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# Epidemiology of venous thromboembolism with focus on risk markers

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## Akademisk avhandling

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### **Abstract**

**Background:** Venous thromboembolism (VTE) is a vascular disease with an incidence of approximately 140 cases per 100,000 person-years in adults. The incidence of VTE has increased over the last decades, and more than 20% of affected individuals die in the first year after diagnosis. To reduce the incidence of VTE, it is important to identify modifiable risk factors for the condition.

**Aims:** The aims of this thesis were a) To study the incidence of first-time VTE and the prevalence of risk markers for VTE at the time of VTE diagnosis, b) To determine the validity of diagnoses of deep vein thrombosis and pulmonary embolism in administrative registries, and c) To study the association between glucose levels, diabetes, alcohol consumption, physical activity and risk of first-time VTE.

**Methods:** To determine the incidence of first-time VTE and the prevalence of risk markers for VTE at the time of VTE diagnosis, a retrospective, population-based cohort study was conducted. The study included all adult residents of Västerbotten County during the year 2006. All other aims were addressed in the prospective, population-based Venous thromboEmbolism In Northern Sweden (VEINS) cohort study. The VEINS cohort included 108,025 residents of Västerbotten County aged 30 to 60 years without previous VTE events. They were included from 1985 onwards and were followed until a VTE event, death, emigration, or the study end on September 5, 2014. All underwent a health examination within the Västerbotten Intervention Programme where weight, height, blood pressure and glucose levels were measured, and answered a questionnaire regarding smoking, education level, medication use, history of diabetes, alcohol intake and physical activity. VTE diagnoses were validated by review of medical records and radiology reports. To study the validity of diagnoses of deep vein thrombosis and pulmonary embolism in administrative registries, a registry search for International Classification of Diseases (ICD) diagnosis codes indicating pulmonary embolism and/or deep vein thrombosis events was made in the Swedish National Patient Registry and the Cause of Death Registry. An additional search using an extended set of ICD diagnosis codes was performed in order to identify misclassified events.

**Results:** The incidence of first-time VTE was 137 (95% confidence interval [CI] 122–154) per 100,000 adults per year. The most common risk markers for VTE were recent hospitalization and concurrent malignancy. The positive predictive value for a diagnosis of pulmonary embolism was 80.7% (95% CI 78.4–82.9), and that of deep vein thrombosis 59.2% (95% CI 56.7–61.7). Misclassification occurred in 1.1% (95% CI 0.4–1.7) of pulmonary embolism events and in 16.4% (95% CI 14.2–18.7) of deep vein thrombosis events. In the VEINS cohort, a total of 2,054 participants experienced an objectively verified first-time VTE event during approximately 1.5 million person-years of follow-up. In univariable analysis, there were associations between fasting plasma glucose, oral glucose tolerance test two-hour post-load plasma glucose, diabetes and increased risk of first-time VTE. These associations were attenuated after adjustment for potential confounders, and were no longer significant. There was an association between alcohol consumption and risk of VTE in men (*P* for trend 0.02 after adjustments for increased risk of first-time VTE over quartiles of weekly alcohol consumption). Alcohol dependence was associated with risk of first-time VTE in men (hazard ratio [HR] 1.30; 95% CI 1.07–1.59 after adjustments). In women, there were no significant associations between alcohol consumption and risk of first-time VTE. Women who performed leisure time physical activity at least once a week had a lower risk of first-time VTE (HR 0.83; 95% CI 0.71–0.98 after adjustments) compared to women with less or no physical activity. Women with high occupational physical activity also had a lower risk of first-time VTE (HR 0.85; 95% CI 0.74–0.98 after adjustments). In men, there were no consistent association between either measure of physical activity and risk of first-time VTE.

**Conclusions:** VTE is a common vascular disease. Registry data on diagnoses of pulmonary embolism, but not deep vein thrombosis, is of acceptable quality and can be considered for use in registry-based studies. Glucose levels and diabetes are not associated with risk of first-time VTE. Alcohol intake and alcohol dependence are associated with an increased risk of first-time VTE in men, whereas high leisure time physical activity and occupational physical activity are associated with a decreased risk of first-time VTE in women.

### **Keywords**

Venous thromboembolism, venous thrombosis, deep vein thrombosis, pulmonary embolism, incidence, risk markers, diabetes, glucose, alcohol consumption, alcohol dependence, physical activity