JAMA | Original Investigation

# Association of Lumbar Puncture With Spinal Hematoma in Patients With and Without Coagulopathy

Jacob Bodilsen, MD; Theis Mariager, BMSc; Hannah Holm Vestergaard, MD; Mikkel Højberg Christiansen, MD; Mikkel Kunwald, MD; Hans Rudolf Lüttichau, MD, PhD; Bo Traberg Kristensen, MD; Carsten Reidies Bjarkam, MD, PhD, DMSc; Henrik Nielsen, MD, DMSc

**IMPORTANCE** Coagulopathy may deter physicians from performing a lumbar puncture.

**OBJECTIVE** To determine the risk of spinal hematoma after lumbar puncture in patients with and without coagulopathy.

**DESIGN, SETTING, AND PARTICIPANTS** Danish nationwide, population-based cohort study using medical registries to identify persons who underwent lumbar puncture and had cerebrospinal fluid analysis (January 1, 2008-December 31, 2018; followed up through October 30, 2019). Coagulopathy was defined as platelets lower than 150 × $10^9$/L, international normalized ratio (INR) greater than 1.4, or activated partial thromboplastin time (APTT) longer than 39 seconds.

**EXPOSURES** Coagulopathy at the time of lumbar puncture.

**MAIN OUTCOMES AND MEASURES** Thirty-day risk of spinal hematoma. Risks were provided as numbers and percentages with 95% CIs. Secondary analyses included risks of traumatic lumbar puncture (>300 × $10^6$ erythrocytes/L after excluding patients diagnosed with subarachnoid hemorrhage). Adjusted hazard rate ratios (HRs) were computed using Cox regression models.

**RESULTS** A total of 83 711 individual lumbar punctures were identified among 64 730 persons (51% female; median age, 43 years [interquartile range, 22-62 years]) at the time of the procedure. Thrombocytopenia was present in 7875 patients (9%), high INR levels in 1393 (2%), and prolonged APTT in 2604 (3%). Follow-up was complete for more than 99% of the study participants. Overall, spinal hematoma occurred within 30 days for 99 of 49 526 patients (0.20%; 95% CI, 0.16%-0.24%) without coagulopathy vs 24 of 10 371 patients (0.23%; 95% CI, 0.15%-0.34%) with coagulopathy. Independent risk factors for spinal hematoma were male sex (adjusted hazard ratio [HR], 1.72; 95% CI, 1.15-2.56), those aged 41 through 60 years (adjusted HR, 1.96; 95% CI, 1.01-3.81) and those aged 61 through 80 years (adjusted HR, 2.20; 95% CI, 1.12-4.33). Risks did not increase significantly according to overall severity of coagulopathy, in subgroup analyses of severity of coagulopathy by pediatric specialty or medical indication (infection, neurological condition, and hematological malignancy), nor by cumulative number of procedures. Traumatic lumbar punctures occurred more frequently among patients with INR levels of 1.5 to 2.0 (36.8%; 95% CI, 33.3%-40.4%), 2.1 to 2.5 (43.7%; 95% CI, 35.8%-51.8%), and 2.6 to 3.0 (41.9% 95% CI 30.5-53.9) vs those with normal INR (28.2%; 95% CI, 27.7%-28.75%). Traumatic spinal tap occurred more often in patients with an APTT of 40 to 60 seconds (26.3%; 95% CI, 24.2%-28.5%) vs those with normal APTT (21.3%; 95% CI, 20.6%-21.9%) yielding a risk difference of 5.1% (95% CI, 2.9%-7.2%).

**CONCLUSIONS AND RELEVANCE** In this Danish cohort study, risk of spinal hematoma following lumbar puncture was 0.20% among patients without coagulopathy and 0.23% among those with coagulopathy. Although these findings may inform decision-making about lumbar puncture by describing rates in this sample, the observed rates may reflect bias due to physicians selecting relatively low-risk patients for lumbar puncture.

*JAMA*. 2020;324(14):1419-1428. doi:10.1001/jama.2020.14895

Supplemental content

CME Quiz at jamacmelookup.com

**Author Affiliations:** Departments of Infectious Diseases, Aalborg University Hospital, Aalborg, Denmark (Bodilsen, Mariager, Vestergaard, Christiansen, Nielsen); Department of Neurosurgery, Aalborg University Hospital, Aalborg, Denmark (Kunwald, Bjarkam); Department of Pulmonary and Infectious Diseases, Herlev Gentofte Hospital, Copenhagen, Denmark (Lüttichau); Department of Neurology, Aalborg University Hospital, Aalborg, Denmark (Kristensen); Department of Clinical Medicine, Aalborg University Hospital, Aalborg, Denmark (Bjarkam, Nielsen).

**Corresponding Author:** Jacob Bodilsen, MD, Department of Infectious Diseases, Aalborg University Hospital, Mølleparkvej 4, 9000 Aalborg, Denmark (jacob.bodilsen@rn.dk).

Lumbar puncture is a commonly performed medical procedure that is crucial for the diagnosis and treatment of central nervous system (CNS) infections, neurological diseases, and certain types of cancer. Spinal hematoma may be caused by lumbar puncture and presents as severe back pain, radiculopathy, urinary incontinence, and inferior paraparesis.[1,2] How often this complication occurs remains unclear, but it has been an increasing concern for clinicians since the 1980s, especially among patients with coagulopathies.[1-9] This may result in deferral or omission of lumbar punctures and, as a consequence, delayed or even erroneous diagnosis and treatment of patients.[2] Studies addressing risks of spinal hematoma after lumbar puncture are scarce and restricted to selected patient groups of small to moderate sample sizes (eg, children[4,10,11] or adults[5,12] with hematological malignancies) or to case series,[3,6,8] so large-scale registry-based data are required for further clarification.[2,13]

Using nationwide and population-based medical registries, this study aimed to determine the risk of spinal hematoma following lumbar puncture in patients with and without coagulopathy in Denmark.

### Key Points

**Question** What is the risk of spinal hematoma after lumbar puncture in patients with coagulopathy?

**Findings** In this Danish registry-based cohort study that included 64 730 patients undergoing 83 711 individual lumbar punctures, the overall 30-day risk of spinal hematoma was 0.20% among patients without coagulopathy at the time of the procedure and 0.23% among patients with coagulopathy.

**Meaning** Although potentially limited by bias due to physicians selecting relatively low-risk patients for lumbar puncture, these findings provide estimates of the risk of spinal hematoma that may inform decision-making about lumbar puncture.

## Methods

### Ethics

The study was approved by the legal representatives of North Denmark Region (reference identification No.: 2018-45) and the Danish Board of Health (reference identification No.: 3-3013-2477/1). To ensure anonymity of patients and according to Danish data regulations, events that involved fewer than 5 individuals were censored from the Danish Registry of Causes of Death. Patient consent or approval from an ethics committee is not required for this type of study in Denmark.

