Appropriate Use of Anticoagulants

(Full update April 2024)

The toolbox below provides information and resources to help you update or develop your institution's policies and protocols for use of anticoagulants in adults. In the US, The Joint Commission's National Patient Safety Goal 03.05.01 is to reduce the likelihood of patient harm associated with the use of anticoagulant therapy (does not apply to short-term prophylactic anticoagulation [e.g., VTE prophylaxis in medical or surgical patients]).[20] For a better understanding of the national patient safety goal requirements see https://www.jointcommission.org/-/media/tjc/documents/standards/r3 reports/r3_19_anticoagulant_therapy_rev_final1.pdf.

Goal	Suggested Strategies or Resources

Ensure appropriate anticoagulant **choice based on indication**.	Consider among the following options for **most patients** with these conditions:
	• A-fib: **apixaban, dabigatran, edoxaban,** or **rivaroxaban** is usually preferred over **warfarin.** When a parenteral agent is needed, choose **heparin** or **LMWH** for most patients.[1] Also see our chart, *Atrial Fibrillation: Focus on Pharmacotherapy* for help determining if an A-fib patient requires anticoagulation.
	  ○ apixaban: for every 1,000 patients treated per year, prevents three more strokes, prevents four more deaths, and avoids ten major bleeds compared to warfarin.[36]
	  ○ rivaroxaban: comparable to warfarin for preventing stroke or systemic embolism in patients with relatively high stroke risk. Comparable major bleeding, but INR only in range 55% of time. Lower rate of hemorrhagic stroke, higher rate of major GI bleed.[37]
	  ○ edoxaban: about as effective as warfarin, with six fewer bleeds per 1,000 patients per year.[38]
	  ○ dabigatran: for every 1,000 patients treated per year, prevents about five more strokes, but was associated with two more heart attacks compared to warfarin. Lower risk of hemorrhagic and ischemic stroke. Similar risk of overall bleeding as warfarin, but higher risk of major GI bleed.[39]
	• VTE treatment or prophylaxis: see section below.
	• Cardiovascular risk reduction in coronary or peripheral artery disease: **rivaroxaban**[8,9]
	• Prosthetic heart valve: see section below.
	• ACS/MI: **enoxaparin**, **heparin**, **fondaparinux**, or **dalteparin** (unstable angina, Non-ST-Elevation ACS)[13,14]
	• PCI: **heparin**, **enoxaparin**, or **bivalirudin**[11]
	• Left ventricular thrombus: **warfarin** (preferred) or **DOAC**[12]
	• Disseminated intravascular coagulation: **heparin**[15]
	• Heparin-induced thrombocytopenia: See our FAQ, *Heparin-Induced Thrombocytopenia*.
	• Extracorporeal circulation: **heparin**[16]

