Saudi Society of Clinical Pharmacy
الجمعية السعودية للصيدلة الإكلينيكية

الهيئة السعودية للتخصصات الصحية
Saudi Commission for Health Specialties

VITAMIN K ANTAGONIST ORAL ANTICOAGULANTS CLINICAL PATHWAY

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Abbreviations:

aPTT	Activated partial thromboplastin time
CBC	Complete blood count
CNS	Central nervous system
FFP	Fresh frozen plasma
GI	Gastrointestinal
GU	Genitourinary
INR	International normalized ratio
IV	Intravenous
LMWH	Low molecular weight heparin
MV	Mechanical valve
PCC	Prothrombin complex concentrate
PO	Orally
PT	Prothrombin time
SC	Subcutaneous
TIA	Transient ischemic attack
UFH	Unfractionated heparin
Vit. K	Vitamin K
VTE	Venothromboembolism

Anticoagulation Pathway
Guide to medication Use

Disclaimer: The following recommendations should be used as a clinical guidance and does not override the clinical judgment of healthcare professionals. The provided recommendations were made based on the best available evidence and are subject to change.

Warfarin

1. **Introduction**
   - **Pharmacologic Category:** Anticoagulant, Vitamin K Antagonist
   - **Targeted Audience:** Physicians in primary, secondary and tertiary hospitals, clinical pharmacists, and nurses

2. **Action**
   - Inhibits hepatic synthesis of coagulation factors II (half-life 42 to 72 hours), VII (half-life 4 to 6 hours), IX, and X (half-life 27 to 48 hours), as well as proteins C and S, which requires the presence of vitamin K.

3. **Baseline lab**
   - International Normalized Ratio (INR), Complete Blood Count (CBC)

4. **Dosing (Table 1&2)**

Infants and Children (Oral): Loading dose: 0.2 mg/kg; maximum: 10 mg; then adjust dose according to results of INR; usual dose: 0.05-0.34 mg/kg/day. Infants <12 months of age may require doses; mean dose of 0.33 mg/kg/day; consistent anticoagulation may be difficult to maintain in children <5 years of age.

Adults (Oral): Initial: 5 mg once daily for most patients. A lower or higher starting dose may be used depending upon patient-specific factors (see example warfarin initiation nomogram below).

Table 1: Adult Target INR Ranges Based Upon Indication

Warfarin is widely used for several off-labeled indications that are not listed below. This might be supported by weak evidence. Please check your institutional policy and procedures for its use for unapproved/off-labeled indications.

Indication	Targeted INR range	Treatment duration
Cardiac		
Myocardial infarction with left ventricular thrombus or high risk for left ventricular thrombus (eg, ejection fraction <40% and severe anteroapical wall motion abnormality on imaging 48 hours after reperfusion) (ACCF/AHA [O'Gara 2013]; ACCP [Vandvik 2012]). Note: Antiplatelet selection and duration of therapy for treatment of myocardial infarction may vary when used in combination with anticoagulation; consider risks of bleeding and thrombotic events when choosing antithrombotic therapy (ACCP [Vandvik 2012]; Lip 2019).	2 to 3	3 months after myocardial infarction (suggested)
Atrial fibrillation or atrial flutter (AHA/ACC/HRS [January 2014, January 2019]). Note: For eligible patients with nonvalvular atrial fibrillation, a direct oral anticoagulant is recommended over warfarin (AHA/ACC/HRS [January 2014, January 2019]).	2 to 3	Indefinite
Valvular – Note: For mechanical valves, aspirin in combination with warfarin is recommended indefinitely (only in patients of low risk of bleeding). For surgically placed bioprosthetic valves, aspirin therapy is recommended indefinitely and concurrent warfarin is suggested for the first 3 to 6 months. When choosing antithrombotic therapy, additional risk factors for thromboembolism (eg, atrial fibrillation, previous thromboembolism, left ventricular systolic dysfunction, hypercoagulable conditions) should be considered. The goal INR is generally the central value in the indicated acceptable range, especially for patients with a mechanical valve (AHA/ACC [Nishimura 2014, Nishimura 2017]).		
On-X mechanical bileaflet aortic valve with no additional risk factors for thromboembolism (AHA/ACC [Nishimura 2017]; Puskas 2014)	1 to 3 months: 2 to 3 Month 4 and after (if aspirin used): 1.5 to 2	Indefinite
Mechanical bileaflet aortic valve (other than On-X) or current-generation single-tilting disc aortic valve with no additional risk factors for thromboembolism (AHA/ACC [Nishimura 2014, Nishimura 2017])	2 to 3	Indefinite
Mechanical aortic valve with additional risk factors for thromboembolism or an older-generation mechanical aortic valve or mechanical mitral valve (including On-X valve) (AHA/ACC [Nishimura 2014, Nishimura 2017])	**2.5 to 3.5**	Indefinite
Surgically placed bioprosthetic aortic or mitral valve at low risk of bleeding (AHA/ACC [Nishimura 2014, Nishimura 2017])	2 to 3	3 to 6 months
Rheumatic mitral stenosis with atrial fibrillation, previous systemic embolism, or left atrial thrombus (AHA/ACC [Nishimura 2014])	2 to 3	Indefinite
Acute venous thromboembolism treatment – Note: For eligible patients, a direct oral anticoagulant is recommended over warfarin. When warfarin is selected for long-term treatment, a parenteral anticoagulant must be used initially as a bridge until INR measurements are therapeutic and stable. Start warfarin on the first or second day of parenteral anticoagulation and overlap until INR is ≥2 for at least 2 days. Duration of overlap is usually 4 to 5 days (ACCP [Ageno 2012]). The optimal duration of warfarin therapy is dependent on several factors, such as presence of provoking events,		

