Socioeconomic status and risk of incident venous thromboembolism

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Abstract

Background: Although venous thromboembolism (VTE) is a leading cause of morbidity and mortality, and socioeconomic status (SES) affects human health and health behavior, few studies have examined the association between SES and VTE.

Objectives: We aimed to investigate the association between SES, assessed individually and in a composite score by levels of education, income, and employment status, and incident VTE.

Methods: We used Danish national registries to identify 51,350 persons aged 25–65 years with incident VTE during 1995–2016. For each case, we used incidence density sampling to select five age-, sex-, and index-year-matched controls from the general Danish population (n = 256,750). SES indicators, including education, income, and employment status, were assessed 1 and 5 years before the VTE. We used conditional logistic regression to compute odds ratios (ORs) with 95% confidence intervals (CIs) for VTE according to individual SES indicators and a composite SES score in analyses adjusted for age, sex, and comorbidities.

Results: Compared with low levels, high educational level (OR 0.74; 95% CI 0.71–0.77), high income (OR 0.70; 95% CI 0.68–0.72), and high employment status (OR 0.66; 95% CI 0.64–0.68) were associated with decreased risk of VTE, even after adjusting for comorbidities. A composite SES score was superior to the individual indicators in assessing VTE risk (OR for high vs. low score: 0.61; 95% CI 0.59–0.63). In sensitivity analysis with SES indicators measured 5 years before the VTE, the risk estimates remained essentially the same.

Conclusion: High levels of both individual SES indicators and a composite SES score were associated with decreased VTE risk.

Keywords
education, employment, income, socioeconomic status, venous thromboembolism
## INTRODUCTION

Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE) is a serious vascular disorder associated with substantially reduced quality of life, morbidity, and mortality.\(^1\)\(^-\)\(^2\) Socioeconomic status (SES) has been demonstrated to affect the risk of arterial cardiovascular diseases such as myocardial infarction and stroke,\(^3\)\(^-\)\(^5\) but less is known of the importance of SES in VTE.

The few studies that have investigated associations between SES indicators and VTE risk report that stress,\(^6\) low income,\(^7\) low educational status,\(^7\)\(^-\)\(^10\) low occupational class,\(^6\)\(^9\)\(^10\) single status,\(^7\) and neighborhood deprivation\(^11\)\(^-\)\(^12\) are associated with increased VTE risk. Even though existing studies suggest that individual SES indicators play a role in the VTE risk, similar to that for other arterial cardiovascular diseases, available evidence is inconsistent and the SES indicators found to be associated with VTE vary within and between studies.\(^3\)\(^-\)\(^10\) The discrepancy in current studies is likely explained by differences in composition of the study populations, study designs, time between SES and VTE assessments, and methods for monitoring SES indicators. Furthermore, because low SES is associated with VTE-related comorbidities such as cancer and cardiovascular diseases,\(^3\)\(^-\)\(^5\)\(^13\) it is likely that these conditions partly explain or mediate the associations reported between SES and VTE.

To tailor VTE prevention at the population level, it is important to assess the strength of the associations between SES and VTE, measured both as individual SES indicators and as a composite SES score, and examine whether these associations are explained by confounding diseases. The aim of this population-based nationwide case-control study was therefore to investigate the impact of the major SES indicators education, income, and employment status, assessed individually and combined, on risk of incident VTE.

## METHODS

### 2.1 Design and setting

Denmark has universal tax-funded health care and educational systems covering all legal Danish residents.\(^14\) In addition, the Danish government maintains nationwide registries containing routinely collected administrative and health data.\(^14\) The unique personal identifier (CPR number) assigned to every Danish resident at birth or upon immigration makes it possible to access and link the nationwide registries to obtain extensive individual-level health care information and current data on civil and vital status.\(^14\)

In the current study we extracted demographic information and data on vital status and migration from the Danish Civil Registration System.\(^14\) Information on VTE and comorbidities was obtained from the Danish National Patient Registry (DNPR) and the Danish Psychiatric Central Research Register both covering all Danish hospitals.\(^14\) Furthermore, we obtained data on income and employment status from the Integrated Database for Labour Market Research, and data on education from the Educational Attainment Register.\(^14\)

