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Admission Rates, Time Trends, Risk Factors, and Outcomes of Ischemic and Hemorrhagic Stroke From German Nationwide Data

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Abstract

Background and Objectives
In the past decade, there have been major improvements in the control of risk factors, acute stroke therapies, and rehabilitation after the availability of high-quality evidence and guidelines on best practices in the acute phase. In this changing landscape, we aimed to investigate the stroke admission rates, time trends, risk factors, and outcomes during the period of 2014–2019 using German nationwide data.

Methods
We obtained data of all acute stroke hospitalizations by the Federal Statistical Office. All hospitalized cases of adults (age 18 years or older) with acute stroke from the years 2014–2019 were analyzed regarding time trends, risk factors, treatments, morbidity, and in-hospital mortality according to stroke subtype (all-cause/ischemic/hemorrhagic).

Results
Between 2014 and 2019, overall stroke hospitalizations in adults (median age = 76 years, [IQR: 65–83 years]) initially increased from 306,425 in 2014 to peak at 318,849 in 2017 before falling to again to 312,692 in 2019, whereas percentage stroke hospitalizations that resulted in death remained stable during this period at 8.5% in 2014 and 8.6% in 2019. In a multivariate model of 1,882,930 cases, the strongest predictors of in-hospital stroke mortality were hemorrhagic subtype (adjusted OR [aOR] = 3.06, 95% CI 3.02–3.10; $p < 0.001$), cancer (aOR = 2.11, 2.06–2.16; $p < 0.001$), congestive heart failure (aOR = 1.70, 1.67–1.73; $p < 0.001$), and lower extremity arterial disease (aOR = 1.76, 1.67–1.84; $p < 0.001$).

Discussion
Despite recent advances in acute stroke care over the past decade, the percentage of stroke hospitalizations resulting in death remained unchanged. Further research is needed to determine how best to optimize stroke care pathways for multimorbid patients.

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Glossary

AKI = acute kidney injury; **CKD** = chronic kidney disease; **LEAD** = lower extremity arterial disease.

Stroke is the second leading cause of death and a major cause of disability worldwide.[1] The global burden of stroke has increased dramatically over the past 30 years in part due to population growth and aging, but also as a result of rising risk factor prevalence including obesity, sedentary lifestyle, hypertension, high alcohol consumption, and chronic kidney disease (CKD).[2] Lower- and middle-income countries continue to account for a large share of this burden.

There have been major developments in stroke care over the past decade with advances in prevention, acute therapies, and neurorehabilitation.[3] Several landmark trials for both ischemic and hemorrhagic stroke were published during this period that led to the widespread implementation of evidence-based interventions. These include mechanical thrombectomy,[4,5] an extended time window for thrombolysis using MRI-based or perfusion-based imaging,[6,7] and intensive blood pressure lowering for intracerebral hemorrhage.[8]

However, it remains unclear whether this progress has translated into improved admission rates, risk factor profiles, and survival for both hemorrhagic and ischemic stroke in the general population. Some studies have observed decline in stroke admissions and mortality,[9-12] but up-to-date, country-specific admissions and survival data by stroke-subtype are scarce, and the most recent Global Burden of Disease study highlights the absence of original, good-quality stroke epidemiologic studies for most countries.[1] Regular monitoring of these trends by stroke subtype is also necessary to monitor the disease burden at a population level.[13]

In Germany, all hospitals are required by federal law to transfer data on all in-patient hospitalizations to the Institute for the Hospital Remuneration System (Institut fur das Entgeltsystem im Krankenhaus, InEK; Siegburg, Germany; g-drg.de) since 2002. The Federal Statistical Office has made a large part of this data set available for scientific purposes. Based on these nationwide data from the years 2014 to 2019, we analyzed recent temporal trends in admission rates, risk factors, and mortality after ischemic and hemorrhagic stroke.

Methods

A diagnosis and procedure-related remuneration system (German Diagnosis Related Groups, G-DRG system) was introduced for all in-hospitalization services in Germany in 2003, enabling accurate and comprehensive acquisition of defined cases of illness.[14] Consistent documentation and billing are achieved by the use of detailed mandatory coding guidelines Owing to federal law, all hospitals are required to transfer patient data on diagnoses, comorbidities, medical services, or procedures and procedure-related complications and to health insurance to receive reimbursement. Afterward, these data were collected by the Institute for the Hospital Remuneration System (InEK) for calculation of the current DRG-system and by the Federal Statistical Office.