### Setting and Study Population

In Denmark, health care is tax financed and free of charge at the point of delivery. At birth or immigration, a unique 10-digit civil registration number is assigned to all residents, which can be used for unambiguous linkage between medical and administrative registries at the individual level. The population of Denmark was 5 827 463 on January 1, 2019.[14]

This study was conducted by (1) using Danish national registries from January 1, 2008, through December 31, 2018 (follow-up through October 30, 2019) to examine the risk of spinal hematoma after lumbar puncture; (2) reviewing the 1998-2018 medical records of all patients with coagulopathy (platelets $<150 \times 10^9$/L, international normalized ratio [INR] >1.4, or activated partial thromboplastin time [APTT] >39 seconds) at the time of the lumbar puncture performed in the North Denmark Region; and (3) reviewing 1998-2018 medical records of all patients admitted with diagnosis codes suggestive of spinal hematoma at the departments of infectious diseases, neurology, or neurosurgery in the North Denmark Region.

First, the Danish Laboratory Database was accessed to identify all 2008-2018 lumbar punctures registered by the use of Nomenclature for Properties and Units (NPU) codes for cerebrospinal fluid (CSF) analyses (eTable 1 in the Supplement). After establishment in 2008, this registry has steadily expanded and now includes most major biochemical laboratories in Denmark since 2015, corresponding to approximately 80% of the population of Denmark.[15] Each lumbar puncture was individually numbered by grouping NPU codes according to the unique personal identifier of each Danish resident and the date of analysis. Thus, patients could only be categorized with 1 lumbar puncture per day, and the date of CSF analysis was considered the index date of each procedure. Traumatic spinal tap was defined as more than $300 \times 10^6$ erythrocytes/L of CSF after excluding patients diagnosed with subarachnoid hemorrhage because many departments of clinical biochemistry in Denmark report all CSF erythrocyte counts lower than this threshold as less than 300. The results of all blood samples that had been performed during the study period were also obtained from this registry. For each measurement of blood platelets, INR, or APTT, the most extreme value each day was included. Measurements of blood platelets, INR, or APTT within 1 day of a performance of a lumbar puncture were included for patients from whom these parameters were not sampled on the index date. Similarly, samples within a 5-day window were also included for patients without such measurements within the first day of the procedure.

The Danish National Patient Registry was used to detect spinal hematoma events, defined as first-time diagnosis codes for inferior paraparesis, medullary compression, or surgical removal of spinal hematoma after each lumbar puncture (eTable 2 in the Supplement).[16] This registry includes information on all somatic admissions in Denmark since 1977 as well as outpatient and emergency department contacts since 1995. Besides dates of admission and discharge, each hospital contact is assigned up to 20 diagnosis codes classified according to the World Health Organization's *International Classification of Diseases, Eighth Revision (ICD-8)* until 1993 when it was replaced by *ICD-10*. Surgical procedures were categorized by the Danish Classification of Surgical Procedures from 1977 to 1996 and by a Danish version of the Nordic Medico-Statistical Committee Classification of Surgical Procedures since then. To avoid misclassification of CSF samples obtained by methods other than lumbar puncture, cases were excluded if they had a procedure code for placement of an external ventricular drain

Table 1. Descriptive Characteristics and 30-Day Risks of Spinal Hematoma in 64 730 Individuals With a Total of 83 711 Lumbar Punctures

| | Danish National Laboratory Database 2008-2018 | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Baseline characteristics, No. (%) | | | 30-d risk of spinal hematoma | | | | |
| | No spinal hematoma | Spinal hematoma | SMD | No./total | % (95% CI) | Risk difference (95% CI) | Crude HR (95% CI)[a] | Adjusted HR (95% CI)[a] |
| No. of study participants | 83 568 | 143 | | 143/83 711[b] | 0.17 (0.14 to 0.20) | | | |
| Sex | | | | | | | | |
| Female | 42 716 (51) | 54 (38) | 0.27 | 54/42 770 | 0.13 (0.09 to 0.16) | 1 [Reference] | 1 [Reference] | 1 [Reference] |
| Male | 40 852 (49) | 89 (62) | 0.27 | 89/40 941 | 0.22 (0.17 to 0.27) | 0.09 (0.03 to 0.15) | 1.89 (1.27 to 2.80) | 1.72 (1.15 to 2.56) |
| Age, y | | | | | | | | |
| 0-20 | 19 565 (23) | 18 (13) | 0.28 | 18/19 583 | 0.09 (0.05 to 0.15) | 1 [Reference] | 1 [Reference] | 1 [Reference] |
| 21-40 | 20 133 (24) | 28 (20) | 0.11 | 28/20 161 | 0.14 (0.09 to 0.20) | 0.05 (−0.02 to 0.11) | 0.91 (0.42 to 1.94) | 0.94 (0.44 to 2.02) |
| 41-60 | 21 444 (26) | 41 (29) | 0.07 | 41/21 485 | 0.19 (0.14 to 0.26) | 0.10 (0.03 to 0.17) | 2.13 (1.11 to 4.08) | 1.96 (1.01 to 3.81) |
| 61-80 | 20 089 (24) | 54 (38) | 0.30 | 54/20 143 | 0.27 (0.20 to 0.35) | 0.18 (0.09 to 0.26) | 2.59 (1.36 to 4.94) | 2.20 (1.12 to 4.33) |
| ≥81 | 2337 (3) | 2 (1) | 0.10 | 2/2339 | 0.09 (0.01 to 0.31) | −0.01 (−0.13 to 0.12) | 1.06 (0.24 to 4.74) | 0.93 (0.20 to 4.23) |
| Charlson Comorbidity Index[c] | | | | | | | | |
| Low | 44 006 (53) | 68 (48) | 0.10 | 68/44 074 | 0.15 (0.12 to 0.20) | 1 [Reference] | 1 [Reference] | 1 [Reference] |
| Moderate | 28 827 (35) | 42 (29) | 0.11 | 42/28 869 | 0.15 (0.10 to 0.20) | −0.01 (−0.07 to 0.05) | 1.34 (0.87 to 2.08) | 1.09 (0.69 to 1.72) |
| High | 10 735 (13) | 33 (23) | 0.27 | 33/10 768 | 0.31 (0.21 to 0.43) | 0.15 (0.04 to 0.26) | 2.31 (1.39 to 3.84) | 1.62 (0.94 to 2.79) |
| Any coagulopathy[d] | | | | | | | | |
| No | 49 427 (59) | 99 (69) | 0.21 | 99/49 526 | 0.20 (0.16 to 0.24) | 1 [Reference] | 1 [Reference] | 1 [Reference] |
| Yes | 10 347 (12) | 24 (17) | 0.12 | 24/10 371 | 0.23 (0.15 to 0.34) | 0.03 (−0.07 to 0.13) | 0.91 (0.48 to 1.71) | 0.73 (0.38 to 1.38) |
| No measurement | 23 794 (28) | 20 (14) | 0.36 | 20/23 814 | 0.08 (0.05 to 0.13) | −0.12 (to −0.06 to −0.17) | 0.39 (0.23 to 0.66) | 0.35 (0.21 to 0.61) |

Abbreviations: HR, hazard ratio; SMD, standardized mean difference.