### 2.2 Cases and controls

We used the International Classification of Diseases (ICD) 8 and 10 codes in the DNPR to identify 51 350 VTE patients aged 25–65 years with a first-time primary or secondary discharge diagnosis of DVT or PE from January 1, 1995, to December 31, 2016. If a patient had simultaneous PE and DVT diagnoses, we categorized the event as PE because of its higher mortality rate.\(^15\) We defined the first hospital admission/outpatient clinic visit date as the VTE date and excluded VTEs registered only in emergency room departments because they often represent working diagnoses with high rates of clinical misclassification.\(^16\) We did not include individuals aged <25 years because they were likely to still be in school and to lack a stable income or employment. We also did not include individuals aged ≥65 years because they would be retired from work and receive an old age pension instead of work-related income.

For each VTE patient, we used the Civil Registration System to individually match five general controls from the general working age population by year of birth, sex, and calendar year (n = 256 750), with replacement based on incidence density sampling.\(^17\) The hospital admission date for the VTE patient was used as the index date for the matched controls.\(^17\) Individuals in the control group could not have been hospitalized for VTE before their index date. Cases and controls with missing SES values (n = 20 398) were not included in the regression analysis.

### 2.3 Variables

We measured educational level, employment status, and income level 1 and 5 years before the VTE/index date. We divided the level of education (i.e., high, medium, low) into age-specific groups based on the distribution of education in each group. (Tables S1 and S2). To avoid the impact of inflation and to account for salary changes over calendar time, we recalculated income values using the new gross domestic product deflators downloaded from the

### Essentials

- Few studies have explored the association between socioeconomic status (SES) and VTE risk.
- We assessed the association between individual SES indicators and a composite SES score, and VTE.
- High levels of SES indicators and a composite SES score were associated with decreased VTE risk.
- The combined SES score performed better than individual indicators in assessing the risk of VTE.
World Bank homepage (www.worldbank.org). After deflation of the income values, we calculated income in quartiles based on the VTE cases and controls and merged the two middle quartiles to obtain three categories (i.e., high, medium, and low). We divided employment status into "employed, unemployed, and outside the workforce." We considered persons pursuing an educational program, those in early retirement, and those receiving other types of public support, except work-related disability pension, to be outside the workforce. Employment status was categorized as high (i.e., employed), medium (i.e., outside the workforce), and low (i.e., unemployed and persons on permanent work-related disability pension).

We used the "low, medium, and high" categorical distributions to create a score for each of the socioeconomic indicators education, income, and employment status. The score for each indicator ranged from 1 to 3 with categories of high (score of 3), medium (score of 2), and low (score of 1), with low serving as the reference. We combined the scores from education, income, and employment status into a composite SES score ranging from 3 to 9. Based on the distribution of the total score, we divided the composite SES score into categories of high (scores of 8 and 9), medium (scores of 5 to 7), and low (scores of 3 and 4), using low SES score as the reference.

We searched the DNPR for information on comorbidities diagnosed before the VTE/index date using ICD-8 codes (1977–1994) and ICD-10 codes (from 1994 onwards) for obesity, cancer, coronary heart disease (including atrial fibrillation, myocardial infarction, and heart failure), diabetes, stroke, chronic obstructive pulmonary disease (COPD), acute kidney failure and chronic kidney disease, mental diseases, surgery and trauma/fractures 3 months before the VTE/index date, and diseases included in the modified Charlson Comorbidity Index (CCI). All ICD codes used in the study are provided in Table S3.

2.4 Statistical analysis

We used conditional logistic regression models to compute crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) as a measure of the incidence rate ratio of VTE, both according to VTE cases and controls aged 25–65 years are presented in Tables 1 and 2. Compared with men, women had a lower educational level and income, a higher prevalence of unemployment, and a lower SES score, with the greatest differences observed in the oldest age groups (Table 2). The following variables were more common among VTE patients than controls: low educational level (37% vs. 31%), low income (32% vs. 24%), and unemployment (20% vs. 11%). Furthermore, a high SES score was less frequent in VTE patients than in matched controls (18% vs. 24%), whereas a low SES score was more frequent (22% vs. 13%) (Table 2). In addition, several comorbidities were more prevalent among VTE patients than among controls: surgery and/or trauma 3 months before the VTE/index date, and CCI score >2 (21% vs. 7%) (Table 1).
3.2 VTE risk by SES indicators

