



Warfarin Management - Adult- Ambulatory Consensus Care Guideline

Population/Problem:

This guideline outlines the evidence for managing anticoagulation therapy with oral vitamin K antagonist (warfarin) for adult patients in the ambulatory setting. For dosing and monitoring of warfarin therapy it is recommended that standardized and validated decision support tools be used for most patients. Evidence has shown improved time in therapeutic INR range and clinical outcomes in patients managed by trained staff using standardized procedures and dosing decision support tools.¹

Recommendations:

1. Indications for use, INR goals and duration of therapy are listed in Table 1
 - 1.1. Alternative INR goals may be chosen when bleeding risk outweighs clotting risk as determined by the individual's provider (*UW Health GRADE very low-quality evidence, conditional recommendation*).

Table 1. Indications for use, INR Ranges, and Duration of Therapy

Table 1. Target INR Ranges and Duration of Therapy			
Indication	INR Goal (Range)	Duration	Evidence Grading
Thrombophilia with Thromboembolic Event¹⁻³			
Antiphospholipid Syndrome	2.5 (2-3)	Indefinite	ACCP Grade 2B
Homozygous Factor V Leiden	2.5 (2-3)	Indefinite	
Protein C, S or Anti-Thrombin deficiency	2.5 (2-3)	Indefinite	
Atrial Fibrillation (AF)/Atrial Flutter⁴⁻⁶			
Note: additional management information is available UW Health Atrial Fibrillation Guidelines			
Prior stroke, transient ischemic attack (TIA)	2.5 (2-3)	Indefinite	AHA/ACC/HRS Grade IA
For AF: CHA ₂ DS ₂ -VASc score of 2 or greater in men or 3 or greater in women	2.5 (2-3)	Indefinite	AHA/ACC/HRS Grade IA

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Table 1. Target INR Ranges and Duration of Therapy (cont)			
Indication	INR Goal (Range)	Duration	Evidence Grading
Atrial Fibrillation (AF)/Atrial Flutter (cont.)⁴⁻⁶			
For AF: CHA ₂ DS ₂ -VASc score of 1 or greater in men or 2 or greater in women	2.5 (2-3)	Indefinite	AHA/ACC/HRS Grade IIb, C-LD
Pre-cardioversion (AF or atrial flutter ≥48 hours or unknown duration) regardless of CHA ₂ DS ₂ -VASc score	2.5 (2-3)	At least 3-weeks unless the need for immediate cardioversion	AHA/ACC/HRS Grade IB
Post-cardioversion to normal sinus rhythm	2.5 (2-3)	At least 4-weeks	AHA/ACC/HRS Grade IB
Cerebral Venous Thrombosis (CVT)^{3,7,8}			
Cerebral venous thrombosis (CVT)	2.5 (2-3)	3-6 months	ACCP Grade 2B
Provoked CVT associated with a transient risk factor (e.g., pregnancy, dehydration, infection)	2.5 (2-3)	3-6 months	AHA/ASA Grade IIb, C
Unprovoked CVT	2.5 (2-3)	6-12 months	AHA/ASA Grade IIb, C
Recurrent CVT, VTE after CVT, or first CVT with severe thrombophilia	2.5 (2-3)	Indefinite	AHA/ASA Grade IIb, C
Venous Thromboembolism (VTE)^{9,10}			
Note: additional management information is available UW Health VTE Diagnosis and Treatment Guideline			
Deep Vein Thrombosis (DVT) or pulmonary embolism (PE)	2.5 (2-3)	At least 3 months	Individualize the duration based upon provoked events, risk factors for thrombosis and bleeding.
Valve Surgical Replacement – Bioprosthetic^{11,12}			
Aortic or Mitral	Aspirin 75 mg to 100 mg per day is reasonable in all patients with a bioprosthetic aortic or mitral valve. AHA/ACC IIa, B		
Aortic or Mitral with low risk of bleeding	2.5 (2-3)	3 to 6 months	AHA/ACC IIa, B-NR
Valve Surgical Replacement – Mechanical¹¹⁻¹³			
Aortic bileaflet or current-generation single-tilting disk and no risk factors for thromboembolism	2.5 (2-3)	Chronic	AHA/ACC IB
Aortic with additional risk factors for thromboembolic events (AF, previous thromboembolism, LV dysfunction, or hypercoagulable conditions) or an older-generation mechanical AVR (such as ball-in-cage)	3 (2.5-3.5)	Chronic	AHA/ACC IB
Mitral	3 (2.5-3.5)	Chronic	AHA/ACC IB
Tricuspid	3 (2.5-3.5)	Chronic	AHA/ACC IB
Dual Aortic and Mitral Valve	3 (2.5 -3.5)	Chronic	AHA/ACC IB
On-X Aortic	2.5 (2-3)	3 months	After 3 months consider decrease the INR goal to 1.5-2.0 (in conjunction with aspirin 81mg daily) AHA/ACC IIb, B-R
On-X Mitral	3 (2.5-3.5)	Chronic	AHA/ACC IB
Aspirin 75 mg to 100 mg daily is recommended in addition to anticoagulation with warfarin in patients with a mechanical valve prosthesis. AHA/ACC IA			
Anticoagulant therapy with oral direct thrombin inhibitors or anti-Xa agents should not be used in patients with mechanical valve prostheses. AHA/ACC III:Harm			