[a] HR analyses are restricted to first-time lumbar punctures only (ie, 64 730) and adjusted for age, sex, and Charlson Comorbidity Index scores.

[b] Seven of the 143 patients diagnosed with spinal hematoma died within 30 days after lumbar puncture.

[c] The score ranges from 0 to 29 and predicts 1-year mortality based on a broad range of 19 medical conditions. A low score (0) indicates a low risk of death and a high score suggests an increased risk of death (≥3).

[d] Assessed by either platelet count lower than 150 × $10^9$/L, international normalized ratio higher than 1.4, activated partial thromboplastin time longer than 39 seconds, or a combination of these parameters.

within 14 days before the index date. The Danish National Patient Registry was also used to compute the Charlson Comorbidity Index (CCI) scores of all patients before the index date.

The Danish Civil Registration System was accessed to obtain information on all-cause mortality and emigration of study participants.[17] This registry was established in 1968 and records data on vital and migration status of all Danish residents on a daily basis.

The Danish Registry of Causes of Death was searched for fatalities ascribed to spinal hematoma as the underlying or contributory causes of death among study participants (eTable 2 in the Supplement).[18] Established in 1875, this registry contains data on all death certificates issued in Denmark. Since 2007, the cause of death has been categorized according to *ICD-10* diagnosis codes and submitted electronically by the physician providing care for the patient at the time of death.

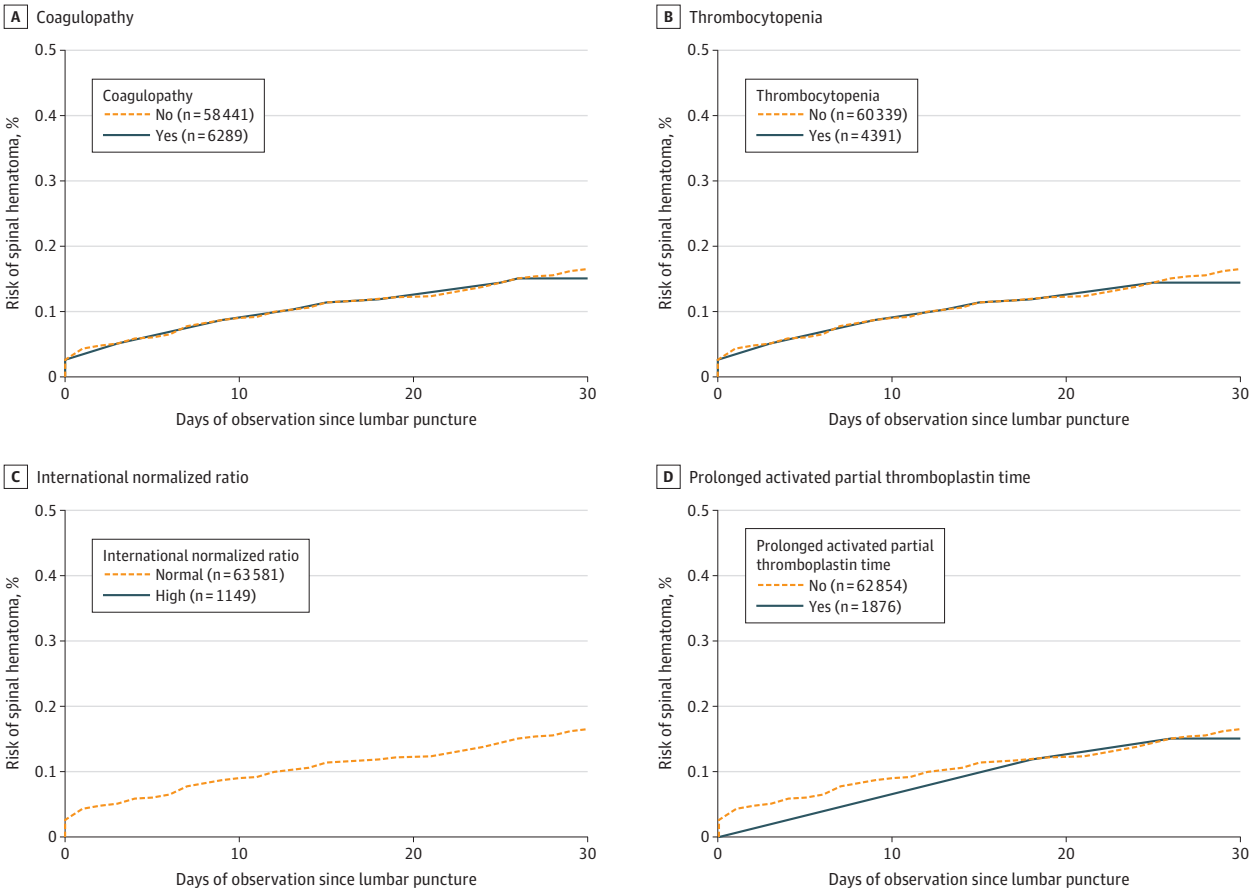
Second, to address potential limitations in identifying cases of spinal hematoma in health care registries, the medical records of all patients with coagulopathy at the time of the procedure in North Denmark Region from 1998 through 2018 were reviewed. All individual lumbar punctures were identified by NPU codes for CSF analyses in the database of the Department of the Clinical Biochemistry at Aalborg University Hospital (eTable 1 in the Supplement), which contains the biochemical results of every resident within the North Denmark Region (n = 589 148 in 2018[14]) (Table1). Besides the occurrence of subsequent spinal hematoma, use of antithrombotic or anticoagulant drugs, reversal of coagulopathy, and the medical indication for lumbar puncture were noted as well as the experience and medical specialty of the physician.

Third, the medical files of all patients with diagnosis and surgical procedure codes suggestive of spinal hematoma admitted at the departments of neurosurgery, neurology, or infectious diseases in the North Denmark Region (1998-2018) were also reviewed to decrease the risk of missed cases caused by lumbar puncture (eTable 3 in the Supplement).