The ORs for VTE risk by SES indicators are shown in Figure 1. High educational level, high income, and high employment status were all associated with a decreased OR for VTE in analyses adjusted for age and sex (Figure 1). Further adjustment for comorbidities had a modest attenuating impact on the association between VTE and high educational level (OR 0.74; 95% CI 0.71–0.77), high income (OR 0.70; 95% CI 0.68–0.72), and high employment status (OR 0.66; 95% CI 0.64–0.68) (Figure 1, model 2). Additional adjustment for the confounding SES indicators further reduced the strength of the associations, but residual increments in ORs remained for all three exposures. When compared with low levels, the ORs for VTE by high educational level (OR 0.74; 95% CI 0.71–0.77), high income (OR 1 OR 0.92; 95% CI 0.89–0.96), and high employment status (OR 0.69; 95% CI 0.67–0.71) remained lowered after adjustments for comorbidities and SES indicators (Figure 1, model 3).

In the composite score model, a high SES score was associated with a lower OR for VTE in analyses adjusted for age and sex. Compared with persons with a low SES score (13% of the control population), individuals with a medium SES score (60% of the control population) had an OR of VTE of 0.71 (95% CI 0.69–0.73) while individuals with a high SES score (24% of the control population) had an OR for VTE of 0.61 (95% CI 0.59–0.63) after adjustments for potential confounders (Figure 1, Model 2).

Figures 2–4 show the unrestricted quadratic spline regression models for income, education, and SES score with adjustment for comorbidities. The OECD average income in Denmark for 2016 was approximately 355 000 DKK. We found that an annual income more than 600 000 DKK was protective against VTE (Figure 2). The corresponding curve with educational level for the age group 25–44 as the exposure variable indicated that an educational level above tertiary education reduced the risk of VTE (Figure 3). With SES score as exposure, the spline curves revealed a clear association between increased VTE risk and below average SES scores (Figure 4).

3.3 VTE risk according to age and sex

The association between VTE and the individual SES indicators, as well as the composite SES score, was strongest in the younger age groups, with the lowest ORs in the age group 35 to 44 years (Tables 3 and 4). ORs for VTE by education, employment status, and the composite

| COMORBITIES | VTE (n = 51 350) | Controls (n = 256 750) |
|-------------|----------------|------------------------|
| Pulmonary embolism | 17 617 (34.3) | 88 085 (34.3) |
| Deep vein thrombosis | 33 733 (67.5) | 168 665 (65.7) |
| Sex (% men) | 26 962 (52.5) | 134 810 (52.5) |
| Comorbidities | | |
| High-risk cancer before VTE/index date | 2754 (5.4) | 1446 (0.6) |
| Low-risk cancer before VTE/index date | 3668 (7.1) | 7571 (2.9) |
| Coronary heart disease | 4641 (9.0) | 12 398 (4.8) |
| Diabetes | 3578 (7.0) | 11 273 (4.4) |
| Chronic obstructive pulmonary disease | 4000 (7.8) | 9228 (3.6) |
| Obesity | 3816 (7.4) | 7625 (3.0) |
| Stroke | 1353 (2.6) | 3328 (1.3) |
| Moderate to severe renal disease | 1206 (2.3) | 1747 (0.7) |
| Surgery 3 months before VTE/index date | 7473 (14.6) | 6511 (2.5) |
| Trauma/fracture 3 months before VTE/index date | 2299 (4.5) | 1711 (0.7) |
| Mental disorders | 6892 (13.4) | 14 491 (5.6) |
| Charlson comorbidity index | | |
| CCI score: 0 | 33 287 (64.8) | 215 092 (83.8) |
| CCI score: 1 | 7151 (13.9) | 23 816 (9.3) |
| CCI score: ≥2 | 10 912 (21.3) | 17 842 (6.9) |
| CCI score: 0b | 43 617 (84.9) | 240 096 (93.5) |
| CCI score: 1b | 5940 (11.6) | 14 074 (5.5) |
| CCI score: ≥2b | 1793 (3.5) | 2580 (1.0) |

Note: Values are numbers, with percentages in brackets.
Abbreviations: CCI, Charlson Comorbidity Index; VTE, venous thromboembolism.
\(^a\)Categorized according to 5-year mortality as high-risk cancer (\(>70\%\)) and low-risk cancer (\(\leq70\%\)).
\(^b\)Modified CCI excluding International Classification of Diseases codes used in the covariate definition.
SES score were lower overall in women than in men (Tables S5-S7). However, subgroup analysis indicated that the associations were stronger in men in the two youngest age groups and stronger in women in the two oldest age groups (Tables S5-S7).