Data Source

The Research Data Centers of the Federal Statistical Office and the Statistical Offices of the Laender (Statistisches Bundesamt, DESTATIS; destatis.de) provided data for the years 2014–2019 for analysis with respect to risk factors, in-hospital outcomes, and time trends related to acute stroke. The database contains all in-patient treated patients on a case base per year, except for treatments in psychiatric or psychosomatic units.[15] We excluded medical care provided by office-based specialists with special admitting. Because of data privacy protection, all subgroups less than 6 cases were excluded from the analysis. There was only remote access to the anonymized original data. A statistical analysis program written in SAS (SAS 9.2: SAS Institute Inc., Cary, NC, USA) was executed by the Research Data Center.

Standard Protocol Approvals, Registrations, and Patient Consents

The data presented here were examined as part of the GenderVasc research project. This project was approved by the Ethics Committee of the Landesaerztekammer Westfalen-Lippe and the Medical Faculty of the University of Muenster (No 2019-21-f-S).

Diagnoses and Procedure Codes

Diagnoses, patient characteristics, comorbidities, and stroke complications are uniformly coded according to the International Statistical Classification of Diseases and Related Health Problems, 10th revision, German modification (ICD-10-GM) (eTable 1 in the supplement, links.lww.com/WNL/C325). Similarly, endovascular and surgical procedures are uniformly coded according to the German Operation and Procedure Classification (OPS) (see eTable 2 in the supplement, links.lww.com/WNL/C325). Coding guidelines and annual adaptation by the German Institute for Medical Documentation and Information (Cologne, Germany) ensure uniform documentation. All hospitalized adult patients with an acute stroke (age 18 years or older, diagnosis code: ICD I60-64) as their principal diagnosis were included in the analysis.

A stroke was defined as a syndrome of rapidly developing clinical symptoms and/or signs of focal, and at times global (applied to patients in deep coma and to those with subarachnoid hemorrhage), loss of brain function, with symptoms lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin.[16] Stroke subtype classification (ischemic or hemorrhagic) corresponded with the ICD-10-GM codes (see eTable 1 in the supplement, links.lww.com/WNL/C325).

Statistical Analysis

Frequencies are given as case number per 100,000 population based on the German population of the respective year. Proportions of hospitalizations are case numbers per 100,000 of total in-hospital cases. Mortality displays the percentage of in-hospital deaths within a designated subgroup. The analysis comprises all in-patient treated acute stroke cases in Germany and does not represent a subgroup or sample. The Mantel-Haenszel χ^2 test was performed to evaluate time trends of categorical variables. Trends over time for continuous variables were analyzed using Spearman correlation analysis. Logistic regression analysis was used to assess the relationship between various demographic factors, vascular risk factors, treatments, and in-hospital stroke mortality, with the final model adjusting for the following covariates: age, sex, hypertension, dyslipidemia, diabetes mellitus, obesity, dementia, smoking, previous stroke, atrial fibrillation/flutter, lower extremity arterial disease (LEAD), cardiovascular disease, congestive heart failure, chronic kidney disease, cancer, carotid interventions, decompressive craniectomy, extracranial/intracranial hematoma evacuations, mechanical thrombectomy, and intravenous (IV) thrombolysis treatment. All analyses were fully explorative, and all *p*-values were interpreted accordingly, that is, all *p*-values are two-sided, and *p*-values <0.05 were considered statistically noticeable. Statistical analysis was performed using SAS software (SAS 9.3: SAS Institute Inc., Cary, NC, USA), IBM SPSS statistics software (IBM SPSS Statistics for Windows, version 28.0. Armonk, NY: IBM Corp) and the web-based statistics software VassarStats (vassarstats.net; R. Lowry).

Data Availability

The data used in this study cannot be made available in the manuscript, the supplemental files, or in a public repository because of German data protection laws ("Bundesdatenschutzgesetz", BDSG). Generally, access to data of statutory health insurance funds for research purposes is possible only under the conditions defined in German Social Law (SGB V § 287). Requests for data access can be sent as a formal proposal specifying the recipient and purpose of the data transfer to the appropriate data protection agency. Access to the data used in this study can only be provided to external parties under the conditions of the cooperation contract of this research project and after written approval by the sickness fund.