## Outcomes

The primary outcome was 30-day risk of first-time spinal hematoma in patients with and without coagulopathy stratified by different levels of thrombocytopenia, high INR levels, and prolonged APTT at time of the lumbar puncture. Prespecified subgroup analysis included risks by medical indication (infection vs neurological condition vs hematological cancer), pediatric specialty, and cumulative number of procedures. Secondary outcomes consisted of the overall cumulative incidence

Figure. Cumulative Incidence of Spinal Hematoma During 30 Days After First-time Lumbar Puncture of 64 730 Individuals




Thirty-day follow-up was complete for more than 99% of all individuals (eFigure 1 in the Supplement). There were no spinal hematomas among patients with a high international normalized ratio at first-time lumbar puncture.

of spinal hematoma after lumbar puncture and 30-day mortality rates. Because traumatic spinal tap is considered a proxy for serious hemorrhagic complications, supplementary analyses were repeated using this variable as the outcome measure after excluding patients diagnosed with subarachnoid hemorrhage within 14 days of their lumbar puncture.[6,7]

## Statistical Analyses

All patients were observed from the index date (date of lumbar puncture) until the date of death, spinal hematoma, loss to follow-up, emigration, or October 30, 2019, whichever came first. Risks were described by numbers and percentages with 95% CIs using the binomial exact method and continuous variables by medians with interquartile ranges (IQRs). Covariate balances were examined using standardized mean differences (SMDs). Risk differences with 95% CIs were also computed for the primary outcome. Missing data for platelets, INR, and APTT were considered unlikely to fulfill the required missing-at-random assumption for multiple imputation due to confounding by indication of obtaining such blood tests at time of the procedure. Thus, risk analyses associated with different levels of thrombocytopenia, high INR, or prolonged APTT only included patients for whom these parameters were available at time of the procedure.

Cox regression was used to compute cause-specific hazard rate ratios (adjusted HRs) of first-time diagnosis of spinal hematoma within 30 days as well as 30-day mortality rate ratios (RRs) for patients with and without coagulopathy at the time of the first lumbar puncture. Adjusted analyses were controlled for age group (0-20, 21-40, 41-60, 61-80, ≥81 years), sex, and CCI scores (0, 1-2, ≥3).[1,7] To assess whether the association with the severity of each coagulopathy differed by age group, sex, or CCI scores, an interaction term was included in regression models and analyzed using the Wald test. The proportional hazards assumption was confirmed by inspection of log(−[log{survival function}]) against time for all exposure variables. Using the stcompet command in Stata, a cumulative incidence curve of the first-time diagnosis of spinal hematoma in all patients was constructed taking death, emigration, and loss to follow-up into account as competing risks.[19] A 2-sided $P$ <. 05 was considered statistically significant.

Stata MP version 16 (StataCorp) was used for all statistical analyses.

Table 2. Thirty-Day Risks of Spinal Hematoma According to Type and Severity of Coagulopathy Following 83 711 Lumbar Punctures in 64 730 Individuals

| | Danish National Laboratory Database 2008-2018, 30-d risk of spinal hematoma | | | | |
|---|---|---|---|---|---|
| | No./total | % (95% CI) | Risk difference (95% CI) | Crude HR (95% CI)[a] | Adjusted HR (95% CI)[a] |
| Blood platelets, $10^9$/L | | | | | |
| ≥151 | 103/51 132 | 0.20 (0.16 to 0.24) | 1 [Reference] | 1 [Reference] | 1 [Reference] |
| 101-150 | 13/3914 | 0.33 (0.18 to 0.57) | 0.13 (−0.05 to 0.32) | 1.82 (0.91 to 3.62) | 1.47 (0.73 to 2.94)[b] |
| 51-100 | 4/2065 | 0.19 (0.05 to 0.50) | −0.01 (0.20 to 0.19) | | |
| 31-50 | 1/789 | 0.13 (0.00 to 0.70) | −0.07 (0.33 to 0.18) | | |
| 11-30 | 2/886 | 0.23 (0.03 to 0.81) | 0.02 (0.29 to 0.34) | 1.80 (0.25 to 12.9) | 1.56 (0.22 to 11.3)[b] |
| 0-10 | 0/221 | 0 (0.00 to 1.66) | | | |
| No measurement | 20/24 704 | 0.08 (0.05 to 0.13) | −0.12 (−0.07 to −0.17) | 0.38 (0.22 to 0.65) | 0.35 (0.20 to 0.60) |
| INR | | | | | |
| 0-1.4 | 106/43 771 | 0.24 (0.20 to 0.29) | 1 [Reference] | 1 [Reference] | 1 [Reference] |
| 1.5-2.0 | 1/957 | 0.10 (0.00 to 0.58) | −0.14 (−0.35 to 0.07) | | |
| 2.1-2.5 | 0/224 | 0 (0.00 to 1.63) | | | |
| 2.6-3.0 | 0/100 | 0 (0.00 to 3.62) | | | |
| 3.1-4.0 | 0/61 | 0 (0.00 to 5.87) | | | |
| ≥4.1 | 0/51 | 0 (0.00 to 6.98) | | | |
| No measurement | 36/38 547 | 0.09 (0.07 to 0.13) | −0.15 (−0.09 to −0.20) | 0.37 (0.24 to 0.58) | 0.38 (0.24 to 0.59) |
| APTT (s) | | | | | |
| 0-39 | 59/19 561 | 0.30 (0.23 to 0.39) | 1 [Reference] | 1 [Reference] | 1 [Reference] |
| 40-60 | 5/2282 | 0.22 (0.07 to 0.51) | −0.08 (0.29 to 0.12) | 0.45 (0.11 to 1.86) | 0.39 (0.09 to 1.62)[c] |
| ≥61 | 0/322 | 0 (0.00 to 1.14) | | | |
| No measurement | 79/61 546 | 0.13 (0.10 to 0.16) | −0.17 (−0.09 to −0.26) | 0.45 (0.30 to 0.67) | 0.45 (0.30 to 0.67) |

Abbreviations: APTT, activated partial thromboplastin time; HR, hazard ratio; INR, international normalized ratio.

[a] HR analyses are restricted to first-time lumbar punctures only (ie, 64 730) and adjusted for age, sex and Charlson Comorbidity Index scores. Few or no events precluded computation of HRs for some strata.

[b] $P$ = .24 for interaction with age group, $P$ = .10 for interaction with sex, and $P$ = .95 for interaction with Charlson Comorbidity Index score.

[c] $P$ = .55 for interaction with age group, $P$ = .71 for interaction with sex, and $P$ = .44 for interaction with Charlson Comorbidity Index score.

## Results

Using medical registries, 83 711 individual lumbar punctures were identified among 64 730 study participants (eFigure 1 in the Supplement). The median age at the time of the procedure was 43 years (IQR, 22-62 years) and 51% were women. Blood platelets were sampled within 5 days of the lumbar puncture among 70% of cases; the INR, among 54%; and APTT, among 26% with the large majority of measurements within a 1-day window of the index date (eTables 4 and 5 in the Supplement). The median number of lumbar punctures was 1 (IQR, 1-2). Follow-up was complete for more than 99% of study participants.

Overall, spinal hematoma was diagnosed in 143 of 83 711 lumbar punctures (0.17%; 95% CI, 0.14%-0.20%); 99 of 49 526 patients (0.20%; 95% CI, 0.16%-0.24%) without coagulopathy, 24 of 10 371 patients (0.23%, 95% CI, 0.15%-0.34%) with coagulopathy, and 20 of 23 814 patients (0.08%, 95% CI, 0.05%-0.13%) without relevant blood samples within 5 days of the procedure (**Table 1**; eTable 6 in the Supplement). A higher proportion of men (62% vs 49%), age group 61-80 years (38% vs 24%), and CCI scores of 3 or higher (23% vs 13%) was observed by comparison of patients with spinal hematoma than those without.