3.4 | Subgroup and sensitivity analysis

Subgroup analysis showed that the ORs for DVT by the high levels of the individual SES indicators, including the composite SES score, were somewhat lower than ORs for PE (Table 5). In analysis restricted on patients with CCI score of zero, the ORs for VTE by high SES levels were slightly attenuated; however, the association remained significant (Table S8). When we assessed SES indicators 5 years before the VTE event/index date, ORs for VTE were essentially the same as in the primary analysis, except for employment status in which the ORs were somewhat lower than 1 year before the VTE event. (Table 6).

4 | DISCUSSION

In this large population-based case-control study, we found that high levels of individual SES indicators (education, income, and employment status), as well as a high composite SES score, were associated with lower odds of VTE even after adjustment for comorbid conditions. Further adjustment for confounding SES indicators, showed that each indicator had an independent effect on VTE risk. Given previous findings underscoring the multidimensional aspect of SES, the independent effects of individual SES indicators on the VTE risk encouraged us to explore whether a composite SES score would improve discrimination between subjects at low and high risk of VTE. We found that the OR for the composite SES score (high vs. low) was consistently lower than the ORs for the individual indicators.

Previous studies have reported divergent results for the association between individual SES indicators and VTE. A Swedish cohort of 6958 men aged 45–55 years with 28 years of follow-up found that self-reported high socioeconomic occupational status measured at index date was associated with lower risk of PE, whereas no association was found with DVT. A Danish cohort (Copenhagen City Health study) of men and women >20 years of age, with median follow-up of 19.5 years, found that medium vs. low household income was associated with reduced risk of VTE, but did not observe an association between education level and VTE risk. A cohort study of Swedish adults (>20 years) followed for 17 years found that those with high educational level and high-status occupations measured at index date had
lower risk of VTE, whereas no association was found between income and VTE risk. Another Swedish cohort of individuals >25 years of age at inclusion, with 13 years of follow-up, showed that low household income, single marital status, and low educational level measured at index date were associated with increased VTE risk. However, there was no adjustment for comorbidities in the analyses.
We found that education, income, and employment status were all associated with VTE. Education, income, and employment are correlated indicators as education often precedes and influences employment level, which in turn affects income. To capture the complexity of influences and the temporal relation among indicators, we applied a composite SES score to measure the association between SES and VTE risk. We found a positive linear relation between the SES score and VTE risk, and the OR for VTE in those with a high SES score was lower than the ORs in those with high levels of any of the individual SES indicators. This may suggest the SES score as a superior tool over individual SES indicators when assessing the risk of VTE.

In modern Western societies, work-related indicators fluctuate over time, especially during life stages such as early and midlife/mature adulthood, for instance because of transition from student to employee or advances in employment and income. The optimal lag time between assessments of SES indicators and disease outcomes, along with the question of reverse causation when good health leads a subsequent high SES, remains subjects of debate. In our study, we assessed SES indicators among individuals of working age (25–65 years) 1 year before the VTE event. To ensure that our results were not influenced substantially by recent changes in SES or health status, we performed sensitivity analyses restricted to persons without comorbidities before the index date. We also performed sensitivity analyses...
## Table 3

Crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) for venous thromboembolism (VTE) according to education, income, and employment status