patient risk factors for recurrence or bleeding, and patient preferences. If indefinite treatment is suggested, reassess need for anticoagulation at periodic intervals (ACCP [Kearon 2012, Kearon 2016]).		
Venous thromboembolism, provoked (ACCP [Kearon 2012, Kearon 2016])	2 to 3	Minimum of 3 months
Venous thromboembolism, unprovoked (ACCP [Kearon 2012, Kearon 2016]; ISTH [Baglin 2012])	2 to 3	Minimum of 3 months and up to indefinite
Thromboprophylaxis		
Idiopathic or inherited pulmonary artery hypertension (ACCF/AHA [McLaughlin 2009]; ACCP [Klinger 2019]; ESC/ERS [Galiè 2016]; Olsson 2014) – Note: Anticoagulation should be considered on an individual basis for patients with idiopathic or inherited pulmonary arterial hypertension after considering risks and benefits. Avoid anticoagulation in patients with scleroderma-associated pulmonary arterial hypertension (Hopkins 2019; Khan 2018; Olsson 2014).	1.5 to 2.5	Indefinite
Chronic thromboembolic pulmonary arterial hypertension (ACCF/AHA [McLaughlin 2009]; ESC/ERS [Galiè 2016])	2 to 3	Indefinite
Antiphospholipid syndrome (ACCP [Holbrook 2012]; Erkan 2019) – Note: Antiphospholipid syndrome is an autoimmune syndrome characterized by venous or arterial thrombosis and/or pregnancy loss in the presence of persistent antiphospholipid antibodies. Patients with antiphospholipid antibodies alone, without a history of thromboembolism, should not receive anticoagulation unless another indication exists. The PT/INR may be prolonged at baseline, in the absence of anticoagulation, in a small percentage of patients due to the presence of antiphospholipid antibodies. This should not be considered a therapeutic effect. An alternative method for monitoring warfarin may be necessary (Erkan 2019).	2 to 3	Indefinite
Total hip arthroplasty or hip fracture surgery – Note: May be used as an alternative to low-molecular-weight heparin or low-dose SubQ heparin (ACCP [Falck-Ytter 2012]).	2 to 3	Minimum of 10 to 14 days and up to 35 days
Total knee arthroplasty – Note: May be used as an alternative to low-molecular-weight heparin or low-dose SubQ heparin (ACCP [Falck-Ytter 2012]).	2 to 3	Typically, 10 to 14 days, but consider up to 35 days if there are multiple or persistent risk factors
Heparin-induced thrombocytopenia – Note: If a patient is taking warfarin at the time of diagnosis, it should be discontinued, and vitamin K should be administered to reverse its effect. Initial therapy should be with a parenteral non-heparin anticoagulant. Warfarin may be initiated after the patient has been stably anticoagulated with a parenteral non-heparin anticoagulant and the platelet count has recovered (eg, ≥150 × 109/L or at the patient's baseline). Starting dose should be ≤5 mg once daily. Overlap the parenteral non-heparin anticoagulant with warfarin for ≥5 days and until INR is therapeutic. Some non-heparin anticoagulants may elevate INR, complicating interpretation. Recheck INR after effects of the non-heparin anticoagulant have worn off to ensure INR remains therapeutic (ACCP [Linkins 2012]; ASH [Cuker 2018]).		
Heparin-induced thrombocytopenia without thrombosis (ACCP [Linkins 2012]; ASH [Cuker 2018])	2 to 3	4 weeks to 3 months (ACCP [Linkins 2012]). Some experts allow for discontinuation of anticoagulation after platelet count recovery, potentially resulting in a shorter duration (ASH [Cuker 2018]).
Heparin-induced thrombocytopenia with thrombosis (ACCP [Linkins 2012]; ASH [Cuker 2018])	2 to 3	Optimal duration not well established. Typically, 3 to 6 months (ACCP [Linkins 2012]; ASH [Cuker 2018]).

Table 2: Example Warfarin Initiation Nomogram Targeting an INR Range of 2 to 3 (for Outpatients or Clinically Stable Inpatients) [a]

INR	Standard dosing for patients who are not expected to be sensitive to warfarin [b]	Reduced dosing for patients expected to be more sensitive to warfarin [c]
	5 mg daily for 3 days [d]	2.5 mg daily for 3 days
	Check INR the morning of day 4	
<1.5	7.5 to 10 mg daily for 2 to 3 days	5 to 7.5 mg daily for 2 to 3 days
1.5 to 1.9	5 mg daily for 2 to 3 days	2.5 mg daily for 2 to 3 days
2 to 3	2.5 mg daily for 2 to 3 days	1.25 mg daily for 2 to 3 days
3.1 to 4	1.25 mg daily for 2 to 3 days	0.5 mg daily for 2 to 3 days
>4	Hold until INR <3	Hold until INR <3

[a] Dosing nomograms offer a reasonable starting point for estimating an initial warfarin dose and subsequent adjustments but should not serve as a substitute for clinical judgment. If the patient received warfarin previously, history of prior dose requirement is useful for guiding re-initiation of therapy.

[b] Patients who are generally started using "standard dosing" include otherwise healthy adults who are not receiving interacting medications.

[c] Patients expected to be more sensitive to warfarin include adults who are frail, elderly, or undernourished; have liver disease, kidney disease, heart failure, or acute illness; or are receiving a medication known to decrease warfarin metabolism.

[d] Some experts suggest starting select younger, otherwise healthy patients at 7.5 or 10 mg for the first 2 days (ACCP [Holbrook 2012]). A higher initial dose may also be appropriate in a patient who was previously treated with warfarin and required high doses or is receiving a medication that increases warfarin metabolism. However, this nomogram has not been validated for starting doses >5 mg/day.