Restricting the analyses to first-time lumbar punctures among the 64 730 study participants, the cause-specific HR of spinal hematoma adjusted for age, sex, and CCI scores was 1.96 (95% CI, 1.01-3.81) for those aged 41 through 60 years; 2.20 (95% CI, 1.12-4.33) for those aged 61 through 80 years, and 1.72 (95% CI, 1.15-2.56) for male sex. Accounting for competing risks (ie, death or loss to follow-up), the overall cumulative incidence of spinal hematoma after first-time lumbar puncture was 0.15% in patients with coagulopathy and 0.17% in those without coagulopathy with a steady temporal increment for 30 days following the procedure (**Figure**).

Examining the full data set stratified by type and severity of coagulopathy—increasing degrees of thrombocytopenia, high INR, or prolonged APTT—and using patients with values within normal ranges as the reference, there was no association of increasing risk of spinal hematoma within 30 days of lumbar puncture (**Table 2**). In addition, risk did not increase by the cumulative number of lumbar punctures in each individual (eTable 7 in the Supplement) or in subgroup analyses of medical indications or pediatric specialty (**Table 3**; eTable 8 in the Supplement). No cases of spinal hematoma were observed among patients admitted with infection and blood platelets lower than 50 × $10^9$/L (n = 344) or INR higher than 1.4 (n = 604) at time of lumbar puncture.

Table 3. Thirty-Day Risks of Spinal Hematoma Following Lumbar Puncture According to Medical Indication

| | Danish National Laboratory Database 2008-2018, 30-d risks of spinal hematoma[a] | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Infectious diseases | | Neurological condition | | Hematological cancer | | Pediatric | |
| | No./total | % (95% CI) | No./total | % (95% CI) | No./total | % (95% CI) | No./total | % (95% CI) |
| Overall | 34/15 216 | 0.22 (0.15-0.31) | 98/19 126 | 0.51 (0.42-0.62) | 19/7976 | 0.24 (0.14-0.37) | 16/17 019 | 0.09 (0.05-0.15) |
| Blood platelets, $\times 10^9$/L | | | | | | | | |
| ≥151 [Reference] | 24/11 631 | 0.21 (0.13-0.31) | 77/13 663 | 0.56 (0.45-0.70) | 9/4682 | 0.19 (0.09-0.36) | 13/11 521 | 0.11 (0.06-0.19) |
| 101-150 | 4/1244 | 0.32 (0.09-0.82) | 7/562 | 1.25 (0.50-2.55) | 5/977 | 0.51 (0.17-1.19) | 1/957 | 0.10 (0.00-0.58) |
| 51-100 | 1/537 | 0.19 (0.00-1.03) | 2/151 | 1.32 (0.16-4.70) | 1/882 | 0.11 (0.00-0.63) | 0/661 | 0 (0.00-0.56) |
| 31-50 | 0/157 | 0 (0.00-2.32) | 0/35 | 0 (0.00-0.10) | 1/477 | 0.21 (0.01-1.16) | 0/310 | 0 (0.00-1.18) |
| 11-30 | 0/145 | 0 (0.00-2.51) | 2/10 | 20.0 (2.52-55.6) | 2/623 | 0.32 (0.04-1.15) | 1/426 | 0.23 (0.01-1.30) |
| 0-10 | 0/42 | 0 (0.00-8.40) | 0/3 | 0 (0.00-70.8) | 0/142 | 0 (0.00-2.56) | 0/91 | 0 (0.00-3.97) |
| No measurement | 5/1460 | 0.34 (0.11-0.80) | 10/4702 | 0.21 (0.10-0.39) | 1/193 | 0.52 (0.01-2.85) | 1/3053 | 0.03 (0.00-0.18) |
| INR | | | | | | | | |
| 0-1.4 [Reference] | 25/10 745 | 0.23 (0.15-0.34) | 76/11 478 | 0.66 (0.52-0.83) | 12/3952 | 0.30 (0.16-0.53) | 10/6430 | 0.16 (0.07-0.29) |
| 1.5-2.0 | 0/403 | 0 (0.00-0.91) | 1/174 | 0.57 (0.01-3.16) | 1/77 | 1.30 (0.03-7.02) | 1/191 | 0.52 (0.01-2.88) |
| 2.1-2.5 | 0/95 | 0 (0.00-3.81) | 0/26 | 0 (0.00-13.2) | 0/10 | 0 (0.00-30.8) | 0/39 | 0 (0.00-9.03) |
| 2.6-3.0 | 0/49 | 0 (0.00-7.25) | 0/17 | 0 (0.00-19.5) | 0/2 | 0 (0.00-84.2) | 0/8 | 0 (0.00-36.9) |
| 3.1-4.0 | 0/26 | 0 (0.00-13.2) | 0/10 | 0 (0.00-30.8) | 0/5 | 0 (0.00-52.2) | 0/6 | 0 (0.00-45.9) |
| ≥4.1 | 0/31 | 0 (0.00-11.2) | 0/9 | 0 (0.00-33.6) | | | 0/8 | 0 (0.00-36.9) |
| No measurement | 9/3867 | 0.23 (0.11-0.44) | 21/7412 | 0.28 (0.18-0.43) | 6/3930 | 0.15 (0.06-0.33) | 5/10 337 | 0.05 (0.02-0.11) |
| APTT, s | | | | | | | | |
| 0-39 [Reference] | 16/3695 | 0.43 (0.25-0.70) | 43/5189 | 0.83 (0.60-1.11) | 10/2482 | 0.40 (0.19-0.74) | 6/2980 | 0.20 (0.07-0.44) |
| 40-60 | 1/796 | 0.13 (0.00-0.70) | 3/395 | 0.76 (0.16-2.20) | 1/351 | 0.28 (0.01-1.58) | 1/473 | 0.21 (0.01-1.17) |
| ≥61 | 0/112 | 0 (0.00-3.24) | 0/34 | 0 (0.00-10.3) | 0/99 | 0 (0.00-3.66) | 0/86 | 0 (0.00-4.20) |
| No measurement | 17/10 613 | 0.16 (0.09-0.26) | 52/13 508 | 0.38 (0.29-0.50) | 8/5044 | 0.16 (0.07-0.31) | 9/13 480 | 0.07 (0.03-0.13) |

Abbreviations: APTT, activated partial thromboplastin time; INR, international normalized ratio.

[a] As indicated by the primary diagnosis codes assigned at discharge. Any patient younger than 18 years at time of the procedure was categorized as pediatric.