|                          | Model 1 OR (95% CI) | Model 2 OR (95% CI) | Model 3 OR (95% CI) |
|--------------------------|---------------------|---------------------|---------------------|
| **Education**            |                     |                     |                     |
| Medium vs. low           |                     |                     |                     |
| Overall                  | 0.76 (0.74–0.78)    | 0.83 (0.81–0.85)    | 0.83 (0.81–0.85)    |
| Age 25–34                | 0.66 (0.62–0.70)    | 0.73 (0.68–0.78)    | 0.73 (0.68–0.78)    |
| Age 34–44                | 0.63 (0.60–0.66)    | 0.71 (0.67–0.75)    | 0.71 (0.67–0.75)    |
| Age 45–54                | 0.74 (0.71–0.77)    | 0.82 (0.79–0.86)    | 0.82 (0.79–0.86)    |
| Age 55–65                | 0.88 (0.86–0.92)    | 0.95 (0.91–0.98)    | 0.95 (0.91–0.98)    |
| High vs. low             |                     |                     |                     |
| Overall                  | 0.62 (0.60–0.64)    | 0.74 (0.71–0.77)    | 0.74 (0.71–0.77)    |
| Age 25–34                | 0.60 (0.54–0.66)    | 0.76 (0.68–0.84)    | 0.76 (0.68–0.84)    |
| Age 34–44                | 0.43 (0.40–0.48)    | 0.55 (0.50–0.61)    | 0.55 (0.50–0.61)    |
| Age 45–54                | 0.56 (0.52–0.61)    | 0.70 (0.64–0.76)    | 0.70 (0.64–0.76)    |
| Age 55–65                | 0.73 (0.69–0.76)    | 0.84 (0.80–0.88)    | 0.84 (0.80–0.88)    |
| **Income**               |                     |                     |                     |
| Medium vs. low           |                     |                     |                     |
| Overall                  | 0.67 (0.66–0.69)    | 0.79 (0.77–0.81)    | 0.95 (0.93–0.98)    |
| Age 25–34                | 0.69 (0.65–0.74)    | 0.73 (0.69–0.78)    | 0.96 (0.89–1.05)    |
| Age 34–44                | 0.54 (0.51–0.57)    | 0.65 (0.61–0.69)    | 0.86 (0.80–0.93)    |
| Age 45–54                | 0.63 (0.60–0.66)    | 0.79 (0.75–0.83)    | 0.97 (0.91–1.03)    |
| Age 55–65                | 0.76 (0.73–0.79)    | 0.88 (0.85–0.92)    | 1.01 (0.96–1.05)    |
| High vs. low             |                     |                     |                     |
| Overall                  | 0.54 (0.52–0.56)    | 0.70 (0.68–0.72)    | 0.92 (0.89–0.96)    |
| Age 25–34                | 0.57 (0.51–0.63)    | 0.67 (0.60–0.75)    | 0.92 (0.81–1.05)    |
| Age 34–44                | 0.41 (0.39–0.44)    | 0.55 (0.51–0.59)    | 0.81 (0.74–0.89)    |
| Age 45–54                | 0.49 (0.47–0.52)    | 0.68 (0.64–0.72)    | 0.90 (0.84–0.97)    |
| Age 55–65                | 0.63 (0.61–0.66)    | 0.81 (0.78–0.85)    | 1.01 (0.95–1.07)    |
| **Employment status**    |                     |                     |                     |
| Medium vs. low           |                     |                     |                     |
| Overall                  | 0.76 (0.74–0.79)    | 0.95 (0.91–0.98)    | 0.96 (0.92–0.99)    |
| Age 25–34                | 0.89 (0.79–0.99)    | 0.99 (0.88–1.12)    | 0.98 (0.87–1.11)    |
| Age 34–44                | 0.90 (0.83–0.98)    | 1.03 (0.94–1.13)    | 1.05 (0.95–1.15)    |
| Age 45–54                | 0.84 (0.78–0.90)    | 0.92 (0.85–1.00)    | 0.93 (0.86–1.01)    |
| Age 55–65                | 0.68 (0.65–0.71)    | 0.87 (0.83–0.91)    | 0.87 (0.83–0.92)    |
| High vs. low             |                     |                     |                     |
| Overall                  | 0.46 (0.45–0.48)    | 0.66 (0.64–0.68)    | 0.69 (0.67–0.71)    |
| Age 25–34                | 0.48 (0.44–0.53)    | 0.62 (0.55–0.69)    | 0.66 (0.59–0.74)    |
| Age 34–44                | 0.40 (0.38–0.43)    | 0.57 (0.53–0.62)    | 0.63 (0.58–0.68)    |
| Age 45–54                | 0.45 (0.43–0.48)    | 0.65 (0.61–0.68)    | 0.67 (0.63–0.71)    |
| Age 55–65                | 0.51 (0.49–0.53)    | 0.71 (0.68–0.74)    | 0.72 (0.69–0.76)    |