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Table 1. Target INR Ranges and Duration of Therapy (cont)			
Indication	INR Goal (Range)	Duration	Evidence Grading
Transcatheter Aortic Valve Replacement (TAVR)^{12,14}			
	Guideline		
	Pivotal Trials (Placement of Aortic Transcatheter Valve Trial [PARTNER] and US CoreValve ¹⁵⁻¹⁷)	American College of Cardiology/American Heart Association Guidelines 2017 ¹²	European Society of Cardiology/ European Association for Cardiothoracic Surgery Guidelines 2017 ¹⁸
First 3 to 6 months	Aspirin plus clopidogrel for first 3 or 6 mo followed by monotherapy	Clopidogrel 75mg daily for the first 6 months in addition to lifelong aspirin 75-100mg (AHA/ACC IIb, C)	Low-dose aspirin plus P2Y12 inhibitor for 3 to 6 months followed by lifelong single antiplatelet therapy in patients without indication for oral anticoagulation (ESC/EACTS IIb, C)
Lifelong treatment	If vitamin K antagonist is indicated, aspirin plus warfarin (without clopidogrel)	Warfarin with an INR of 2.5 (2-3) for at least 3 months in patients with low bleeding risk (AHA/ACC IIb,B)	Lifelong oral anticoagulants for patients with indication (ESC/EACTS IC)
Orthopedic Surgery¹⁹			
Indication	INR Goal (Range)	Duration	
Total Knee or Hip Arthroplasty*	1.8-2.2	10-14 days	INR goal per surgeon
Hip Fracture Surgery*	1.8-2.2	10-14 days	INR goal per surgeon
Trauma Surgery*	1.8-2.2	35 days	INR goal per surgeon
* If other indication for anticoagulation exist - INR goal should be clarified			

Patient Assessment

2. Patients should be assessed for risk factors that may make them more sensitive to the effects of warfarin. If multiple high sensitivity risk factors are present then a lower initiation dose or reduced maintenance dose may be needed.²⁰ (UW Health GRADE high quality evidence, strong recommendation) (see Table 2)

Table 2. Warfarin sensitivity factors
<p>Increases sensitivity (usually require lower doses)</p> <ul style="list-style-type: none"> • Baseline (pre-warfarin) PT/INR (e.g., greater than 1.4) • Advanced age (e.g., 60 years of age or older)²¹⁻³⁰ • Underweight (e.g., BMI less than 18kg/m²)^{29,31,32} • Nutritional status (e.g., malnourished, low vitamin K intake/stores) • Genetic factors (e.g., CYP2C9, VKORC1 phenotypes) • Drug-drug interactions • Hypoalbuminemia^{33,34} • Ethnicity (Asian)^{30,35,36} • Liver disease^{30,37} • Thyroid Disease (e.g., hyperthyroidism, Graves' disease)³⁸⁻⁴¹ • Heart Failure^{42,43} • Febrile illness • Prolonged vomiting and diarrhea • Cannabinoids • Alcohol •