Goal	Suggested Strategies or Resources
Choose an appropriate anticoagulant for VTE treatment or prophylaxis.	• VTE treatment phase: **apixaban**, **dabigatran**, **edoxaban**, or **rivaroxaban** is usually preferred over **warfarin** or **LMWH**.[2-4] Apixaban and rivaroxaban **do not** require initial treatment with a parenteral agent (heparin, LMWH, or fondaparinux).[2-4] • VTE, prevention of recurrence: **apixaban** (reduced dose), **dabigatran**, **rivaroxaban** (reduced dose), or **warfarin.**[2,4] o After the three-month treatment phase, determine if the patient is a candidate for extended-phase prophylaxis. See our chart, *Venous Thromboembolism Prophylaxis*, for help. o When choosing treatment, consider patient preferences, bleeding risk, and risk of recurrent VTE.[2] o A reduced DOAC dosing option lacks data for patients with clearer indications for long-term anticoagulation (e.g., A-fib, antiphospholipid syndrome, cancer).[45] Also, it has not been studied after standard anticoagulant dosing for only three months.[45,46] Study durations were about two to four years, so net benefit of longer duration is not clear.[2] • VTE, recurrent while on anticoagulant therapy:[47] o If taking warfarin and INR is therapeutic, suggest changing to treatment-does LMWH for at least one month. o If taking a DOAC and adherent, suggest changing to treatment-dose LMWH for at least one month. o If using LMWH and adherent, recommend increasing the dose by one-quarter to one-third. • VTE prophylaxis, post-arthroplasty: **LMWH** (preferred), **fondaparinux**, **apixaban**, **dabigatran** (off-label in US for knee replacement), **rivaroxaban**, **low-dose heparin**, **warfarin**[5,6,17] o Apixaban and dabigatran have efficacy and major bleeding risk similar to LMWH.[5] Rivaroxaban has greater efficacy but higher bleeding risk compared to LMWH.[5] • VTE prophylaxis, hip fracture surgery: **LMWH** (preferred), **fondaparinux**, **low-dose heparin**, **warfarin**[5,6] • VTE prophylaxis, surgery or at-risk medical patients: see our chart, *Venous Thromboembolism Prophylaxis*.
Choose an oral anticoagulant for a patient with a prosthetic heart valve. *Continued…*	• Mechanical heart valve: use warfarin[10] o Mechanical mitral valve: INR 2.5 to 3.5 o Older ball-in-cage valve: INR 2.5 to 3.5 o Mechanical On-X aortic valve and no thrombosis risk factors, for the first three months after surgery, INR 2 to 3 plus aspirin 75 to 100 mg daily may be reasonable. An INR target is 1.5 to 2 is reasonable after the first three months, with continuation of aspirin 81 mg daily, if the patient has no thrombotic risk factors. o Mechanical bileaflet or current-generation single tilting disc aortic valve: INR 2 to 3 (INR 2.5 to 3.5 if thromboembolic risk is high: A-fib, VTE history, left ventricular dysfunction, hypercoagulable state) • Bioprosthetic heart valve[10] o Aspirin indefinitely. For patients at low risk of bleeding, warfarin (INR 2 to 3) may be used for three to six months, followed by aspirin indefinitely. o If the patient has an indication for long-term anticoagulation, either a DOAC or warfarin can be used, but warfarin is preferred for A-fib presenting within the first three months after valve replacement. • TAVI

Goal	Suggested Strategies or Resources
Choose an oral anticoagulant for a patient with a prosthetic heart valve, continued	○ If the patient has a reason for anticoagulation, either warfarin or a DOAC can be used, but for TAVI patients with A-fib, DOACs have not been shown superior to warfarin (unlike other A-fib patients).[40] ○ If the TAVI patient does not have an indication for anticoagulation, options are (depending on bleeding risk):[10] ▪ warfarin for three to six months, then aspirin indefinitely ▪ antiplatelet therapy (e.g., aspirin, or DAPT stepping down to aspirin after three to six months)
Ensure safe and effective anticoagulant use in patients with potential adherence issues.	• For patients who tend to miss doses, consider warfarin.[60] • Avoid alternating daily doses of warfarin; this can lead to confusion.[59] • For patients who cannot adhere to INR monitoring, or who have a history of difficult-to-control INR, consider a DOAC.[7] • For patients in whom cost is a potential adherence barrier, consider warfarin. • For more tips see our toolbox, *Medication Adherence Strategies*.
Ensure appropriate anticoagulant choice for **special populations** *Continued…*	• **Kidney function** considerations: ○ General considerations for DOACs: ▪ In kidney impairment, DOACs require caution, dose reduction, or avoidance, depending on drug, kidney function, indication, and concomitant medications. ▪ The lower the kidney function, the lesser the benefit of DOACs over warfarin.[41] ▪ DOAC clinical trial inclusion of patients with CrCl <30 mL/min is limited.[41] ▪ Dabigatran and edoxaban have the most reliance on kidney function.[41] ○ Considerations for anticoagulant choice based on kidney function: ▪ CrCl >95 mL/min: avoid edoxaban for A-fib (US labeling)[17] ▪ CrCl <30 mL/min: ○ Dabigatran contraindicated per Canadian labeling.[17] ○ Consider heparin over LMWH.[21] ○ Fondaparinux contraindicated (US; Canada: avoid).[18,19] ○ Avoid dalteparin (treatment doses), or nadroparin (treatment doses; Canada).[24,31] ▪ CrCl <15 mL/min or hemodialysis: ○ Most DOACs are either not recommended or dosing information is not available. ○ Consider apixaban, warfarin, or rivaroxaban, with some considerations:[17] ▪ Apixaban dosage adjustment is not needed, but these patients were excluded from clinical trials, and use is not recommended per Canadian labeling.[17]