5. Monitoring (Pathway 1&2)

Example Frequency of Monitoring by Clinical Setting (Adapted From Wittkowsky 2018)a

Initiation of therapy	Frequency of monitoring INR
Inpatient initiation	Daily
After hospital discharge	If stable, within 3 to 5 days. If unstable, within 1 to 3 days
Outpatient flexible initiation	Daily through day 4, then within 3 to 5 days
Outpatient average daily dosing method	Every 3 to 5 days until INR reaches lower limit of therapeutic range, then within 1 week
First month of therapy	At least weekly
Maintenance therapy	**Frequency of monitoring**
Medically stable inpatients	Every 1 to 3 days
Medically unstable inpatients	Daily
After hospital discharge	If stable, within 3 to 5 days. If unstable, within 1 to 3 days
Routine follow-up in medically stable and reliable patients	Every 4 to 12 weeks
Routine follow-up in medically unstable or unreliable patients	Every 1 to 2 weeks
Dose held today for significant over-anticoagulation	Recheck in 1 to 2 days
Dosage adjustment today	Recheck within 1 to 2 weeks
Dosage adjustment ≤2 weeks ago	Recheck within 2 to 4 weeks

aThese example suggestions should not replace clinical judgment; more frequent monitoring

6. **Dose adjustment**
   - **Renal impairment:** No dosage adjustment necessary. However, patients with renal impairment have an increased risk for bleeding diathesis; monitor INR closely. Hemodialysis: Not dialyzable
   - **Hepatic impairment:** There are no dosage adjustments provided in the manufacturer's labeling. However, the response to oral anticoagulants may be markedly enhanced in obstructive jaundice, hepatitis, and cirrhosis. INR should be closely monitored.

7. **Contraindications**
   - Hypersensitivity to warfarin or any component of the formulation; hemorrhagic tendencies (eg, active GI ulceration, patients bleeding from the GI, respiratory, or GU tract; cerebral aneurysm; CNS hemorrhage; dissecting aortic aneurysm; spinal puncture and other diagnostic or therapeutic procedures with potential for significant bleeding); recent or potential surgery of the eye or CNS; major regional lumbar block anesthesia or traumatic surgery resulting in large, open surfaces; blood dyscrasias; malignant hypertension; pericarditis or pericardial effusion; bacterial endocarditis; unsupervised patients with conditions associated with a high potential for noncompliance; eclampsia/preeclampsia, threatened abortion, pregnancy (except in women with mechanical heart valves at high risk for thromboembolism)

8. **Caution**
   - Acute kidney injury, Anaphylaxis/hypersensitivity, Bleeding, Calciphylaxis, Atheroemboli/cholesterol microemboli, Bariatric surgery, Dietary insufficiency, Heparin-induced thrombocytopenia, Hepatic impairment, Infection, Renal impairment, Thyroid disease

9. **Drug-Drug and Food-drug interactions (most common /serious) Table 3:**

Interacting drug	Effect	Management
Allopurinol	May enhance the anticoagulant effect of Vitamin K Antagonists	Consider therapy modification
Amiodarone	May enhance the anticoagulant effect of Vitamin K Antagonists	Consider therapy modification
Androgens	May enhance the anticoagulant effect of Vitamin K Antagonists	Consider therapy modification
Barbiturates	May increase the metabolism of Vitamin K Antagonists	Consider therapy modification
CarBAMazepine	May decrease the serum concentration of Vitamin K Antagonists	Consider therapy modification
Cimetidine	May enhance the anticoagulant effect of Vitamin K Antagonists	Consider therapy modification
Clopidogrel	May enhance the anticoagulant effect of Warfarin	Consider therapy modification
Estrogen Derivatives	May diminish the anticoagulant effect of Anticoagulants	Consider therapy modification
Fenofibrate and Derivatives	May enhance the anticoagulant effect of Warfarin	Consider therapy modification
Fluconazole	May increase the serum concentration of Vitamin K Antagonists	Consider therapy modification
Herbs (Anticoagulant/Antiplatelet Properties) (eg, Alfalfa, Anise, Bilberry)	May enhance the adverse/toxic effect of Anticoagulants	Consider therapy modification
MetroNIDAZOLE	May increase the serum concentration of Vitamin K Antagonists	Consider therapy modification
MiFEPRIStone	May enhance the adverse/toxic effect of Anticoagulants	Avoid combination
Nonsteroidal Anti-Inflammatory Agents (Nonselective)	May enhance the anticoagulant effect of Vitamin K Antagonists	Consider therapy modification
Phenytoin	May enhance the anticoagulant effect of Vitamin K Antagonists	Consider therapy modification
Posaconazole	May diminish the anticoagulant effect of Vitamin K Antagonists	Monitor therapy
Tamoxifen	May increase the serum concentration of Vitamin K Antagonists	Avoid combination
Thrombolytic Agents	May enhance the anticoagulant effect of Anticoagulants	Monitor therapy

Urokinase	May enhance the anticoagulant effect of Anticoagulants	Avoid combination
Vorapaxar	May enhance the adverse/toxic effect of Anticoagulants	Avoid combination

Food	Effect	Management
foods rich in vitamin K	The anticoagulant effects of warfarin may be decreased	Maintain a consistent diet; consult prescriber before making changes in diet. Take warfarin at the same time each day
Vitamin E	May increase warfarin effect	
Cranberry juice	May increase warfarin effect	
Ethanol **Acute ethanol ingestion** **Chronic daily ethanol use**	 Decreases metabolism of PO anticoagulants & increases PT/INR Increases the metabolism of oral anticoagulants and decreases PT/INR	Limit alcohol consumption; monitor INR closely

10. Peri-procedural Bridging Management of warfarin (Pathway 3)

Bridging anticoagulation refers to giving a short-acting anticoagulant given parenterally around the time of the surgery/procedure, when warfarin is interrupted and its anticoagulant effect is outside a therapeutic range. The aim of bridging is minimizing the risk for thromboembolism.