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Table 2. Warfarin sensitivity factors (cont)
Decrease warfarin sensitivity (may require higher doses)
<ul style="list-style-type: none"> • Enteral feedings • High-vitamin K intake • Drug interactions • Chewing tobacco

3. The HAS-BLED score can assist with predicting the risk of major bleeding in warfarin patients.⁴⁴ (*UW Health GRADE moderate quality evidence, strong recommendation*)
 - 3.1 This score should not automatically exclude patients from receiving warfarin if clinically indicated. It should be used to identify modifiable risk factors that can be corrected to decrease risk. (*UW Health GRADE moderate quality evidence, strong recommendation*)

Table 3: HAS-BLED Score⁴⁴

Factors	Points	Scoring
Hypertension (SBP >160 mmHg)	1	Score = 0-1: Low risk Score = 2: Moderate risk Score ≥3: High risk High bleed risk considerations: <ul style="list-style-type: none"> - Optimize blood pressure control - Check INRs frequently - Utilize anticoagulation clinic - Focus on fall prevention - Utilize direct oral anticoagulants
Abnormal lab values <ul style="list-style-type: none"> - Creatinine >2.26 mg/dL - Bilirubin >2x the upper limit of normal (ULN) <i>and</i> AST/ALT/AP >3x ULN 	1	
Stroke history	1	
Bleeding history or predisposition	1	
Labile INRs: Time in Therapeutic Range <60%	1	
Elderly: > 65 years	1	
Drugs <ul style="list-style-type: none"> - EtOH abuse - ASA or NSAID use 	1	

4. Initial warfarin dosing should be tailored based on baseline INR, patient bleed risk, potential sensitivity to warfarin (see Table 2), indication, goal INR range and if potential drug interactions are present²⁰ (*UW Health GRADE high quality evidence, strong recommendation*)
5. If therapeutic anticoagulation is needed immediately, patients should receive another form of anticoagulation such as LMWH until they are therapeutic on warfarin for 24-48 hours^{7,20} (*UW Health GRADE high quality evidence, strong recommendation*)
6. Prior to making a dose adjustment, assess for missed doses, recent INR trends, changes in diet and activity level, potential drug interactions, symptoms of bleeding or clotting, pregnancy status and other changes that may affect INR level as described in Appendix A. Patient Assessment Tool^{1,20} (*UW Health GRADE moderate quality evidence, strong recommendation*)
 - 6.1 Pregnant patients should not take warfarin and should be transitioned to an alternative anticoagulant (e.g. low molecular weight heparin) (*UW Health GRADE high quality evidence, strong recommendation*)

Table 4. Warfarin Initiation (Week 1) with INR Goal 2-3⁴⁵

Day Therapy	INR Value	Dose Adjustment
Day 1		5 mg daily (2.5 mg daily if high sensitivity to warfarin identified)
In 2-3 days after initiation	< 1.5 1.5-1.9 2.0-2.5 > 2.5	5 – 7.5 mg daily 2.5 - 5 mg daily 1 - 2.5 mg daily Hold and recheck INR next day
In additional 2-3 days after last INR check	< 1.5 1.5-1.9 2.0-3.0 > 3.0	7.5 – 10 mg daily 5 – 10 mg daily 2.5 – 5 mg daily Hold warfarin, recheck in 1-2 days
*If patient is started on 2.5 mg then target lower warfarin dose adjustments to avoid overshooting INR goal		

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Table 5. Warfarin Maintenance Dosing Protocol with INR Goal 1.5-2.0⁴⁵

INR less than 1.5	INR 1.5 – 2.0	INR 2.1 – 3.0	INR 3.1 – 3.9	INR 4.0-4.9	INR 5.0-8.9	INR greater than or equal to 9.0
Increase weekly dose 5%	No Change	Decrease weekly dose 5%	Half dose x 1 and Decrease weekly dose 10%	Hold 1 dose Decrease weekly dose by 10-20%	Order required Consider: Hold 2-3 doses, when able recheck INR before resuming warfarin Decrease weekly dose 10-20%; Check HCT or Hgb	Contact MD for urgent patient evaluation