Goal	Suggested Strategies or Resources
Ensure appropriate anticoagulant choice for **special populations**, continued	▪ Warfarin has been associated with calciphylaxis (calcific uremic arteriolopathy; vascular calcification) in end-stage kidney disease patients.[42] ▪ Rivaroxaban should be avoided for VTE indications if CrCl <15 mL/min (US; Canada: avoid for all indications).[8,9] Pharmacokinetic data suggest rivaroxaban 10 to 15 mg once daily in hemodialysis patients provides levels similar to patients in the pivotal A-fib trial, but there are limited clinical outcomes data.[8,43] • **Liver impairment** o Avoid DOACs in patient with **severe liver impairment**.[30] They can be considered for compensated cirrhosis (e.g., Child-Pugh A and early B.[30] ▪ For labeled recommendations for specific DOACs in relation to severity of hepatic impairment, see our chart, *Comparison of Oral Anticoagulants*. o Warfarin, LMWH, or heparin can be used, but cirrhosis-associated elevation in INR or antithrombin deficiency may complicate monitoring.[30,44] • In patients with **low body weight**: o avoid fondaparinux for VTE **prophylaxis** (contraindicated [US] if <50 kg).[18] o it may be prudent to avoid DOACs in patients <50 kg due to limited clinical trial data in this population.[50] • In **pregnancy**, LMWH is the anticoagulant of choice. Heparin is also considered safe. Warfarin and heparins are considered safe in **breastfeeding**.[51] • For more information on anticoagulants in special populations, see the following resources: o for patients with cancer, see our *Cancer -Associated Thrombosis FAQ*. o after a bleed, see our FAQ, *Managing Bleeding with Anticoagulants*. o in patients post-bariatric surgery, see our *Bariatric Surgery and Medication Use*.
Take steps to prevent anticoagulant dosing errors.	• Use only oral unit-dose, prefilled syringes, or premixed bags of anticoagulants when available.[20] • Keep in mind that dosing for DOACs is based on factors such as indication, age, weight, kidney function, and use of interacting medications. • Require DOAC indications on orders to help prevent dosing errors. • Be aware that some DOACs (apixaban, rivaroxaban) have **initial dosing** for **VTE** that is different from maintenance dosing.[23] • For VTE prevention post-arthroplasty, use dabigatran 110 mg (half the usual maintenance dose) if started on the day of surgery.[23] • Administer **heparin infusions** using a programmable pump.[20] Nurse-driven heparin protocols may help get patients titrated to their goal faster, and stay at their goal dose longer, than prescriber-driven protocols.[25]

