

Doctor, I have finished 6 months of treatment for my blood clot. Can I start taking a reduced-dose of anticoagulant now?

After 6 months, some people can safely switch to a reduced dose of a direct oral anticoagulant (DOAC). In these cases, reduced-dose DOACs are just as good at preventing new clots as full-dose DOACs and appear to cause less bleeding. The bleeding risk of reduced-dose DOACs is similar to that of taking a daily aspirin. We should talk about whether that is a good plan for you.

What's the evidence?

Understanding the problem

Anticoagulants protect people who have deep vein thrombosis (DVT) or pulmonary embolism (PE) from forming new blood clots while their body works on breaking down the old blood clots. How long people with DVT or PE should take an anticoagulant is not based on when the clot is gone. Instead, it is based on when the risk factor that caused the blood clot is gone.

For example, Alice develops a DVT one week after hip replacement surgery. She is treated with anticoagulants for 3 months, and then her doctor tells her she can stop taking them. Alice's risk factor for DVT was surgery. Her DVT is called "provoked".

For many people, the risk factor that caused the DVT or PE is either weak (e.g., travel) or unknown. This type of DVT or PE is called "unprovoked". These people remain at risk for forming new blood clots for the rest of their lives. To protect themselves from another clot, they may decide to take anticoagulants indefinitely.

Anticoagulants also have safety concerns because they increase the risk of bleeding.

For example, Sam has an ulcer in his stomach that is bleeding but so slowly, he hasn't noticed it. When Sam is diagnosed with a PE and starts taking anticoagulants, the bleeding from his ulcer increases and he vomits up blood.

Researchers are always looking for ways to protect people from blood clots while lowering the risk of bleeding. One possible way to do this is to reduce the dose of the anticoagulant. Previous studies showed that reduced-dose DOACs appear to be just as good at preventing new blood clots as full-dose DOACs but with a lower risk of bleeding.

A meta-analysis is a statistical method used to get more accurate information about a treatment by combining the results of studies together. This is similar to judging a sports team based on how they perform over an entire season rather than just one game.

The meta-analysis described below was designed to find out more about how reduced-dose DOACs compare to 1) full-dose DOACs, and 2) stopping DOACs or substituting a DOAC with aspirin.

The research

A summary of 2 studies published up to March 2017.

Who? The studies included 5847 people who completed 6 to 12 months of full-dose anticoagulation for venous thromboembolism (VTE; collective term for blood clots within the venous system). Patients were excluded if their doctor thought it was unsafe for them to stop anticoagulation or if they had had severe medical illnesses that would prevent them from safely remaining on a full-dose DOAC. Very few patients with cancer were included in the studies.

What? The studies compared reduced-dose DOACs with full-dose DOACs and with placebo or aspirin.

Reduced-dose DOAC	vs	Full-dose DOAC	vs	Placebo or aspirin
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Reduced-dose DOAC	vs	Full-dose DOAC	vs	Placebo or aspirin
Rivaroxaban (Xarelto®), 10 mg once a day <u>or</u> Apixaban (Eliquis®), 2.5 mg twice a day		Rivaroxaban (Xarelto®), 20 mg once a day <u>or</u> Apixaban (Eliquis®), 5 mg twice a day		Placebo: A pill containing an inactive substance that has no effect on the outcome. Sometimes, it is referred to as a “sugar pill.” <u>or</u> Aspirin, 81 mg once a day

What the researchers found

The quality of the studies was moderate to high with low risk of bias.

People who took reduced-dose DOACs did not have more new blood clots than people who continued to take full-dose DOACs. As well, people who took reduced-dose DOACs had fewer new blood clots than did people who switched to placebo or aspirin.

People who took reduced-dose DOACs did not bleed more than people on placebo or aspirin.

Summary of findings

Reduced-dose DOAC vs full-dose DOAC vs placebo or aspirin in people who have been treated for VTE for 6 months

Outcomes at 1 year	Rate of events with:			Result of reduced-dose DOAC compared with:		Number of studies and quality of the evidence
	Reduced-dose DOAC	Full-dose DOAC	Placebo or aspirin	Full-dose DOAC	Placebo or aspirin	
Recurrent VTE	2 out of 100 people	1 out of 100 people	6 out of 100 people	No effect*	About 4 fewer people who took reduced-dose DOAC had another DVT or PE	Moderate-quality - 2 studies
Major Bleeding or Clinically relevant nonmajor bleeding	3 out of 100 people	4 out of 100 people	2 out of 100 people	About 1 less person who took reduced-dose DOAC had bleeding that was life-threatening or required seeing a doctor	No effect*	Moderate-quality to High-quality - 2 studies

*Although the rates for the 2 groups look different, the differences were not statistically significant—this means that the difference could simply be due to chance rather than due to the different treatments.

This Evidence Summary is based on the following article:

Vasanthamohan L, Boonyawat K, Chai-Adisaksopha C, et al. **Reduced-dose direct oral anticoagulants in the extended treatment of venous thromboembolism: a systematic review and meta-analysis.** *J Thromb Haemost.* 2018 Jul;16(7):1288-1295. doi: 10.1111/jth.14156. Epub 2018 Jun 17. PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/29772108?dopt=Abstract>)

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Glossary

anticoagulant	medications that prevent blood clots from forming or travelling (aka blood thinner)
anticoagulants	medications that prevent blood clots from forming or travelling (aka blood thinner)
anticoagulation	medications that prevent blood clots from forming or travelling (aka blood thinner)
apixaban	Eliquis® (aka DOAC)
Clinically relevant nonmajor bleeding	bleeding that is not as serious as major bleeding but still required assesment by a doctor OR a medical intervention (e.g. scope) OR interruption of the medication OR caused discomfort or impairment of activities of daily living
deep vein thrombosis (DVT)	formation of a blood clot within a vein deep within the leg
DOAC	anticoagulant pill that does not require blood tests to monitor the effect (aka novel oral anticoagulant, NOAC); examples include apixaban, dabigatran, edoxaban, rivaroxaban
DVT	formation of a blood clot within a vein deep within the leg
High-quality	Additional studies are very likely to have the same result
major bleeding	serious bleeding (e.g. requiring a visit to the doctor or hospital, an invasive test to find the source of bleeding or a blood transfusion)
meta-analysis	advanced statistical method that combines the results of different studies together
Moderate-quality	Additional studies are likely to have the same result
PE	blood clot(s) that cause obstruction of blood vessels within the lungs (pulmonary artery), after travelling from veins, most commonly within the leg or arm or pelvis
placebo	a harmless, inactive, and simulated treatment
provoked	DVT or PE that is associated with (or thought to be caused by) a strong risk factor such as cancer or recent surgery
pulmonary embolism (PE)	blood clot(s) that cause obstruction of blood vessels within the lungs (pulmonary artery), after travelling from veins, most commonly within the leg or arm or pelvis
risk factor	characteristics that increase the chance that a person will develop a disease or condition or experience a bad outcome
risk of bias	possibility that study has an error(s) that deviates the results away from the truth
rivaroxaban	Xarelto® (aka DOAC)
ulcer	open sore
unprovoked	a DVT or PE that is unexplained or not associated with a strong risk factor (aka idiopathic VTE)
venous thromboembolism	the collective term referring to blood clots within the veins, most commonly deep vein thrombosis and pulmonary embolism
VTE	venous thromboembolisms; collective term referring to blood clots within the veins