**Note:**
- Model 1: Crude model controlled for matching variables (age, sex) by study design.
- Model 2: Adjusted model controlled for matching variables (age, sex) by study design and adjusted for obesity, cancer, coronary heart disease (including atrial fibrillation and heart failure), diabetes, stroke, chronic obstructive pulmonary disorder, acute kidney failure, chronic kidney disease, mental diseases, surgery 3 months before the VTE/index date and Charlson Comorbidity Index score, excluding comorbidities already adjusted for.
- Model 3: Adjusted model controlled for matching variables (age, sex) by study design and adjusted for model 2 and socioeconomic status indicators.
### TABLE 4 Crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) for venous thromboembolism (VTE) according to SES score

|          | Model 1 OR (95% CI) | Model 2 OR (95% CI) |
|----------|---------------------|---------------------|
| Low      | 1.00 (ref)          | 1.00 (ref)          |
| Medium vs. low |                   |                     |
| Overall  | 0.55 (0.54–0.56)    | 0.71 (0.69–0.73)    |
| Age 25–34| 0.48 (0.45–0.52)    | 0.58 (0.54–0.63)    |
| Age 34–44| 0.41 (0.39–0.44)    | 0.55 (0.51–0.59)    |
| Age 45–54| 0.51 (0.48–0.53)    | 0.69 (0.65–0.73)    |
| Age 55–65| 0.65 (0.63–0.68)    | 0.82 (0.79–0.86)    |
| High vs. low |                   |                     |
| Overall  | 0.43 (0.41–0.44)    | 0.61 (0.59–0.63)    |
| Age 25–34| 0.42 (0.37–0.46)    | 0.56 (0.49–0.62)    |
| Age 34–44| 0.30 (0.27–0.32)    | 0.44 (0.40–0.48)    |
| Age 55–65| 0.38 (0.36–0.41)    | 0.58 (0.54–0.62)    |
| Age 45–54| 0.52 (0.50–0.55)    | 0.73 (0.69–0.76)    |

Note: Model 1: Crude model controlled for matching variables (age, sex) by study design. Model 2: Adjusted model controlled for matching variables (age, sex) by study design and adjusted for obesity, cancer, coronary heart disease (including atrial fibrillation and heart failure), diabetes, stroke, chronic obstructive pulmonary disorder, acute kidney failure, chronic kidney disease, mental diseases, surgery 3 months before the VTE/index date and Charlson Comorbidity Index score, excluding comorbidities already adjusted for.

### TABLE 5 Crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) for pulmonary embolism (PE) and deep vein thrombosis (DVT) according to education, income, employment, and SES score

|          | PE (OR 95% CI) | DVT (OR 95% CI) |
|----------|---------------|----------------|
|          | Low           | Medium         | High           | Low           | Medium         | High           |
| Education| Model 1       | 1.00 (ref)     | 0.80 (0.77–0.83) | 0.67 (0.63–0.71) | 1.00 (ref)     | 0.74 (0.72–0.76) | 0.59 (0.57–0.62) |
|          | Model 2       | 1.00 (ref)     | 0.87 (0.84–0.91) | 0.79 (0.75–0.84) | 1.00 (ref)     | 0.81 (0.79–0.83) | 0.71 (0.68–0.74) |
|          | Model 3       | 1.00 (ref)     | 0.87 (0.84–0.91) | 0.79 (0.75–0.84) | 1.00 (ref)     | 0.81 (0.79–0.83) | 0.71 (0.68–0.74) |
| Income   | Model 1       | 1.00 (ref)     | 0.70 (0.67–0.73) | 0.56 (0.54–0.59) | 1.00 (ref)     | 0.66 (0.64–0.68) | 0.53 (0.51–0.55) |
|          | Model 2       | 1.00 (ref)     | 0.81 (0.78–0.85) | 0.73 (0.69–0.77) | 1.00 (ref)     | 0.78 (0.75–0.80) | 0.69 (0.66–0.71) |
|          | Model 3       | 1.00 (ref)     | 0.99 (0.94–1.04) | 0.96 (0.90–1.03) | 1.00 (ref)     | 0.94 (0.90–0.97) | 0.90 (0.86–0.95) |
| Employment status | Model 1 | 1.00 (ref) | 0.76 (0.72–0.80) | 0.46 (0.44–0.48) | 1.00 (ref) | 0.76 (0.73–0.80) | 0.47 (0.45–0.48) |
|          | Model 2       | 1.00 (ref)     | 0.94 (0.89–1.00) | 0.66 (0.62–0.69) | 1.00 (ref)     | 0.94 (0.90–0.99) | 0.66 (0.64–0.69) |
|          | Model 3       | 1.00 (ref)     | 0.95 (0.90–1.01) | 0.67 (0.64–0.71) | 1.00 (ref)     | 0.96 (0.92–1.00) | 0.70 (0.67–0.72) |
| SES score | Model 1       | 1.00 (ref)     | 0.57 (0.55–0.60) | 0.45 (0.42–0.47) | 1.00 (ref)     | 0.54 (0.52–0.56) | 0.42 (0.40–0.43) |
|          | Model 2       | 1.00 (ref)     | 0.74 (0.70–0.77) | 0.64 (0.60–0.68) | 1.00 (ref)     | 0.69 (0.67–0.72) | 0.59 (0.57–0.62) |