Goal	Suggested Strategies or Resources
Ensure appropriate anticoagulant **dosing in special populations**.	• Choose the correct anticoagulant dose for the patient's **kidney function**. o See our chart, *Comparison of Oral Anticoagulants* for details. o **Heparin**: for VTE **prophylaxis**, consider 5,000 units every eight to 12 hours SQ.[26] o **LMWH:** ▪ Enoxaparin, CrCl <30 mL/min: for VTE **treatment** or ACS, dose is 1 mg/kg SQ once daily (for ST-elevation MI, add 30 mg IV bolus x 1 with first dose if <75 years of age).[23,24] For VTE **prophylaxis**, consider 30 mg SQ once daily (Canada: 20 to 30 mg once daily).[23,24] ▪ Dalteparin, CrCl <30 mL/min: for VTE **prophylaxis**, consider 5,000 units SQ once daily.[31] ▪ Tinzaparin (Canada) can be used at CrCl 20 to 30 mL/min with caution.[22] ▪ For nadroparin (Canada): for VTE **prophylaxis**, reduce dose by 25% to 33% for CrCl <30 mL/min, and also consider dose reduction for CrCl 30 to 50 mL/min.[24] For VTE **treatment**, reduce dose by 25% to 33% for CrCl 30 to 50 mL/min. Do not use treatment doses if CrCl <30 mL/min.[24] • Dose anticoagulants correctly for patients with **low body weight** (also see dosing for kidney impairment, if applicable) o Low body weight patients may be at increased bleeding risk due to advanced age, frailty, or comorbidities.[48] o **DOACs**: ▪ In low body weight patients, kidney function may be overestimated; DOAC dosing/choice is based in part on kidney function.[48] ▪ Apixaban and edoxaban may require dose reduction in patients ≤60 kg, but appear at least as safe as warfarin in patients ≤60 kg based on RCT data.[17,49] ▪ See our toolbox, *Comparison of Oral Anticoagulants* for details on **DOAC** dosing in patients with low body weight. o **Heparin**: for VTE **prophylaxis**, consider 5,000 units SQ every 12 hours.[26] o **LMWH**: ▪ For VTE **prophylaxis** in patients ≤50 kg or with BMI ≤18.5 kg/m^2, consider **enoxaparin** 30 to 40 mg SQ once daily, or **dalteparin** 5,000 units SQ once daily.[26,31] o **Fondaparinux:** for VTE **treatment** in patients <50 kg, a dose of 5 mg once daily is recommended.[18,19] • Dose anticoagulants correctly for patients with **obesity**. o **Heparin**: for VTE **prophylaxis**, consider 7,500 units SQ every eight hours (BMI >40 kg/m^2).[26] o **LMWH**: ▪ For VTE **prophylaxis** in patients with BMI >40 kg/m^2, consider **enoxaparin** 40 mg SQ every 12 hours (if CrCl >30 mL/min).[26] ▪ For VTE **treatment** in patients >100 kg or with BMI ≥40 kg/m^2, consider **enoxaparin** 0.75 to 0.85 mg/kg SQ every 12 hours,[28,29] or dalteparin 100 units/kg SQ every 12 hours for patients ≥99 kg.[31] o **Fondaparinux: f**or VTE **treatment** in patients >100 kg, a dose of 10 mg once daily is recommended.[18,19] • Ensure DOACs (apixaban, dabigatran, warfarin [see below]) are dosed appropriately in **older age**. See our chart, *Comparison of Oral Anticoagulants*, for DOAC dosing.
Continued…	

Goal	Suggested Strategies or Resources
Dosing in special populations, continued	
Dose **warfarin** correctly.	• Consider using a tool for estimating initial warfarin dose. One is available at http://www.warfarindosing.org. • Consider referring warfarin patients to an anticoagulation clinic, if available. Warfarin patients managed by anticoagulation clinics have fewer adverse events and hospitalizations [Evidence level B-3].[55] • Consider starting warfarin at a dose of 5 mg once daily for most patients.[56] Some protocols start with 1 to 2.5 mg in older adults, or in patients with certain comorbidities (e.g., heart or kidney failure, liver disease, malnutrition, cancer).[56] • Overlap heparins and warfarin for at least five days after warfarin is started, even if the INR value is therapeutic sooner, The antithrombotic effect of warfarin isn't present until about the fifth day of therapy, based on the clearance of prothrombin (factor II); it has the longest half-life of the vitamin K-dependent clotting factors.[57] • In previously stable patients with a single INR ≤0.5 below or above target, continue dose and repeat INR in one to two weeks.[58] During maintenance, if INR is subtherapeutic (INR more than 0.5 below target), increase warfarin dose by no more than 15% and wait four to five days before making further increases.[59]

Minimize **GI bleeding risk** in patients taking anticoagulants.	• Consider apixaban for patients with other GI bleed risk factors [Evidence level B-3].[52]
	  ○ Dabigatran's tartaric acid component may cause direct mucosal injury.[52] The site of bleeding with dabigatran tends to be lower GI (vs upper GI with rivaroxaban or warfarin), which may have implications for patients with lower GI lesions (e.g., angiodysplasia, erosions, diverticulosis).[53]
	• Consider adding a proton pump inhibitor for patients with:
	  ○ HAS-BLED score ≥3[53]
	  ○ History of upper GI bleed or peptic ulcer disease[54]
	  ○ Age >75 years with a DOAC or age >65 years with warfarin.[54]
	  ○ Antiplatelet[54]
	  ○ NSAID[54]
	• Use aspirin only when clearly needed (e.g., recent MI)[53]
	• Avoid NSAIDs.[53]
	• Use the correct dose.[53]
	• Eliminate modifiable risk factors (e.g., uncontrolled hypertension, excessive alcohol use, *Helicobacter pylori*).[53,54]
	• Consider referring warfarin patients to an anticoagulant clinic, if available.[55]
	• Watch for drug interactions.[54]