Table 6. Warfarin Maintenance Dosing Protocol with INR Goal 2-3⁴⁵

INR less than 1.5	INR 1.5 - 1.9	INR 2.0 - 3.0	INR 3.1- 3.9	INR 4.0-4.9	INR 5.0- 8.9	INR greater than or equal to 9.0
Extra Dose Increase weekly dose 10-20%	Increase weekly dose 5-10%	No change	Decrease weekly dose 5-10%	Hold 1 dose Decrease weekly dose 10%	Order required Consider: Hold 2-3 doses, when able recheck INR before resuming warfarin Decrease weekly dose 10-20% Check HCT or Hgb	Contact MD for urgent patient evaluation

Table 7. Warfarin Maintenance Dosing Protocol with INR Goal 2.5-3.5⁴⁵

INR less than 1.9	INR 1.9 - 2.4	INR 2.5 - 3.5	INR 3.6 - 4.5	INR 4.6-4.9	INR 5.0- 8.9	INR greater than or equal to 9.0
Extra Dose Increase weekly dose 10-20%	Increase weekly dose 5-10%	No change	Decrease weekly dose 5-10%	Hold 1 dose Decrease weekly dose 10%	Order required Consider: Hold 1-2 doses, when able recheck INR before resuming warfarin Decrease weekly dose 10-20% Check HCT or Hgb	Contact MD for urgent patient evaluation

Table 8. Warfarin Dosing Pearls (UW Health GRADE low quality evidence, conditional recommendation)

INR range without a dosing table	Use same concept of adjusting the weekly dose by 5-10% based on the INR result
INR minimally out of range	If there is a transient reason for INR to be out of range (e.g. missed dose) or patient previously stable with unknown reason to be out of range, then may consider rechallenging the dose before making a weekly dose adjustment. Recheck the INR in 1-2 weeks.
Considerations for extra doses	An extra dose can be either an extra partial dose or extra full dose based on the INR and patient's known response to warfarin. The extra dose should not be included in the weekly dose adjustment
Considerations for held doses	A held dose should not be included in the weekly dose adjustment
Point of Care (POC) INR	If the INR is above 3.9, a repeat venipuncture is required to verify INR

INR < 2.0 AND mechanical valve with an INR goal of 2.5-3.5	Consider bridging with a low molecular weight heparin or as directed per the periprocedural guidelines
Variations in INR	Daily low dose vitamin K supplement should not be used to improve INR control