Note: Model 1: Crude model controlled for matching variables by study design. Model 2: Adjusted model controlled for matching variables by study design and adjusted for obesity, cancer, coronary heart disease (including atrial fibrillation and heart failure), diabetes, stroke, chronic obstructive pulmonary disorder, acute kidney failure, chronic kidney disease, mental diseases, surgery 3 months before the VTE/index date and Charlson Comorbidity Index score, excluding comorbidities already adjusted for. Model 3: Adjusted model controlled for matching variables by study design and adjusted for Model 2 and SES indicators.

With SES score as the exposure, there were no additional SES variables; therefore, models 2 and 3 are identical and model 3 is not included in the table.
Our study has several strengths and some limitations. We conducted the study in a setting that provides government-funded educational and health care services free of charge to all citizens, thus preventing selection and referral bias. We used a large sample from the general working age population with highly accurate and validated data for exposures, outcomes, and comorbidities, which allowed a detailed interpretation of the association between SES and VTE. In addition, we were able to perform repeated measurements of SES close to the VTE/index date, thereby avoiding misclassification and potential attenuation of associations. Unfortunately, we were unable to measure modifiable risk factors such as body mass index, physical activity, or diet that could act as confounders or intermediate variables for the association between SES and VTE. We also did not have access to relevant SES indicators such as occupational category, household income or length of employment. Although we found that the composite SES score might provide a common and improved measure of SES for assessment of VTE risk, the score has not been validated.

In conclusion, we found that high SES was associated with decreased VTE risk even after accounting for comorbidities. As compared with measuring individual SES indicators (education, income, and employment), we found that a composite SES score improved the risk assessment of VTE. Our findings may help healthcare providers improve preventive strategies diminishing the burden of VTE on public health and healthcare systems.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Helle Jørgensen, Erzsébet Horváth-Puhó, Kristina Laugesen, Sigrid K. Brækkan, John-Bjarne Hansen, and Henrik T. Sørensen contributed to the planning and design of the study and to the analysis and interpretation of the data. Helle Jørgensen drafted the manuscript. All authors critically revised the manuscript for intellectual content and approved the final version before submission.

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REFERENCES

1. White RH. The epidemiology of venous thromboembolism. Circulation. 2003;107(23 Suppl 1):I4-8.
2. Raskob GE, Angchaisukiri P, Blanco AN, et al. Thrombosis: a major contributor to global disease burden. Arterioscler Thromb Vasc Biol. 2014;34(11):2363-2371.
3. de Mestral C, Stringhini S. Socioeconomic status and cardiovascular disease: an update. Curr Cardiol Rep. 2017;19(11):115.
4. Addo J, Ayerbe L, Mohan KM, et al. Socioeconomic status and stroke: an updated review. Stroke. 2012;43(4):1186-1191.
11. Kort D, van Rein N, van der Meer FJM, et al. Relationship between physical activity and venous thromboembolism: results from the Copenhagen City Heart Study. *Circulation*. 2010;121(17):1896-1903.

12. Zoller B, Li X, Sundquist J, Sundquist K. Socioeconomic and occupational risk factors for venous thromboembolism in Sweden: a nationwide epidemiological study. *Thromb Res*. 2012;129(5):577-582.