Traumatic spinal tap (>300 × $10^6$ erythrocytes/L in the CSF) occurred in 27.8% (95% CI, 27.4-28.1) of all lumbar punctures. Using this parameter as a surrogate for risk of spinal hematoma, there was no increased risk associated with all degrees of thrombocytopenia (eTable 9 in the Supplement). However, traumatic lumbar punctures occurred more frequently among patients with INR levels of 1.5 to 2.0 (36.8%; 95% CI, 33.3%-40.4%), 2.1 to 2.5 (43.7%; 95% CI, 35.8%-51.8%), and 2.6 to 3.0 (41.9%; 95% CI, 30.5%-53.9%) vs those with normal INR (28.2%; 95% CI, 27.7%-28.7%). Traumatic spinal tap was also more common in patients with an APTT of 40 to 60 seconds (26.3%; 95% CI, 24.2%-28.5%) vs those with normal APTT (21.3%; 95% CI, 20.6%-21.9%) yielding a risk difference of 5.1% (95% CI, 2.9%-7.2%).

Thirty-day mortality RRs, adjusted for age, sex, and CCI scores, increased significantly according to severity of coagulopathy (eTable 10 in the Supplement). By searching the Danish Registry of Causes of Death, fewer than 5 deaths were categorized with spinal hematoma as the primary or secondary causes of death. Among another 13 deaths attributable to unintentional complications of surgical or medical care, none were caused by procedures of aspiration or puncture.

Secondary analyses consisted of medical record review of 1694 identified lumbar punctures in 1237 patients with coagulopathy at time of procedure in the North Denmark Region from 1998 through 2018 (**Table 4**). The patients had a median age of 46 years (IQR 8-66 years) and 45% were female. Fluoroscopy was not used in any of the reviewed lumbar punctures. Spinal hematoma was found in 1 of 1694 procedures equivalent to 0.06% (95% CI, 0.001%-0.33%) of all lumbar punctures (see the Supplement for case description). No spinal hematomas were observed among a limited number of cases with ongoing antithrombotic or anticoagulant treatment at the time of the procedure.

In addition, medical record review of patients at departments of neurosurgery, neurology, or infectious diseases in the North Denmark Region from 1998 to 2018 did not reveal any cases of spinal hematoma preceded by lumbar puncture (eFigure 2 in the Supplement).

## Discussion

In this Danish nationwide population-based cohort study, the absolute risk of spinal hematoma within 30 days after lumbar puncture was low and did not differ substantially between patients with and without coagulopathy at the time of procedure.

Previous studies of risk of spinal hematoma following lumbar puncture primarily consist of case series of limited size.[3,6-8,13] Two reports involving 941 children and 66 adults who had undergone lumbar punctures to treat acute leukemia

Table 4. Characteristics of 1694 Lumbar Punctures in 1237 Individuals in North Denmark Region From 1998 Through 2018

| | North Denmark Region 1998-2018, No. (%)[a] |
|---|---|
| No. of punctures | 1694 |
| Overall risk of spinal hematoma | 1 (0.06) |
| 95% CI | 0.001-0.33 |
| Females | 755 (45) |
| Males | 939 (55) |
| Age, y | |
| No. | 1694 |
| Median (IQR) | 46 (8-66) |
| No. of lumbar punctures in each patient | |
| No. | 1237 |
| Median (IQR) | 1 (1-1) |
| Planned lumbar puncture (elective) | 624/1643 (38) |
| Medical indication for lumbar puncture | |
| Diagnostic[b] | 1126 (66) |
| Infectious diseases | 964 (86) |
| Neurological condition | 162 (14) |
| Malignancy | 194 (17) |
| Therapeutic (eg, instillation of chemotherapy) | 465 (27) |
| Diagnostic and therapeutic | 95 (6) |
| Needle | |
| Traumatic | 188 (11) |
| Atraumatic | 93 (5) |
| Unknown | 1413 (83) |
| Gauge | |
| No. | 127 |
| Median (IQR) | 22 (22-22) |
| No. of attempts per procedure | |
| No. | 609 |
| Median (IQR) | 1 (1-1) |
| Consultant performing the procedure (yes/no) | 506/1043 (49) |
| Medical specialty | |
| Pediatrics | 524 (31) |
| Anesthesia | 305 (18) |
| Hematology | 292 (17) |
| Neurology | 99 (6) |
| Infectious diseases | 93 (5) |
| Emergency and accidents | 52 (3) |
| Neurosurgery | 11 (0.6) |
| Oncology | 3 (0.2) |
| Other departments | 145 (9) |
| Unknown | 170 (10) |
| Medication affecting coagulation[c] | 437/1580 (28) |
| Acetylsalicylic acid[d] | 144 (9) |
| Dipyridamole | 5 (0.3) |
| Ticagrelor | 0 (0) |
| Clopidogrel | 8 (0.5) |
| Vitamin K antagonist | 177 (11) |
| Direct oral anticoagulants[e] | 16 (1) |
| Low-molecular-weight heparin[f] | 171 (11) |
| Intravenous heparin (dialysis) | 8 (0.5) |

(continued)

Table 4. Characteristics of 1694 Lumbar Punctures in 1237 Individuals in North Denmark Region From 1998 Through 2018 (continued)

| | North Denmark Region 1998-2018, No. (%)[a] |
|---|---|
| Platelets, × $10^9$/L[g] | |
| ≥151 | 477 (28) |
| 101-150 | 124 (7) |
| 51-100 | 605 (36) |
| 31-50 | 196 (12) |
| 11-30 | 209 (12) |
| 0-10 | 38 (2) |
| No measurement | 45 (3) |
| Platelet transfusion | 299/1039 (29) |
| No. of platelet transfusions +/− 2 d of index date | |
| No. | 257 |
| Median (IQR) | 1 (1-2) |
| INR[h] | |
| 0-1.4 | 516 (30) |
| 1.5-2.0 | 509 (30) |
| 2.1-2.5 | 121 (7) |
| 2.6-3.0 | 56 (3) |
| 3.1-4.0 | 47 (3) |
| ≥4.1 | 18 (1) |
| No measurement | 427 (25) |
| Antidote (eg, vitamin K or fresh frozen plasma) +/− 2 d of index date | 99/717 (14) |
| APTT (s)[i] | |
| 0-39 | 368 (22) |
| 40-60 | 380 (22) |
| ≥61 | 141 (8) |
| No measurement | 805 (48) |

Abbreviations: APTT, activated partial thromboplastin time; INR, international normalized ratio.

[a] Unless otherwise stated.

[b] Reason could not be determined for 8 cases. Some patients had several diagnostic indications.

[c] All anticoagulants and antiplatelets not specifically listed as held in the days before lumbar puncture. Some patients were administered several medications.

[d] Other nonsteroidal anti-inflammatory drugs in 8 patients.

[e] Rivaroxaban in 11, dabigatran in 3, and apixaban in 2 patients.

[f] Dalteparin in 102, tinzaparin in 48, and enoxaparin in 21 patients.

[g] A total of 1278 were measured on the index date, 252 within 1 day, and 119 within 5 days.

[h] A total of 869 were measured on index date, 165 within 1 day, and 233 within 5 days.