10.1 Procedures That May Be Safely Performed Without Warfarin Interruption:

- Simple Dental extraction
- Bone marrow biopsy
- Endoscopy (±mucosal biopsy)
- Cataract surgery
- Pacemaker placement
- Venography
- Minor dermatologic surgery
- Joint aspiration

10.2 Patients with low thrombosis risk include:

- Aortic bileaflet MV in sinus rhythm and no previous thromboembolism
- AF without previous thromboembolism, intracardiac thrombus, and CHADS2 score ≤2
- VTE ≥3 month previously without active cancer

10.3 Perioperative thrombotic risk assessment (Table4):

- A higher thromboembolic risk increases the importance of minimizing the interval without anticoagulation.
- For patients with >1 condition that predisposes to thromboembolism, the condition with the highest thromboembolic risk takes precedence

Table 4 perioperative thromboembolic risk assessment and management:

VTE Risk	Patient stratification	Bridging recommendation
Low VTE risk	- Chronic atrial fibrillation (valvular or non-valvular) *and* no major stroke risk factors -Prior venous thromboembolism over 12 months ago	No bridging anticoagulation suggested
Intermediate VTE risk	-Newer generation (bileaflet) mechanical aortic valve -Bioprosthetic aortic valve -Chronic atrial fibrillation (valvular or nonvalvular) *and* at least 1 major stroke risk factor: Prior stroke/TIA, left ventricular dysfunction, hypertension, diabetes, or age >75 years -Prior venous thromboembolism within last 3-12 months	Bridging anticoagulation optional and based on individual patient Characteristics
High VTE risk	-Any mechanical prosthetic mitral valve -Older generation (cage-ball, tilting disc) mechanical aortic valve -Recent (within 3 months) arterial thromboembolism (stroke, systemic embolism, -Transient ischemic attack [TIA]) -Recent (within 3 months) venous thromboembolism (deep vein thrombosis, pulmonary embolism) † -Prior arterial or venous thromboembolism during interruption of warfarin -Severe thrombophilia (e.g. Deficiency of protein c, protein s or antithrombin, antiphospholipid antibodies)	Bridging anticoagulation suggested
†Consider a temporary inferior vena cava filter to be inserted after warfarin interruption and prior to surgery for patients in whom surgery is planned within 1 month of thromboembolic episode; it can be left in situ for 1-2 weeks until therapeutic anticoagulation is re-established.		

10.4 Procedural bleeding risk (Table 5):

- The risk of bleeding is dominated by the type of surgery or invasive procedure. Patient comorbidities (eg, older age, decreased renal function) and medications that affect hemostasis.

Table 5 Procedural bleeding risk stratification

	Procedural bleeding risk
Very Low-risk (warfarin interruption not needed)	- Simple dental extractions (1 or 2 teeth) or teeth cleaning - Skin biopsy or skin cancer removal - Cataract removal
Low-risk	- Laparoscopic cholecystectomy - Laparoscopic inguinal hernia repair - Dental procedures - Dermatologic procedures - Ophthalmologic procedures - Coronary angiography - Gastroscopy or colonoscopy - Selected invasive procedures (bone marrow aspirate and biopsy, lymph node biopsy, thoracentesis, paracentesis, arthrocentesis)
Intermediate-Risk	- Other intra-abdominal surgery - Other intrathoracic surgery - Other orthopedic surgery - Other vascular surgery
High-Risk	- Neurosurgery (intracranial or spinal surgery) - Cardiac surgery (coronary artery bypass or heart valve replacement) - Major vascular surgery (abdominal aortic aneurysm repair, aortofemoral bypass) - Major urologic surgery (prostatectomy, bladder tumor resection) - Major lower limb orthopedic surgery (hip/knee joint replacement surgery) - Lung resection surgery - Intestinal anastomosis surgery - Permanent pacemaker insertion or internal defibrillator placement - Selected invasive procedures (kidney biopsy, prostate biopsy, cervical cone biopsy, pericardiocentesis, colonic polypectomy)

10.5 Bridging anticoagulation options are as follows:

a) **In normal renal function:** Subcutaneous (SC) therapeutic-dose LMWH: enoxaparin 1 mg/kg twice daily or 1.5 mg/kg once daily; dalteparin 100 IU/kg twice daily or 200 IU/kg once daily; or tinzaparin 175 IU/kg once daily. (*dose adjustment is required in renal impairment*)

b) Intravenous (IV) unfractionated heparin (UFH) to achieve a therapeutic activated partial thromboplastin time (aPTT) defined according to local laboratory parameters.

c) In **high-bleeding-risk surgery/procedure**, an alternate post-operative management option is SC low-dose LMWH: enoxaparin 40 mg once daily; dalteparin 5000 IU once daily; or tinzaparin 4500 IU once daily.

d) In **very-high-bleeding-risk surgery/procedure**, post-operative therapeutic dose LMWH bridging should be avoided; alternate options are low-dose LMWH or resuming warfarin alone.

10.6 Post-Operative Resumption of Bridging Anticoagulation:

Resumption of therapeutic doses of any anticoagulant should not occur earlier than the time periods suggested below.

a) Low bleeding risk procedure:

- Start therapeutic-dose of LMWH/UFH 12-24 hours after surgery (i.e. day after surgery)

b) Moderate bleeding risk procedure:

- Start therapeutic-dose of LMWH/UFH 24-48 hours after surgery

c) High bleeding risk procedure:

- Start therapeutic-dose of LMWH/UFH 48-72 hours after surgery
- Alternate management: low-dose LMWH, starting 12-24 hours after surgery (i.e. Day after surgery) or resume warfarin alone with no post-operative LMWH/UFH