Goal	Suggested Strategies or Resources
Identify and respond to potential **food** and **drug interactions** with anticoagulants.	• Most DOACs are not good choices in patients who require use of drugs that strongly induce their metabolism (e.g., through CYP3A4 and/or p-glycoprotein; rifampin, phenytoin, carbamazepine). See our chart, *Comparison of Oral Anticoagulants*, for specific drug interactions to be aware of with DOACs and warfarin. • Ensure DOAC doses are adjusted for **drug interactions.** DOACs are often significantly affected by p-glycoprotein inhibitors and inducers. Additionally, **apixaban** and **rivaroxaban** may interact with CYP3A4 inducers/inhibitors.[23] • Ensure **rivaroxaban** doses >10 mg are given with a meal to improve absorption.[23] • Screen warfarin patients with significant drugs interactions with inducers/inhibitors of CYP2C9, 2C19, 1A2, and 3A4. • Screen for interactions when an antibiotic is prescribed for a patient taking warfarin. • Assess risk/benefit of concomitant antiplatelet use. For more information, see our FAQ, *Combination Antithrombotic Therapy*. • Use education resources (see below) to explain warfarin drug and food interactions to patients and caregivers.
Perform appropriate baseline and follow-up **labs**.	• Develop a policy for baseline and ongoing lab tests to monitor and adjust anticoagulant therapy.[20,32] • See our charts, *Lab Monitoring for Common Medications* and *Comparison of Oral Anticoagulants* for information on monitoring DOACs and warfarin. Also consider monitoring liver function in patients taking DOACs.[20] Other labs may be appropriate in specific situations (e.g., patient is bleeding or requires emergency/urgent surgery; see our FAQ, *Managing Bleeding With Anticoagulants*). • Use activated partial thromboplastin time (aPTT) or anti-Xa levels to monitor heparin.[23] • In warfarin patients, confirm acceptable INR before neuraxial anesthesia.[33] • Monitor complete blood count to detect problems such as heparin-induced thrombocytopenia, increased bleeding risk, or subclinical bleeding.
Switch between anticoagulants safely.	• See our chart, *Comparison of Oral Anticoagulants*, for details on switching to/from DOACs and warfarin. • For information on switching from a DOAC to intravenous heparin, see https://bpb-us-e1.wpmucdn.com/sites.uw.edu/dist/8/9473/files/2023/11/UWMC-DOAC-to-Heparin-Transition-Guidelines-11.28.23.pdf.
Manage bleeding in patients taking anticoagulants.	• Develop protocols for anticoagulant reversal.[32] For help, see our: o FAQ, *Managing Bleeding With Anticoagulants* o Chart, *Clotting Factors*

Goal	Suggested Strategies or Resources
Manage anticoagulants **perioperatively**.	• Determine if the patient requires the anticoagulant at all. • Determine if the procedure requires discontinuation of the anticoagulant. • If warfarin is to be continued perioperatively, ensure the INR is not supratherapeutic. If warfarin will be held, determine if bridging is required. • If anticoagulant discontinuation is required, determine when it can be restarted. • Confer with anesthesia regarding stopping/restarting anticoagulants in patients who will have or have had regional anesthesia. • Ensure that the patient and caregivers understand if/when to stop/restart the anticoagulant. • Ensure that everyone caring for the patient is aware that the patient is taking an anticoagulant, and which one they are taking. • Develop protocols that address perioperative use of anticoagulants.[13] Consult our resources for help: o See our FAQ, *Managing Bleeding With Anticoagulants*, for pre-operative washout and laboratory assessment of bleeding risk. This chart also contains information to help in situations where a washout isn't feasible. o See our chart, *Perioperative Management of Chronic Medications in Noncardiac Surgery*, for considerations about holding, bridging, and restarting anticoagulants around surgery or procedures.
Make decisions regarding thrombolytics in stroke patients taking an anticoagulant.	• See our checklist, *Acute Ischemic Stroke Pharmacotherapy*.
Educate patients and families about anticoagulation.	• Points that should be addressed in education include adherence, follow-up (e.g., next INR), interactions (with foods and drugs), and adverse effects.[20,32] • Suggest tools to promote anticoagulation adherence, such as phone apps like Medisafe (https://www.medisafeapp.com/). • Resources for patients include: o "What are Direct-Acting Oral Anticoagulants (DOACs)?" (https://www.heart.org/-/media/Files/Health-Topics/Answers-by-Heart/What-are-DOACs.pdf) o "Foods that are High and Low in Vitamin K" (https://www.heart.org/-/media/Files/Health-Topics/Atrial-Fibrillation/warfarin-card.pdf). o "A Patient's Guide to Taking Warfarin" (https://www.heart.org/en/health-topics/arrhythmia/prevention--treatment-of-arrhythmia/a-patients-guide-to-taking-warfarin).
Ensure safe use of	**General Considerations**