[i] 591 were measured on index date, 128 within 1 day, and 170 within 5 days.

did not observe any serious hemorrhagic complications related to the procedure,[4,5] whereas another study showed that spinal hematoma occurred in 2 of 271 patients (0.7%) treated with aspirin at time of procedure.[20] In comparison, 3 cases (0.2%) of spinal hematoma were observed in the current study among 1896 procedures performed with blood platelets less than 50 × $10^9$/L across a range of medical indications and patient groups.

Consistent with the present study, a systematic review and meta-analysis of 613 patients with spinal hematoma found a male predominance of 2:1 and a peak incidence among patients in their 60s.[1] Moreover, only 63 cases (10%) were attributed to lumbar puncture or spinal blockade, most of whom were treated with intravenous heparin.

A recent large meta-analysis of 110 randomized clinical trials totaling 31 412 patients observed a decreased risk of all adverse outcomes including traumatic spinal tap when an atraumatic needle was used for lumbar puncture vs a traumatic needle, but the meta-analysis did not report on risk of spinal hematoma.[21] Although the different nature of central neuraxial blockades and the concomitant injection of anesthetics precludes direct translation to patients undergoing lumbar puncture, risks of spinal hematoma ranging from 1 of 3600 to 1 of 220 000 in such patients also lend some support to the very low-risk estimates observed in the current study.[22-29]

Thirty-day mortality was significantly increased across all ranges of coagulopathy, which is likely due to the severe underlying medical conditions compared with patients without coagulopathy. This is supported by a search in the Danish Registry of Causes of Death, in which fewer than 5 deaths involving spinal hematoma were identified among all of the study participants.

Lumbar puncture is a common procedure and was performed approximately 18 750 times annually corresponding to 1.4% of all 1 336 803 hospital contacts in Denmark in year 2018,[14] which is comparable with the results of a recent French study.[30] In clinical practice, the possibility of undiagnosed CNS infection or neurological disease needs to be balanced against a risk of spinal hematoma that appears relatively small. Guidelines suggest platelet thresholds should be higher than 20 × $10^9$/L or 50 × $10^9$/L for lumbar puncture and INR levels lower than 1.5 for removal of epidural catheters.[13,31-34] However, some experts recommend proceeding with lumbar puncture regardless of coagulation status if the medical indication is acute bacterial meningitis.[35]

## Limitations

This study has several limitations. First, misclassification bias may be present due to the reliance upon diagnosis codes for paraparesis, medullary compression, and surgical removal of

intraspinal bleeding as proxies for spinal hematoma. Combined with potential missed diagnosis during clinical practice including in fatal cases, this could lead to an underestimation of risk if patients were not assigned one of these diagnosis codes. Conversely, the risk of 0.06% found by a medical record review of 1694 lumbar punctures among patients with coagulopathy suggests that an overestimation is more likely. Lack of registry-based data on use of antiplatelet and anticoagulant treatment at the time of the procedure, especially those not affecting INR or APTT, may also have led to misclassification of patients categorized without coagulopathy. However, interpretation of such data would also require access to information on medication adherence and planned pauses in treatment in the days before lumbar puncture, which is not possible using Danish registries. Still, observations of treatment with anticoagulants and antiplatelets was accounted for by medical record review and may offer some insights into their contribution to the proportion of patients with coagulopathy in Denmark. Second, despite the registry-based design, numbers remained limited for those with severe coagulopathy and data on platelets, INR, and APTT were missing in a sizeable proportion of patients. Yet, risks among patients with unknown coagulation status was lower than that of other patients. Third, although this study was unable to address reversal of coagulopathies in registry-based analyses, data from the medical record review showed that corrections took place for 14% of patients with high INR and for 29% with thrombocytopenia providing a basis for comparison to other settings. Fourth, the study was unable to assess risks in patients with functional coagulopathy or in lumbar punctures performed by fluoroscopy, which is rarely used in Denmark. Fifth, study inclusion was restricted to cases for whom CSF was sent for laboratory analysis meaning that complications due to (multiple) failed attempts of lumbar puncture were not included. Sixth, patients, in whom physicians chose not to do a lumbar puncture, eg due to a perceived high risk of bleeding complications, were not included.

## Conclusions

In this Danish cohort study, risk of spinal hematoma following lumbar puncture was 0.20% among patients without coagulopathy and 0.23% among those with coagulopathy. Although these findings may inform decision-making about lumbar puncture by describing rates in this sample, the observed rates may reflect bias due to physicians selecting relatively low-risk patients for lumbar puncture.


### ARTICLE INFORMATION

**Accepted for Publication:** July 23, 2020.

**Author Contributions:** Dr Bodilsen had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
*Concept and design:* Bodilsen.
*Acquisition, analysis, or interpretation of data:* Bodilsen, Mariager, Vestergaard, Christiansen, Kunwald, Bjarkam, Nielsen.
*Drafting of the manuscript:* Bodilsen.
*Critical revision of the manuscript for important intellectual content:* Bodilsen, Mariager, Vestergaard, Kunwald, Lüttichau, Kristensen, Bjarkam, Nielsen.
*Statistical analysis:* Bodilsen.
*Administrative, technical, or material support:* Bodilsen, Mariager, Kunwald, Nielsen.
*Supervision:* Lüttichau, Bjarkam, Nielsen.

**Conflict of Interest Disclosures:** None reported.


### REFERENCES


1. Kreppel D, Antoniadis G, Seeling W. Spinal hematoma: a literature survey with meta-analysis of 613 patients. *Neurosurg Rev*. 2003;26(1):1-49. doi:10.1007/s10143-002-0224-y

2. Estcourt LJ, Malouf R, Hopewell S, Doree C, Van Veen J. Use of platelet transfusions prior to lumbar punctures or epidural anaesthesia for the prevention of complications in people with thrombocytopenia. *Cochrane Database Syst Rev*. 2018;4:CD011980. doi:10.1002/14651858.CD011980.pub3

3. Owens EL, Kasten GW, Hessel EA II. Spinal subarachnoid hematoma after lumbar puncture and heparinization: a case report, review of the literature, and discussion of anesthetic implications. *Anesth Analg*. 1986;65(11):1201-1207. doi:10.1213/00000539-198611000-00018

4. Howard SC, Gajjar A, Ribeiro RC, et al. Safety of lumbar puncture for children with acute lymphoblastic leukemia and thrombocytopenia. *JAMA*. 2000;284(17):2222-2224. doi:10.1001/jama.284.17.2222

5. Vavricka SR, Walter RB, Irani S, Halter J, Schanz U. Safety of lumbar puncture for adults with acute leukemia and restrictive prophylactic platelet transfusion. *Ann Hematol*. 2003;82(9):570-573. doi:10.1007/s00277-003-0707-0

6. Brem SS, Hafler DA, Van Uitert RL, Ruff RL, Reichert WH. Spinal subarachnoid hematoma: a hazard of lumbar puncture resulting in reversible paraplegia. *N Engl J Med*. 1981;304(17):1020-1021. doi:10.1056/NEJM198104233041705

7. Ruff RL, Dougherty JH Jr. Complications of lumbar puncture followed by anticoagulation. *Stroke*. 1981;12(6):879-881. doi:10.1161/01.STR.12.6.879

