

Venous Thromboembolism (VTE)

What is Venous Thromboembolism (VTE)?

Venous thromboembolism (VTE) is the third most common cardiovascular disease worldwide, after ischaemic heart disease and stroke¹ and is the most common avoidable cause of hospital death². VTE encompasses two serious conditions:

- ◆ **Deep vein thrombosis (DVT)** is a blood clot in a vein, usually in the leg that partially or totally blocks the flow of blood³. If all or part of a DVT breaks off, it can travel to the lungs and cause a pulmonary embolism (see below)
- ◆ Symptoms of DVT include pain, swelling, redness of the area, and dilation of the surface veins. The skin may also be warm to the touch
- ◆ **Pulmonary embolism (PE)** is a blood clot blocking one or more vessels in the lungs. Once in the lung, the blood clot may block the circulation, causing sudden death or long-term damage to the lungs and other vital organs. About a third (34%) of VTE deaths are from sudden fatal PE⁴
- ◆ Symptoms of PE include acute shortness of breath, chest pain, and rapid heart rate; some people also cough blood
- ◆ About 1 in 10 deaths that occur in the hospital is caused by pulmonary emboli⁵

Who is at Risk of VTE?

Populations at high risk of VTE include patients undergoing major orthopaedic surgery for hip or knee replacement and those admitted to hospital for an acute medical condition.

- ◆ The risk of symptomatic VTE after major orthopaedic surgery is higher than in the general population for at least two months after surgery²
- ◆ Patient-related, or predisposing, risk factors include inherited thrombophilia, advanced age, obesity, prior VTE and varicose veins²
- ◆ Without preventative treatment, the absolute DVT risk after hip or knee surgery is between 40% and 60%²

VTE is difficult to diagnose, as up to half of patients have no specific symptoms. Consequently, avoiding venous blood clots by preventative measures is the most economical and effective approach in current clinical practice.

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How Common is VTE?

The worldwide incidence of VTE is 1 per 1000⁶.

- ◆ In the US, the annual prevalence of DVT is estimated at up to 2 million cases a year⁷. The estimated incidence of acute PE is approximately 60-70 per 100,000 patients⁸
- ◆ In the EU, the estimated incidence of DVT is approximately 700,000 every year⁹. The estimated incidence of PE is approximately 400,000 every year⁹

What is the Disease Burden of VTE?

Mortality and morbidity

VTE kills one person every 37 seconds, which is more than 843,000 deaths every year^{4,10}. This includes over 540,000 deaths in Europe alone¹¹. In the EU, more than twice as many people die from VTE than from breast cancer, prostate cancer, AIDS and traffic accidents combined⁴.

- ◆ 10–25% of PEs are rapidly fatal^{12,13}, usually within 2 hours of the onset of symptoms¹⁴. PE can reoccur, and if it does, it is usually fatal¹⁵
- ◆ Even in the absence of a PE, DVT alone can have burdensome and costly consequences such as post-thrombotic syndrome¹³ and an increased risk of reoccurrence

Economic burden

The complications associated with VTE and its treatment are frequent and costly. The main drivers of these VTE costs are initial and recurrent events requiring hospitalisation.

- ◆ The total estimated cost for VTE associated care in Europe is €3.1bn per year¹⁶
- ◆ In Europe, the annual cost of managing all-cause VTE has been estimated at approximately €4,000 per patient¹⁷
- ◆ In the US, the total estimated costs for VTE associated care is up to \$15.5 billion annually¹⁸
- ◆ With hospital readmission for DVT at 19%, the rate of VTE recurrence remains high¹⁹





How is VTE Prevented and Treated?

Anticoagulants are the cornerstone of therapy for prevention of potentially deadly blood clots, but widely-used traditional therapies are associated with significant drawbacks.

- ◆ The traditional standard therapy for **prevention of VTE** associated with orthopaedic surgery is a class of anticoagulant drugs known as heparins. Heparins require administration by injection, which can cause inconvenience and discomfort. In addition, some patients taking heparin experience a severe reaction known as HIT (heparin-induced thrombocytopenia), which can lead to new or worsening thrombosis
- ◆ The current standard of care for **treatment of VTE** is the complex dual drug approach of heparin followed by a vitamin K antagonist (VKA), such as warfarin. As well as the difficulties associated with heparins mentioned above, managing patients on VKAs such as warfarin can also be challenging. VKAs have a narrow therapeutic window (meaning there is a small gap between the dose that provides effective anticoagulation and a dose that increases bleeding events or can increase the rate of blood clots) and therefore can require frequent dose adjustments, as well as a need for routine coagulation monitoring. Furthermore, VKAs have a slow onset of action, as well as many food and drug interactions^{20,21}

Limitations of current VTE therapies may contribute to their under-utilisation²², creating challenges for patients and leaving them at risk.

New oral anticoagulants hold the promise of overcoming the limitations of traditional anticoagulants, thereby enabling their use to prevent and or treat more venous thromboembolic (VAT) conditions.

- ◆ Benefits of new oral anticoagulants include predictable anticoagulation without the need for routine coagulation monitoring or frequent dose adjustment, low risk of drug-drug interactions and no dietary restrictions
- ◆ Xarelto[®] (rivaroxaban) is a highly effective, oral, once daily anticoagulant approved for the prevention of VTE in adult patients undergoing elective hip or knee replacement surgery
- ◆ 'Xarelto' has been recommended for approval by the European Committee for Medicinal Products for Human Use (CHMP) for the treatment of DVT and prevention of recurrent DVT and PE following an acute DVT in adults





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About Rivaroxaban (Xarelto®)

Rivaroxaban is an oral anticoagulant that was discovered in Bayer HealthCare's Wuppertal laboratories in Germany, and is being jointly developed by Bayer HealthCare and Johnson & Johnson Pharmaceutical Research & Development, L.L.C. It has a rapid onset of action with a predictable dose response and high bioavailability, no requirement for routine coagulation monitoring, and a limited potential for food and drug interactions.

Rivaroxaban is marketed under the brand name Xarelto® for VTE prevention in adult patients following elective hip or knee replacement surgery, and it is the only oral anticoagulant that has consistently demonstrated superior efficacy over enoxaparin in this indication. Rivaroxaban is approved in more than 110 countries worldwide and marketed outside the U.S. by Bayer HealthCare in this indication.

In the U.S., where rivaroxaban has been available since July 2011 for VTE prevention in adult patients following elective hip or knee replacement surgery, Janssen Pharmaceuticals, Inc. (a Johnson & Johnson Company) holds marketing rights. The Bayer HealthCare sales force is supporting Janssen Pharmaceuticals, Inc. in designated hospital accounts. On November 4, Xarelto® received further marketing approval in the U.S. for the prevention of stroke in patients with Atrial Fibrillation.

The extensive clinical trial programme supporting rivaroxaban makes it the most studied and widely published oral, direct Factor Xa inhibitor. The studies, reported and ongoing, involve over 75,000 patients for the prevention and treatment of venous and arterial thromboembolic (VAT) disorders across a broad range of acute and chronic conditions, including stroke prevention in patients with Atrial Fibrillation, DVT treatment and the prevention of recurrent DVT or PE, and the secondary prevention of Acute Coronary Syndrome.

**To learn more about thrombosis, please visit www.thrombosisadviser.com
To learn more about 'Xarelto' please visit www.xarelto.com**

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