11. Anticoagulant Reversal (Pathway 4&5):

A. General Principles of Management of Anticoagulant-Associated Bleeding

HASHTI

1. Hold further doses of anticoagulant
2. Consider Antidote
3. Supportive treatment
   a. Volume resuscitation (intravenous fluids)
   b. Hemodynamic support (inotropes, monitoring)
4. Local or surgical Hemostatic measures
   a. Anti-fibrinolytic agents can be considered (aminocaproic acid, tranexamic acid)
5. Transfusion
   a. Red blood cells for severe or symptomatic anemia
   b. Platelets if thrombocytopenia (<50 x 109/L) or patient on long-acting antiplatelet agents
6. Investigate for bleeding source

B. Definitions Used for Reversal Situations

a. Non-urgent: Reversal is elective (procedures >5 days away)

b. Urgent (without bleeding): Reversal needed within hours

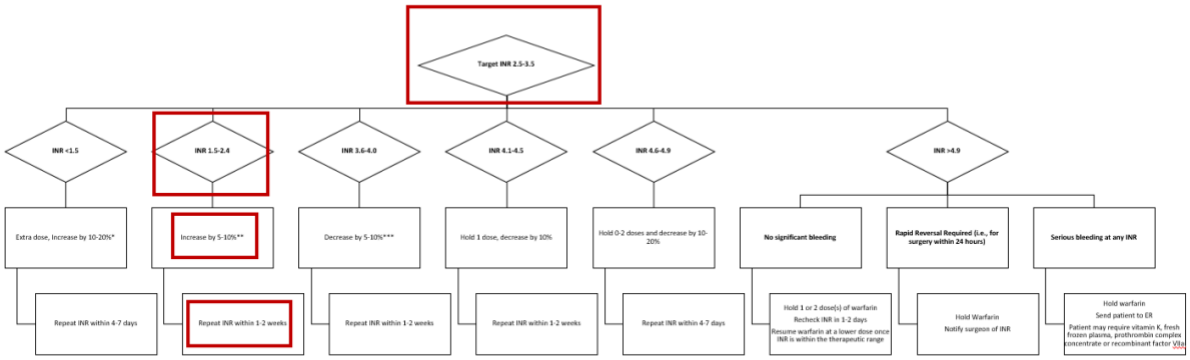
c. Urgent (with bleeding): Immediate reversal

Patient case examples:

Case 1:

S.M is a 45-year-old woman with a history of rheumatic fever, s/p mitral valve replacement with a St. Jude's prosthesis (mechanical) maintained on warfarin 5 mg po daily, came in to your clinic for her routine checkup. She has no history of bleeding, thrombotic, or embolic complications and all her labs are within normal limits. Her current dose of warfarin is 5 mg daily and her INRs over the past year have ranged between 2.6 and 3.7. Her INR for today is 2.2, she denied taking any new OTC meds or antibiotics, and she reassures that she's complaint with her medications. How will you adjust her warfarin? When will you repeat her INR?

Pathway 2 Chronic Warfarin Dose Adjustment in Non-Bleeding Patients[5]



* If recent mechanical heart valve within 6-8 weeks, consider bridging therapy with therapeutic dose low molecular weight heparin
** If INR 2.3-2.4, consider no dose change, and repeat INR in 7-14 days
*** If INR 3.6-3.7, consider no dose change, and repeat INR in 7-14 days

Answer:

1- The patient has a mechanical valve which makes her target INR from 2.5-3.5

2- Since the patient has a sub-therapeutic INR the dose should be increased according to the pathway the total weekly dose should be increased by 5-10%

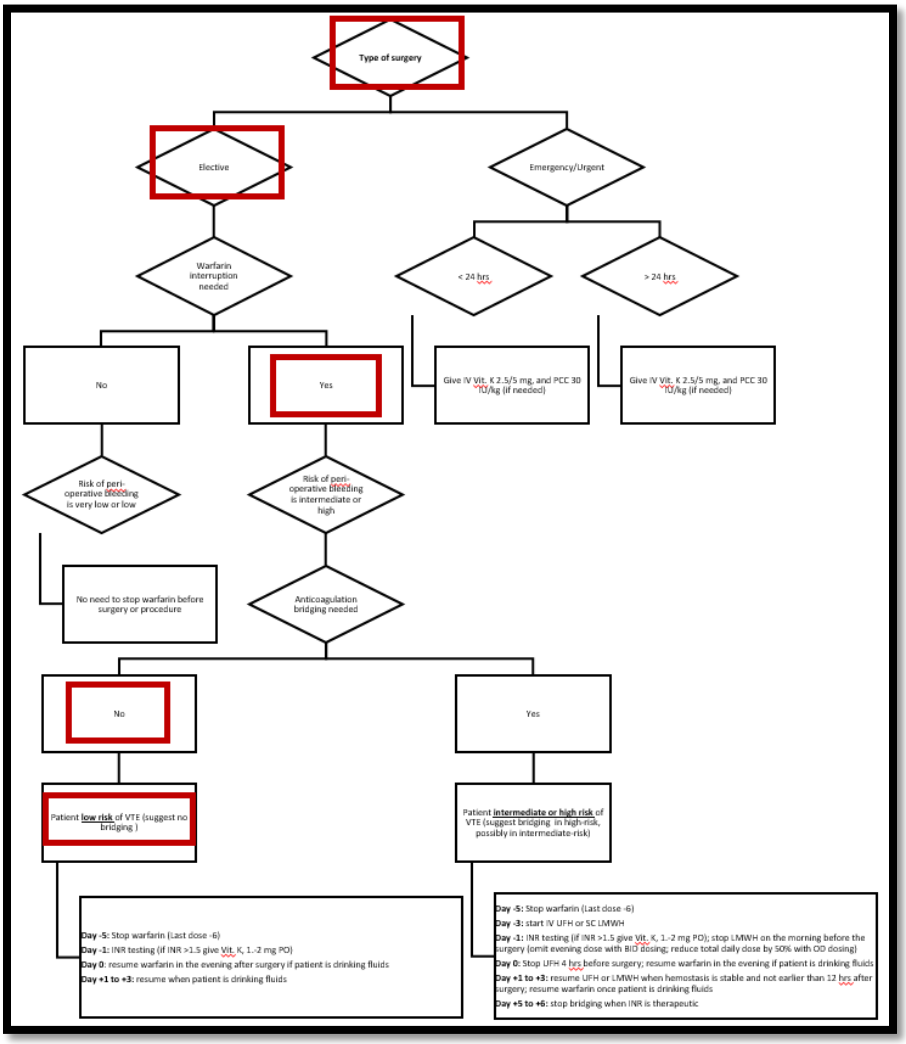
4- Patient is currently receiving 5 mg po daily (35 mg/week) the recommendation would be to take 5 mg po daily on week days and 6 mg on weekends (37 mg/week)