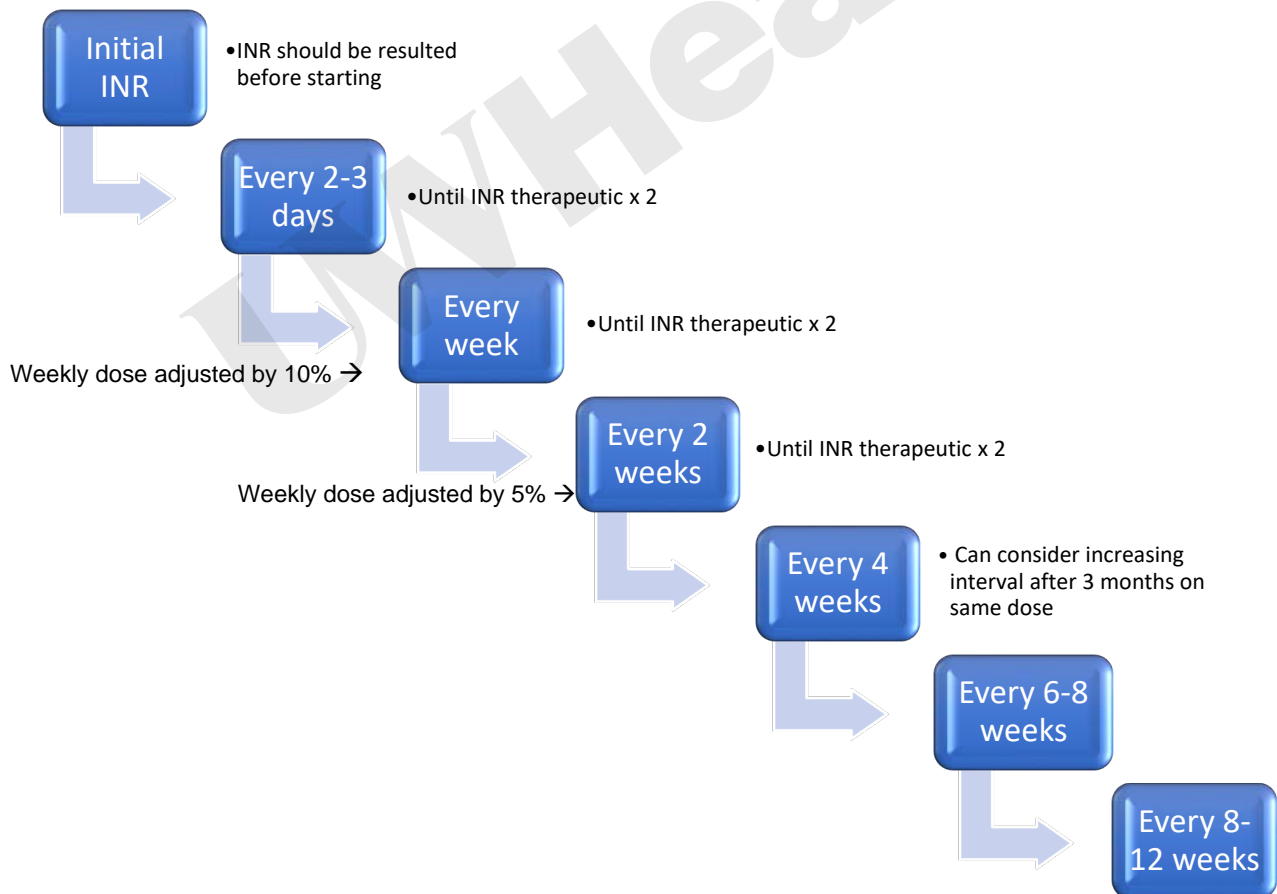
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Laboratory Monitoring^{1,20} (UW Health GRADE low quality evidence, conditional recommendation)

Table 9. Laboratory monitoring recommendations for warfarin

Baseline		
Within the past 30 days	<ul style="list-style-type: none"> • Baseline INR • Pregnancy test* 	*Pregnancy test is not needed if: <ol style="list-style-type: none"> 1. Are postmenopausal (12 months of amenorrhea in a woman > 45 years old in the absence of other biological or physiological causes) 2. Had a hysterectomy or bilateral salpingo-oophorectomy 3. Have ovarian failure 4. Had a bilateral tubal ligation or other surgical sterilization procedure 5. Are known to be pregnant 6. Have had a miscarriage or abortion in the last 7 days 7. Have given birth within the past 4 weeks
Within the past 90 days	<ul style="list-style-type: none"> • Hemoglobin • Platelet count • 	
Annually		
	<ul style="list-style-type: none"> • Hemoglobin • Platelet count • 	

Frequency of INR Monitoring After Initiation of Warfarin^{1,20,46,47} (UW Health GRADE low quality evidence, conditional recommendation)



Patient Assessment

7. Any significant signs or symptoms of major bleeding or clotting should be referred to a primary care provider or urgent care/emergency department for evaluation. Common signs and symptoms are listed in Table 10. (*UW Health GRADE high quality evidence, strong recommendation*).

Table 10. Common Signs and Symptoms of Major Bleeding and Clotting^{9,48}

Signs and Symptoms of Bleeding	Signs and Symptoms of Clotting
Blood in sputum	Chest or unilateral leg pain
Bloody emesis (bright red or coffee ground-like)	Unilateral lower extremity swelling
Blood in urine or stool (enough to color toilet water)	Warm, red or discolored skin of lower extremity
Bleeding that has not resolved or slowed within 10 minutes	Elevated heart rate (HR > 100 bpm)
	Shortness of breath
	Coughing or coughing up blood

Drug Interactions

8. Most drug interactions with warfarin will start to have an effect within 3-5 days of concomitant therapy. In general, it is recommended to check an INR 3-4 days after starting a medication that has the potential to interact with warfarin. If the INR is affected at that time, then a dose adjustment can be made. There are some notable exceptions to this that are listed in Table 11.