13. Stringhini S, Carmeli C, Jokela M, et al. Socioeconomic status and cardiovascular outcomes for different approaches. *Assessment*. 2002;9(2):145-155.

14. Schmidt M, Schmidt SAJ, Adelborg K, et al. The Danish health care system and epidemiological research: from health care contacts to database records. *Clin Epidemiol*. 2019;11:563-591.

15. Sogaard KK, Schmidt M, Pedersen L, Horvath-Puho E, Sorensen HT. 30-year mortality after venous thromboembolism: a population-based cohort study. *Circulation*. 2014;130(10):829-836.

16. Adelborg K, Corraini P, Darvalis B, et al. Risk of thrombembolic and bleeding outcomes following hematological cancers: a Danish population-based cohort study. *J Thromb Haemost*. 2019;17(8):1305-1318.

17. Heide-Jørgensen U, Adelborg K, Kahlert J, Sorensen HT, Pedersen L. Sampling strategies for selecting general population comparison cohorts. *Clin Epidemiol*. 2018;10:1325-1337.

18. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383.

19. Darin-Mattsson A, Fors S, Kärholt I. Different indicators of socioeconomic status and their relative importance as determinants of health in old age. *Int J Equity Health*. 2017;16(1):173.

20. Geyer S, Hemström Ö, Peter R, Vägerö D. Education, income, and occupational class cannot be used interchangeably in social epidemiology. Empirical evidence against a common practice. *J Epidemiol Community Health*. 2006;60(9):804-810.

21. Braveman P, Gottlieb L. The social determinants of health: it’s time to consider the causes of the causes. *Public Health Rep*. 2014;129:19-31.

22. Cirino PT, Chin CE, Sevick RA, Wolf M, Lovett M, Morris RD. Measuring socioeconomic status: reliability and preliminary validity for different approaches. *Assessment*. 2002;9(2):145-155.

23. Galobardes B, Lynch J, Smith GD. Measuring socioeconomic position in health research. *Br Med Bull*. 2007;81-82:21-37.

24. Mackenbach JP. *Health inequalities: Persistence and change in European welfare states*. Oxford University Press; 2019:252.

25. Pampel FC, Krueger PM, Denney PD, Nyden JT. Socioeconomic disparities in health behaviors. *Annu Rev Sociol*. 2010;36:349-370.

26. Shavers VL. Measurement of socioeconomic status in health disparities research. *J Natl Med Assoc*. 2007;99(9):1013-1023.

27. Levesque JF, Harris MF, Russell G. Patient-centred access to health care: conceptualising access at the interface of health systems and populations. *Int J Equity Health*. 2013;12:18.

28. Havranek EP, Mujahid MS, Barr DA, et al. Social determinants of risk and outcomes for cardiovascular disease. *Circulation*. 2015;132(9):873-898.

29. Sobal J, Stunkard AJ. Socioeconomic status and obesity: a review of the literature. *Psychol Bull*. 1989;105(2):260-275.

30. Stalsberg R, Pedersen AV. Are differences in physical activity across socioeconomic groups associated with choice of physical activity variables to report? *Int J Environ Res Public Health*. 2018;15(5):922.

31. Evensen LH, Braekkan SK, Hansen JB. Regular physical activity and risk of venous thromboembolism. *Semin Thromb Hemost*. 2018;44(8):765-779.

32. von Känel R, Mills PJ, Fainman C, Dimsdale JE. Effects of psychological stress and psychiatric disorders on blood coagulation and fibrinolysis: a biobehavioral pathway to coronary artery disease? *Psychosom Med*. 2001;63(4):531-544.

33. Ramsay S, Lowe GDO, Whincup PH, Rumley A, Morris RW, Wannamethee SG. Relationships of inflammatory and haemostatic markers with social class: results from a population-based study of older men. *Atherosclerosis*. 2008;197(2):654-661.

34. Kumari M, Marmot M, Brunner E. Social determinants of venous thromboembolism. *J Thromb Haemost*. 2000;20(7):1842-1847.

35. Sundbøll J, Adelborg K, Munch T, et al. Positive predictive value of cardiovascular diagnoses in the Danish National Patient Registry: a validation study. *BMJ open*. 2016;6(11):e012832.

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