5- Repeat INR in 1-2 weeks

Case 2:

A 66-year-old male k/c of long standing AF on warfarin came into your clinic and informed you that he has a scheduled a knee replacement in 2 weeks and asks you when should he stop and resume his warfarin? Is bridging required for this patient?

All his labs are within normal limit and his INR for today is 2.7



Answer:

1- According to the Procedural bleeding risk stratification table the patient is at high risk of bleeding since he is undergoing knee replacement

2- Patient is at low risk of VTE since he has chronic atrial fibrillation and no major stroke risk factors and no bridging anticoagulation is needed

3- According to the Bridging pathway #3:

Day -5: Stop warfarin (Last dose -6)

Day -1: INR testing (if INR >1.5 give Vit. K, 1.-2 mg PO)

Day 0: resume warfarin in the evening after surgery if patient is drinking fluids

Day +1 to +3: resume when patient is drinking fluid

References:

Baron TH, et al. Management of antithrombotic therapy in patients undergoing invasive procedures. N Engl J Med 2013;368(22):2113-2124.

Cushman M, et al. 2014 Clinical Practice Guide on Anticoagulant Dosing and Management of Anticoagulant-Associated Bleeding Complications in Adults. American Society of Hematology, February 2014. Accessible at: http://www.hematology.org/Clinicians/Guidelines-Quality/Quick-Reference.aspx

Douketis JD et al, Perioperative bridging anticoagulation in patients with atrial fibrillation. N Engl J Med 2015;373(9):823-833.

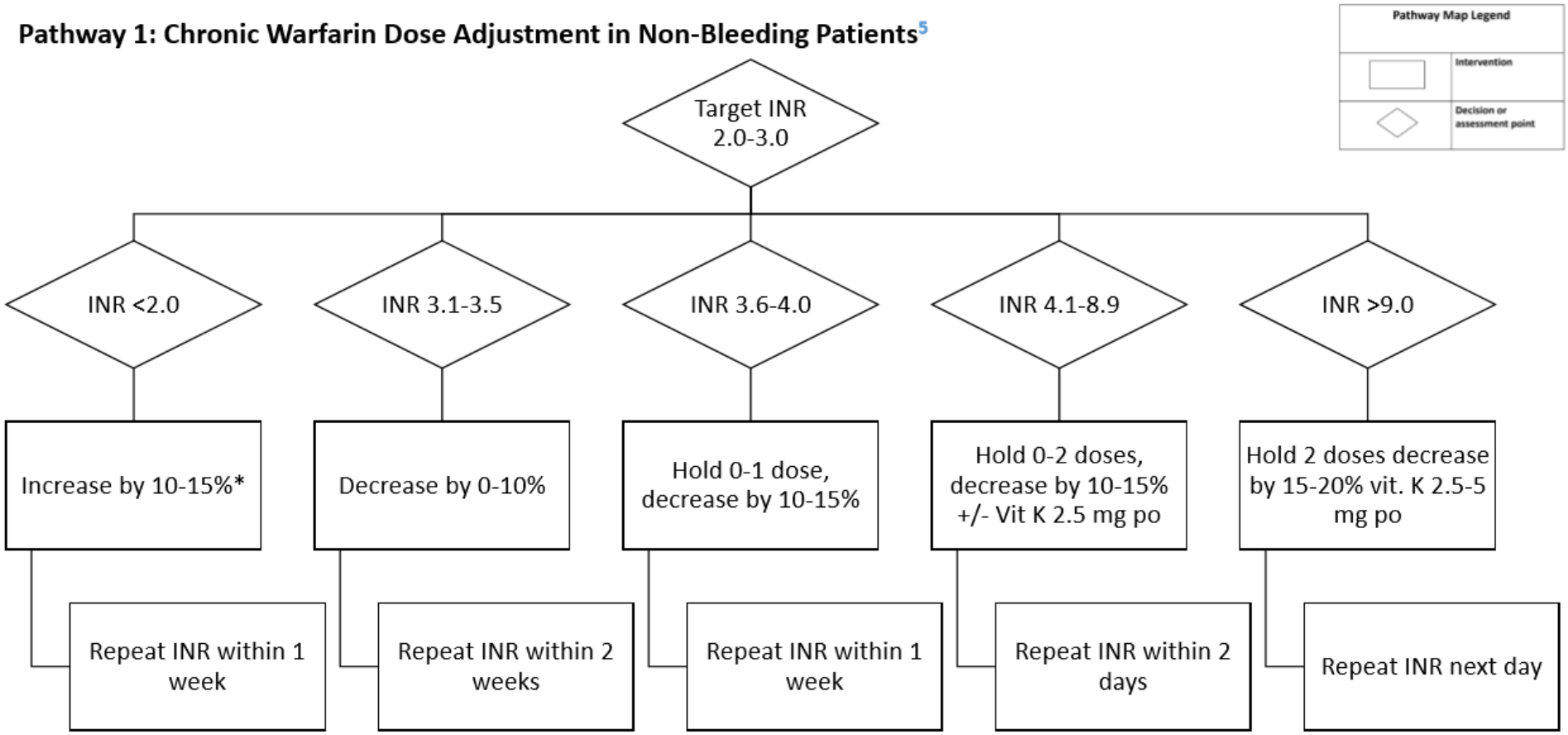
Douketis JD, et al. Perioperative management of antithrombotic therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141(2 Suppl):e326S-350S.