Table 11. Dose adjustment recommendations for common/significant warfarin – drug interactions

Medication	INR check after starting	Adjustment
Amiodarone	Every 7 days	Target a 25-50% weekly dose reduction over 2-4 weeks
Rifampin	Every 7 days	Target a 50% weekly dose increase over 2 weeks
Fluconazole	2 – 3 days	Target a 30% weekly dose decrease
Metronidazole	2 – 3 days	Target a 30% weekly dose decrease
Sulfamethoxazole/ Trimethoprim	2 days	Target a 30% weekly dose decrease <i>Should reduce dose prior to starting medication to avoid critical INR elevation</i>

(*UW Health GRADE moderate quality evidence, strong recommendation*)

Tables 12 and 13 outline potential drug-drug, drug-food, and drug-herb interactions. Bolded medications are considered significant interactions. The tables are **not** all inclusive.

Table 12. Medications, Dietary Supplements and Food that **INCREASE** INR or Bleeding Risk^{1,20,30,49}

Drug Class	Known Interaction	Probable Interaction	Possible Interaction	Unlikely Interaction
Anti-Infective	Ciprofloxacin Erythromycin Fluconazole* Isoniazid Metronidazole* Miconazole Miconazole Vaginal Suppository Moxifloxacin Sulfamethoxazole* Voriconazole	Amoxicillin/clavulanate Azithromycin Clarithromycin Itraconazole Ketoconazole Levofloxacin Ritonavir Tetracycline	Amoxicillin Chloramphenicol Darunavir Daptomycin Etravirine Ivermectin Nitrofurantoin Norfloxacin Ofloxacin Saquinavir Telithromycin Terbinafine	Cefotetan Cefazolin Tigecycline
Cardiovascular	Amiodarone* Clofibrate Diltiazem Fenofibrate Propafenone Propranolol	Aspirin Fluvastatin Quinidine Ropinirole Simvastatin	Disopyramide Gemfibrozil Metolazone	
Analgesics, Anti-Inflammatory	Piroxicam	Acetaminophen Aspirin Celecoxib Tramadol	Indomethacin Propoxyphene Sulindac Tolmentin Topical Salicylates	Methylprednisolone Nabumetone
CNS Drugs	Alcohol Citalopram Entacapone Sertraline	Disulfiram Chloral hydrate Fluvoxamine Phenytoin	Felbamate	Diazepam Fluoxetine Quetiapine
GI Drugs and Food	Cimetidine Mango Omeprazole	Grapefruit	Orlistat	
Herbal Supplement	Fenugreek Feverfew Fish Oil Ginkgo Quiltinggao	Dandelion Danshen Don Quai Lycium PC-SPES Red or Sweet Clover	Capsicum Forskolin* Garlic Ginger Turmeric	
Other	Anabolic Steroids Capecitabine Zileuton	Fluorouracil Gemcitabine Levamisole Paclitaxel Tamoxifen Tolterodine	Acarbose Cyclophosphamide Danazol Iphosphamide Trastuzumab	Etoposide Carboplatin Levonorgestrel

*Indicates significant interaction

Table 13. Medications, Dietary Supplements and Food that **DECREASE INR**^{1,20,30,49}