8. Edelson RN, Chernik NL, Posner JB. Spinal subdural hematomas complicating lumbar puncture. *Arch Neurol*. 1974;31(2):134-137. doi:10.1001/archneur.1974.00490380082011

9. Carabenciov ID, Hawkes MA, Hocker S. Safety of lumbar puncture performed on dual antiplatelet therapy. *Mayo Clin Proc*. 2018;93(5):627-629. doi:10.1016/j.mayocp.2018.02.005

10. Ruell J, Karuvattil R, Wynn R, Will A. Platelet count has no influence on traumatic and bloody lumbar puncture in children undergoing intrathecal chemotherapy. *Br J Haematol*. 2007;136(2):347-348. doi:10.1111/j.1365-2141.2006.06433.x

11. Veen JJ, Vora AJ, Welch JC. Lumbar puncture in thrombocytopenic children. *Br J Haematol*. 2004;127(2):233-234. doi:10.1111/j.1365-2141.2004.05178.x

12. Breuer AC, Tyler HR, Marzewski DJ, Rosenthal DS. Radicular vessels are the most probable source of needle-induced blood in lumbar puncture: significance for the thrombocytopenic cancer patient. *Cancer*. 1982;49(10):2168-2172. doi:10.1002/1097-0142(19820515)49:10<2168::AID-CNCR2820491031>3.0.CO;2-O

13. Horlocker TT, Vandermeuelen E, Kopp SL, Gogarten W, Leffert LR, Benzon HT. *Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines*. Vol 43. 4th ed. BMJ Publishing Group Ltd; 2018:263-309.

14. Statistics Denmark website. Accessed December 10, 2019. http://www.statbank.dk

15. Trier-Poulsen D. Dokumentation af labdatabasens forskertabel. November 23, 2018. Accessed May 20, 2020. https://sundhedsdatastyrelsen.dk/da/registre-og-services/om-de-nationale-sundhedsregistre/doedsaarsager-og-biologisk-materiale/laboratoriedatabasen

16. Schmidt M, Schmidt SAJ, Sandegaard JL, Ehrenstein V, Pedersen L, Sørensen HT. The Danish National Patient Registry: a review of content, data quality, and research potential. *Clin Epidemiol*. 2015;7:449-490. doi:10.2147/CLEP.S91125

17. Schmidt M, Pedersen L, Sørensen HT. The Danish Civil Registration System as a tool in epidemiology. *Eur J Epidemiol*. 2014;29(8):541-549. doi:10.1007/s10654-014-9930-3

18. Helweg-Larsen K. The Danish Register of Causes of Death. *Scand J Public Health*. 2011;39(7)(suppl):26-29. doi:10.1177/1403494811399958

19. Coviello V, Boggess M. Cumulative incidence estimation in the presence of competing risks. *Stata Journal*. 2004;4(2):103-112. doi:10.1177/1536867X0400400201

20. Lee PW, Levy M. Risk of hematoma from aspirin or clopidogrel owing to lumbar puncture.

*Mayo Clin Proc*. 2019;94(8):1552-1555. doi:10.1016/j.mayocp.2019.05.018

**21**. Nath S, Koziarz A, Badhiwala JH, et al. Atraumatic versus conventional lumbar puncture needles: a systematic review and meta-analysis. *Lancet*. 2018;391(10126):1197-1204. doi:10.1016/S0140-6736(17)32451-0

**22**. Ruppen W, Derry S, McQuay H, Moore RA. Incidence of epidural hematoma, infection, and neurologic injury in obstetric patients with epidural analgesia/anesthesia. *Anesthesiology*. 2006;105(2):394-399. doi:10.1097/00000542-200608000-00023

**23**. Moen V, Dahlgren N, Irestedt L. Severe neurological complications after central neuraxial blockades in Sweden 1990-1999. *Anesthesiology*. 2004;101(4):950-959. doi:10.1097/00000542-200410000-00021

**24**. Li S-L, Wang D-X, Ma D. Epidural hematoma after neuraxial blockade: a retrospective report from China. *Anesth Analg*. 2010;111(5):1322-1324. doi:10.1213/ANE.0b013e3181f1b9ea

**25**. Vandermeulen EP, Van Aken H, Vermylen J. Anticoagulants and spinal-epidural anesthesia. *Anesth Analg*. 1994;79(6):1165-1177. doi:10.1213/00000539-199412000-00024

**26**. Cook TM, Counsell D, Wildsmith JAW; Royal College of Anaesthetists Third National Audit Project. Major complications of central neuraxial block: report on the Third National Audit Project of the Royal College of Anaesthetists. *Br J Anaesth*. 2009;102(2):179-190. doi:10.1093/bja/aen360

**27**. Cameron CM, Scott DA, McDonald WM, Davies MJ. A review of neuraxial epidural morbidity: experience of more than 8000 cases at a single teaching hospital. *Anesthesiology*. 2007;106(5):997-1002. doi:10.1097/01.anes.0000265160.32309.10

**28**. Wulf H. Epidural anaesthesia and spinal haematoma. *Can J Anaesth*. 1996;43(12):1260-1271. doi:10.1007/BF03013437

**29**. Pöpping DM, Zahn PK, Van Aken HK, Dasch B, Boche R, Pogatzki-Zahn EM. Effectiveness and safety of postoperative pain management: a survey of 18 925 consecutive patients between 1998 and 2006 (2nd revision): a database analysis of prospectively raised data. *Br J Anaesth*. 2008;101(6):832-840. doi:10.1093/bja/aen300

**30**. Moisset X, Ruet A, Brochet B, et al. Who performs lumbar puncture, how many do they perform, how and why? a retrospective study of 6594 cases. *Eur Neurol*. 2016;76(1-2):8-11. doi:10.1159/000447452

**31**. Gibson BES, Todd A, Roberts I, et al; British Commitee for Standards in Haematology Transfusion Task Force: Writing Group. Transfusion guidelines for neonates and older children. *Br J Haematol*. 2004;124(4):433-453. doi:10.1111/j.1365-2141.2004.04815.x

**32**. German Medical Association. Platelet Concentrates. *Transfus Med Hemother*. 2009;36(6):372-382. doi:10.1159/000268058

**33**. Kaufman RM, Djulbegovic B, Gernsheimer T, et al; Platelet transfusion: a clinical practice guideline from the AABB. *Ann Intern Med*. 2015;162(3):205-213. doi:10.7326/M14-1589

**34**. British Committee for Standards in Haematology, Blood Transfusion Task Force. Guidelines for the use of platelet transfusions. *Br J Haematol*. 2003;122(1):10-23. doi:10.1046/j.1365-2141.2003.04468.x

**35**. McGill F, Heyderman RS, Michael BD, et al. The UK joint specialist societies guideline on the diagnosis and management of acute meningitis and meningococcal sepsis in immunocompetent adults. *J Infect*. 2016;72(4):405-438. doi:10.1016/j.jinf.2016.01.007