Macle L et al, 2016 Focused update of the Canadian Cardiovascular Society guidelines for the management of atrial fibrillation. Can J Cardiol 2016;32(10):1-16.

Mehta SR, et a. 2018 Canadian Cardiovascular Society/Canadian Association of Interventional Cardiology focused update of the Guidelines for the Use of Antiplatelet Therapy. Can J Cardiol 2018;34:214-233.

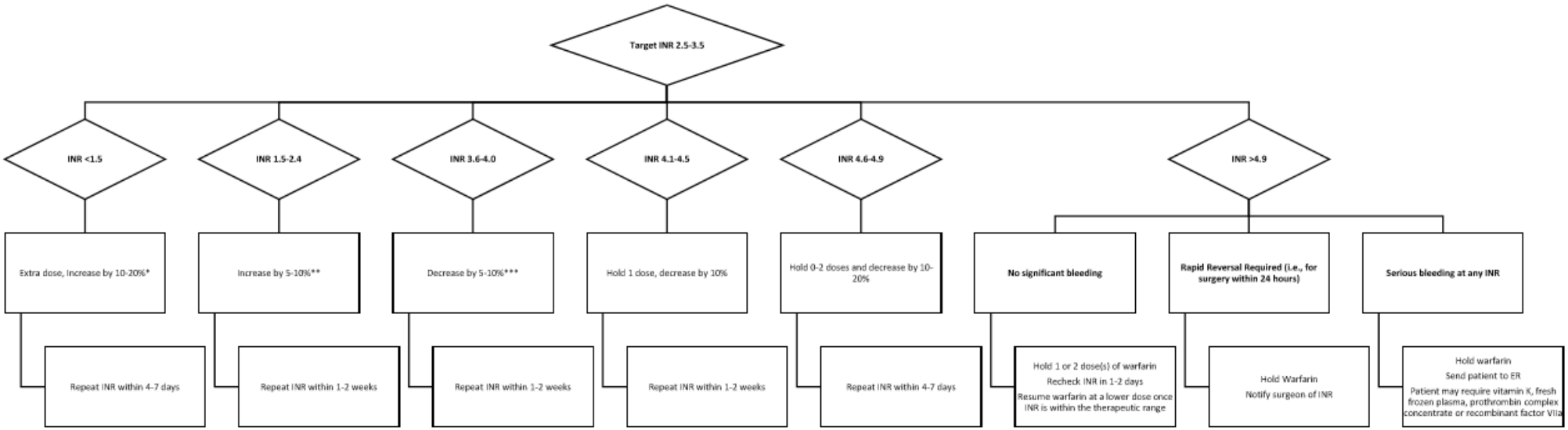
Monagle P, et al. Antithrombotic therapy in neonates and children: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141(2 Suppl):e737S-801S.

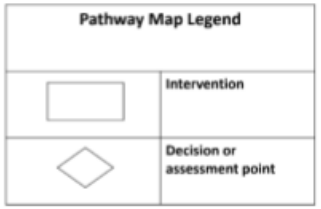
Pathway 1: Chronic Warfarin Dose Adjustment in Non-Bleeding Patients[5]



* Consider 15% increase if INR ≤1.5 without explanation

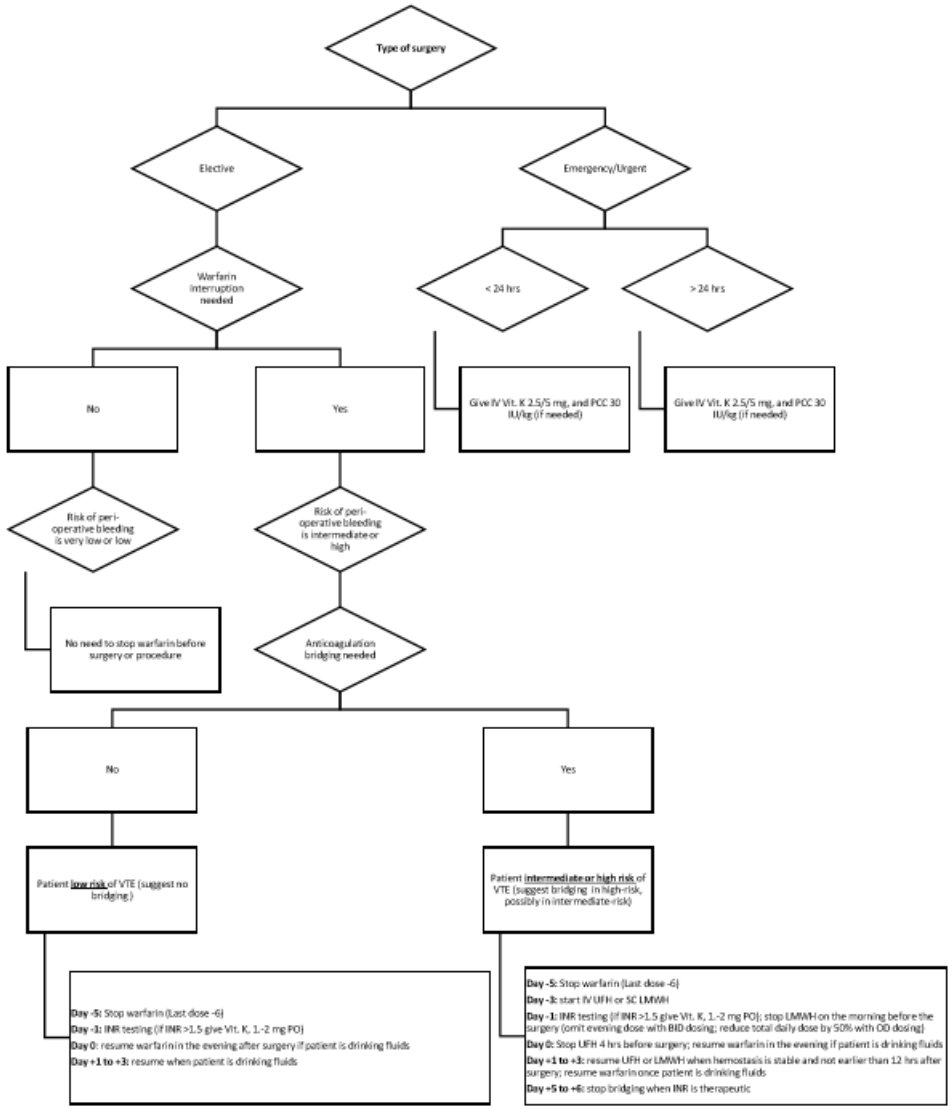
Pathway 2 Chronic Warfarin Dose Adjustment in Non-Bleeding Patients[5]