Drug Class	Known Interaction	Probable Interaction	Possible Interaction	Unlikely Interaction
Anti-Infective	Griseofulvin Nafcillin Ribavirin Rifampin*	Dicloxacillin Ritonovir Rifapentine	Terbinafine Nelfinavir Nevirapine	Cloxacillin Rifaximin Teicoplanin
Cardiovascular	Cholestyramine	Bosentan	Telmisartan	Furosemide
Analgesics, Anti-Inflammatory	Mesalamine	Azathioprine	Sulfasalazine	
CNS Drugs	Barbiturates Carbamazepine	Chlordiazepoxide		Propofol
GI Drugs and Food	High content vitamin K food Avocado	Soy milk Sucralfate	Sushi containing seaweed	
Herbal Supplement	Alfalfa	Ginseng Multivitamin St. John's Wort Parsley Chewing Tobacco	Co-Enzyme Q10 Yarrow Licorice	Green Tea
Other	Mercaptopurine	Chelation Therapy Influenza vaccine Raloxifene	Cyclosporine Etretinate Ubidecarenone	

*Indicates significant interaction

Dietary Interactions

Fluctuating levels of vitamin K from both external dietary sources and internal gastrointestinal sources can significantly alter the INR. Increased dietary intake of vitamin K from either food sources or nutritional supplement sources can reduce the effectiveness of warfarin and decrease the INR. Since warfarin is a high protein bound drug with up to 99% of the drug bound to plasma proteins, patients who are malnourished with low albumin levels will have higher concentrations of unbound drug and may experience faster INR response. Conversely, patients receiving enteral nutrition will have more bound drug due to the high protein concentration in these products.^{20,30,50-52}

9. Promote consistent intake of dietary vitamin K and not avoidance¹ (*UW Health GRADE high quality evidence, strong recommendation*)
10. For enteral nutrition hold the tube feed 1 hour before and 1 hour after warfarin administration.^{50,52} (*UW Health GRADE moderate quality evidence, strong recommendation*)
 - 10.1 If unable to hold enteral nutrition, increase warfarin dose until a therapeutic INR is achieved.⁵² (*UW Health GRADE low quality evidence, conditional recommendation*)
 - 10.2 If on cycled tube feeding, administer warfarin at a time when tube feeds are off.^{52,53} (*UW Health GRADE moderate quality evidence, strong recommendation*)
11. A significant decrease ($\geq 50\%$) in total dietary intake for ≥ 3 days may cause an increase in INR.

Warfarin Reversal

For information on reversing the effects of warfarin, see [“Antithrombotic Reversal- Adult-Inpatient- Clinical Practice Guideline”](#)

Disclaimer

Consensus care models assist clinicians by providing a framework for the evaluation and treatment of patients. This guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

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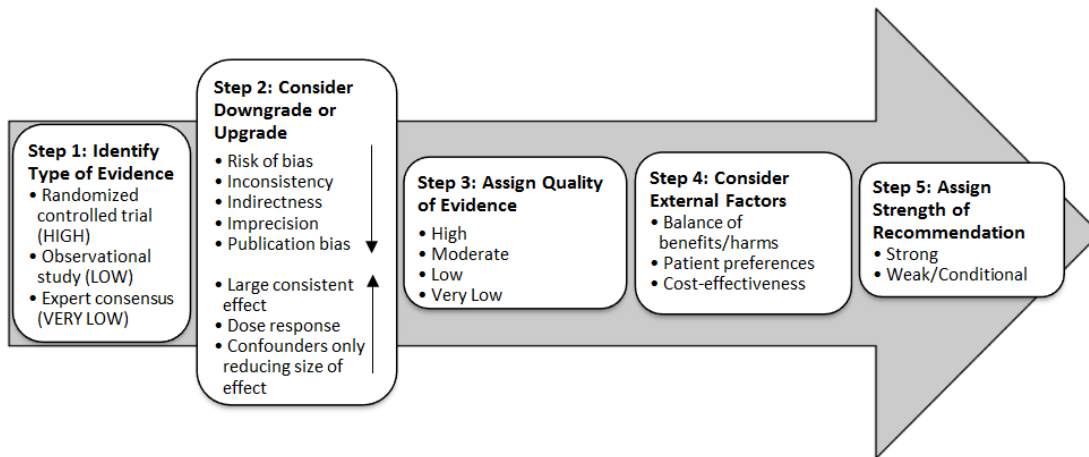


Table 1. GRADE Ranking of Evidence

High	We are confident that the effect in the study reflects the actual effect.
Moderate	We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different.
Low	The true effect may differ significantly from the estimate.
Very Low	The true effect is likely to be substantially different from the estimated effect.