Goal	Suggested Strategies or Resources
anticoagulants at **transitions of care**.	• Use our checklist, *Transitions of Care*, for important considerations at admission, upon transfer between units, before discharge, and at follow-up outpatient visits to help keep patients on track with the medications and to reduce readmissions.[34] • Watch for duplicate anticoagulation orders (i.e., prophylaxis and treatment). **Considerations on Admission** • If a patient is admitted on an anticoagulant document and: o assess **adherence and timing of last dose** to know when doses are due and to interpret laboratory tests (e.g., INR). o confirm the dose. For example, patients' current warfarin dose may be different than what is on the bottle label. o ensure that the **dose is appropriate** based on any changes in kidney function (e.g., DOACs). o verify the indication and ensure that the anticoagulant is still needed for that **indication** (i.e., VTE treatment). **Considerations During Transfers** • If patients transfer to your hospital on a heparin drip, continue the drip in units/hr or units/kg/hr instead of mL/hr. Heparin concentrations may differ between hospitals. • Use a validated tool to ensure VTE prophylaxis is still appropriate when patients transfer to the floor (e.g., IMPROVE [https://www.mdcalc.com/improve-risk-score-venous-thromboembolism-vte]). **Discharge Considerations** • Ensure anticoagulants prescribed solely for VTE prevention in at-risk medical patients are **discontinued before discharge**. Inform new provider of time of last dose of discontinued anticoagulants, due to possibility of persistent effect.[35] • Ensure outpatient provider or transfer facility is aware of date of previous and next INR and the INR target.[12] • Document kidney function (preferably as CrCl) in communication to outpatient providers.[35] • Iron out any issues with third party DOAC coverage or cost barriers **before** discharge. This might involve discharge planners and the patient's outpatient pharmacist. • Include **indication** and **time of last dose** on discharge orders/prescriptions for oral anticoagulants.[35] • If an anticoagulant is prescribed for a finite **duration** (e.g., VTE treatment, VTE prevention post-arthroplasty), ensure that the outpatient prescriber, patient/caregiver, and pharmacist are aware of the **stop date** and any need for **step-down** in dosage (e.g., for VTE treatment).
Consider **anticoagulation stewardship**	• If your hospital does not already have one, consider a stewardship program for anticoagulation to optimize the quality and safety of anticoagulation use, similar to programs for opioids and antimicrobials.[27] • Access and review the o Checklist for Core Elements of Anticoagulation Stewardship Programs at https://acforum.org/web/downloads/ACF-Anticoagulation-Stewardship-Checklist.pdf. o Core Elements of Anticoagulation Stewardship at https://acforum.org/web/education-stewardship.php, to see what areas can be improved at your facility.

Abbreviations: ACS = acute coronary syndrome; CrCl = creatinine clearance; DAPT = dual antiplatelet therapy; DOAC = direct oral anticoagulant; GI = gastrointestinal; IV = intravenous; LMWH = low molecular weight heparin; MI = myocardial infarction; PCI = percutaneous coronary intervention; SQ = subcutaneous; TAVI = transcatheter aortic valve implantation

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician* 2004;69:548-56. https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html.]

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