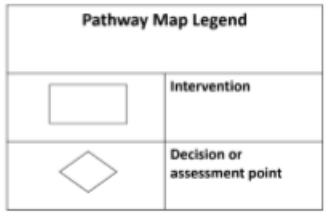




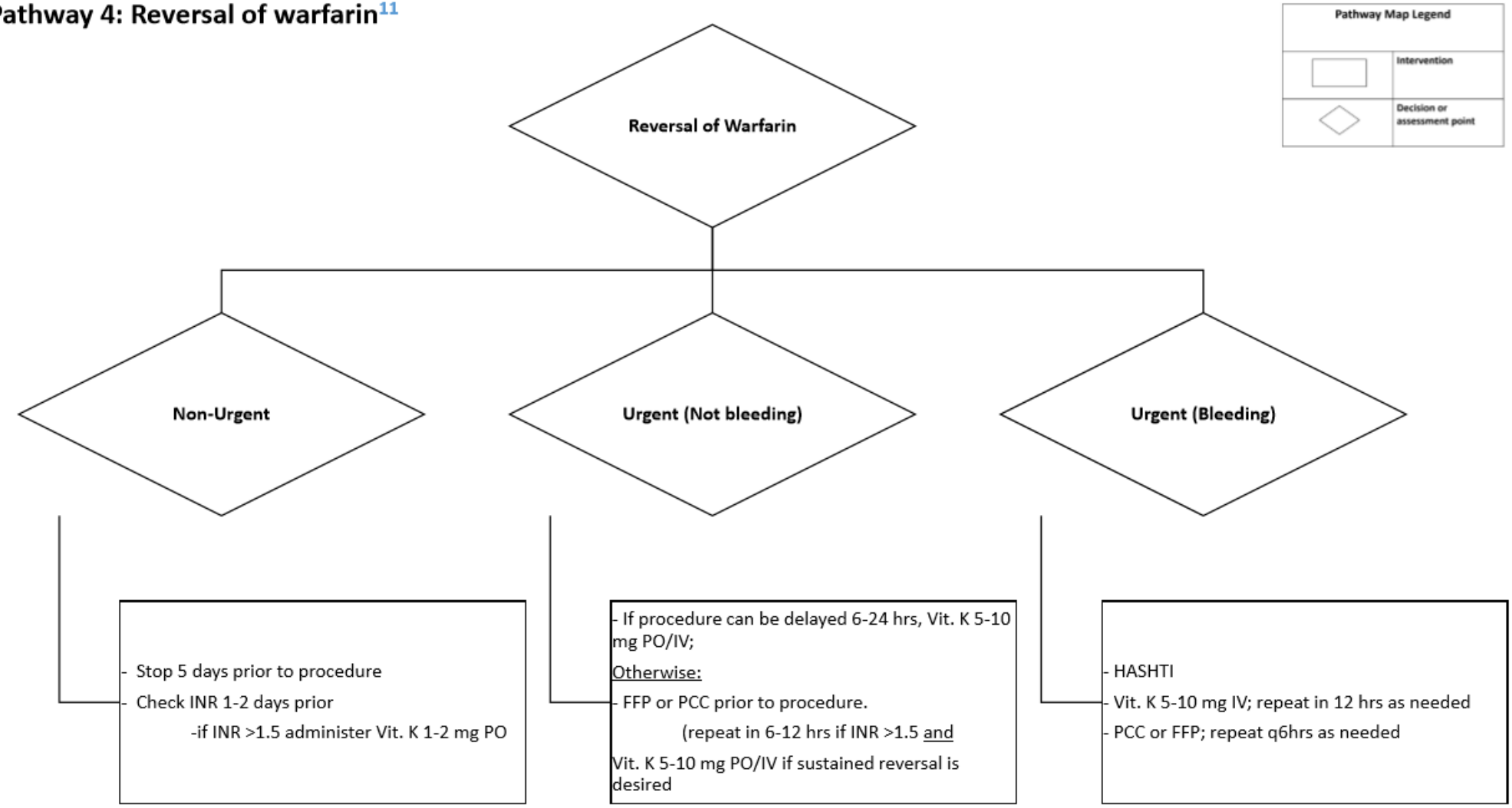
* If recent mechanical heart valve within 6-8 weeks, consider bridging therapy with therapeutic dose low molecular weight heparin
** If INR 2.3-2.4, consider no dose change, and repeat INR in 7-14 days
*** If INR 3.6-3.7, consider no dose change, and repeat INR in 7-14 days

Pathway 3: Bridging[10]





Pathway 4: Reversal of warfarin[11]



Pathway 5: Reversal agents[11]