Table 2. GRADE Ratings for Recommendations for or Against Practice

Strong (S)	Generally, should be performed (i.e., the net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.)
Conditional (C)	May be reasonable to perform (i.e., may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented.)

TABLE 1 Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care* (Updated August 2015)

CLASS (STRENGTH) OF RECOMMENDATION	LEVEL (QUALITY) OF EVIDENCE†
CLASS I (STRONG) Benefit >>> Risk Suggested phrases for writing recommendations: ■ Is recommended ■ Is indicated/useful/effective/beneficial ■ Should be performed/administered/other ■ Comparative-Effectiveness Phrases‡: ○ Treatment/strategy A is recommended/indicated in preference to treatment B ○ Treatment A should be chosen over treatment B	LEVEL A ■ High-quality evidence‡ from more than 1 RCT ■ Meta-analyses of high-quality RCTs ■ One or more RCTs corroborated by high-quality registry studies
CLASS IIa (MODERATE) Benefit >> Risk Suggested phrases for writing recommendations: ■ Is reasonable ■ Can be useful/effective/beneficial ■ Comparative-Effectiveness Phrases‡: ○ Treatment/strategy A is probably recommended/indicated in preference to treatment B ○ It is reasonable to choose treatment A over treatment B	LEVEL B-R (Randomized) ■ Moderate-quality evidence‡ from 1 or more RCTs ■ Meta-analyses of moderate-quality RCTs
CLASS IIb (WEAK) Benefit ≥ Risk Suggested phrases for writing recommendations: ■ May/might be reasonable ■ May/might be considered ■ Usefulness/effectiveness is unknown/unclear/uncertain or not well established	LEVEL B-NR (Nonrandomized) ■ Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies ■ Meta-analyses of such studies
CLASS III: No Benefit (MODERATE) Benefit = Risk (Generally, LOE A or B use only) Suggested phrases for writing recommendations: ■ Is not recommended ■ Is not indicated/useful/effective/beneficial ■ Should not be performed/administered/other	LEVEL C-LD (Limited Data) ■ Randomized or nonrandomized observational or registry studies with limitations of design or execution ■ Meta-analyses of such studies ■ Physiological or mechanistic studies in human subjects
CLASS III: Harm (STRONG) Risk > Benefit Suggested phrases for writing recommendations: ■ Potentially harmful ■ Causes harm ■ Associated with excess morbidity/mortality ■ Should not be performed/administered/other	LEVEL C-EO (Expert Opinion) Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).
 A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.
 * The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).
 † For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.
 ‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.
 COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

Grade of Recommendation/ Description	Benefit vs Risk and Burdens	Methodological Quality of Supporting Evidence	Implications
1A/strong recommendation, high-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1B/strong recommendation, moderate quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1C/strong recommendation, low-quality or very low-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Observational studies or case series	Strong recommendation but may change when higher quality evidence becomes available
2A/weak recommendation, high-quality evidence	Benefits closely balanced with risks and burden	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2B/weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burden	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2C/weak recommendation, low-quality or very low-quality evidence	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

Collateral Tools & Resources

The following collateral tools and resources support staff execution and performance of the evidence-based model recommendations in everyday clinical practice.

Metrics

- Time within therapeutic INR range (%): goal > 70%
- % of patients with critical INR results

Patient Resources

1. Health Facts For You #6900: Warfarin (Coumadin, Jantoven)
2. Health Facts For You #322: Food-Drug Interactions: Coumadin & Warfarin Diet Interactions
3. Health Facts For You #6915: Heparin (Unfractionated and Low Molecular Weight)

Policies

1. UWHC Policy #2.3.1 Anticoagulation Monitoring by UW Anticoagulation Clinic Pharmacists
2. UW Health Policy #7.98 Entering Test Results into UW Health Link (EPIC)

Protocols

Initiation and Management of Warfarin – Adult -Ambulatory [7]

Reporting Workbench Reports

Anticoagulation Responsible Pool [7364099]
AC Clinic Outreach Report [7594473]

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