Results

Overall, between 2014 and 2019, there were a total of 1,882,930 hospitalizations coded as acute stroke in Germany, corresponding to an average 1.62% of all in-patient admissions. The frequency of hospitalized stroke cases remained relatively constant from 377.38 per 100,000 population in 2014 to 375.98 in 2019. Table 1 shows the absolute ischemic and hemorrhagic stroke admission rates for this period according to age group and year. The absolute number of ischemic stroke admissions peaked at 323.28 per 100,000 population in 2016 and then fell steadily to 317.75 in 2019. The ICH admission rate also had its nadir in 2019 at 58.23 per 100,000 population. During this time period, there were decreases in the stroke admission rates in the 40–49 and 70–79 year age groups while rates increased for those aged 60–69 and 80–89 years (Table 1 and Figure 1).

Summary statistics for baseline demographic and clinical characteristics according to stroke subtype during this time period are shown in Table 2. Patients presenting with ischemic stroke were slightly older than those with a hemorrhagic stroke (median age 76 vs 74 years). In total, 905,667 (48.1%) of all patients were female with comparable rates between the subtypes. Hypertension was the most prevalent comorbidity, affecting 74.4% of all acute stroke patients. Comorbidities were generally more prevalent in ischemic stroke patients apart from cancer, which was more common in ICH (3.5 vs 2.9%). Time trends of demographic characteristics and vascular risk factors remained stable throughout the study period for both ischemic and hemorrhagic stroke subtypes (see eTables 3 and 4 in the supplement, links.lww.com/WNL/C325).

The therapies received and the complications and outcomes experienced by those hospitalized with acute stroke from 2014 to 2019 are summarized in eTable 5, links.lww.com/WNL/C325 in the supplement and detailed according to year and subtypes in Tables 3 and 4. During this period, 27,097 (1.7%) and 16,479 (1%) of ischemic stroke patients were treated with carotid endarterectomy and stenting, respectively. The rate of carotid stenting increased steadily from 0.7% in 2014 to 1.3% in 2019 ($p < 0.001$) (Table 3). Craniectomy rates remained stable throughout this period. Mechanical thrombectomy rates progressively increased from 1.9% in 2014 to 6.1% in 2019 ($p < 0.001$). Similarly, IV thrombolysis rates rose from 11.2% in 2014 to 14.1% in 2019 ($p < 0.001$). In line with these changes, there was also a trend toward greater bleeding and hemorrhagic transformation events (1.3%–1.6% and 2.8%–5.1% from 2014 to 2019, both $p < 0.001$). However, there was no change in the requirement for blood transfusions. There was a small rise in the incidence of acute kidney injury (AKI) (1.4%–2.7%; $p < 0.001$). Associated health care costs also rose during this period to peak at €7,634.42 in 2019 ($p < 0.001$).

Among patients hospitalized with acute hemorrhagic stroke, the rate of neurosurgical interventions remained stable over the 6-year period at approximately 1.9% and 10% for craniectomy and evacuation procedures, respectively (Table 4 and eTable 5 in the supplement, links.lww.com/WNL/C325). 6.6% of patients had other bleeding events or required a blood transfusion. The rate of AKI or need for renal replacement therapy increased from 2.5% in 2014 to 3.7% in

Table 1 Absolute Annual Stroke Admission Rates According to Age Group and Crude Rates per 100,000 Population

	2014	2015	2016	2017	2018	2019	Total
Ischemic							
Younger than 40 y, N (%) =	3,569 (1.4%)	3,552 (1.4%)	3,827 (1.4%)	3,973 (1.5%)	3,775 (1.4%)	3,833 (1.5%)	22.529 (1.4%)
40–49 y, N (%) =	9,910 (3.9%)	9,405 (3.6%)	9,723 (3.6%)	9,288 (3.5%)	8,649 (3.3%)	8,312 (3.2%)	55,287 (3.5%)
50–59 y, N (%) =	25,331 (9.9%)	26,412 (10.2%)	27,272 (10.2%)	27,664 (10.4%)	27,574 (10.4%)	26,806 (10.1%)	161,059 (10.2%)
60–69 y, N (%) =	40,675 (15.9%)	42,402 (16.3%)	45,658 (17.1%)	46,718 (17.5%)	47,311 (17.9%)	47,313 (17.9%)	270,077 (17.1%)
70–79 y, N (%) =	83,717 (32.8%)	83,735 (32.2%)	82,134 (30.8%)	80,143 (30.0%)	76,475 (28.9%)	73,965 (28.0%)	480,169 (30.4%)
80–89 y, N (%) =	74,313 (29.1%)	75,981 (29.3%)	79,272 (29.7%)	80,445 (30.1%)	81,802 (30.9%)	84,858 (32.1%)	476,671 (30.2%)
90 y or older, N (%) =	17,761 (7.0%)	18,219 (7.0%)	18,892 (7.1%)	19,144 (7.2%)	18,899 (7.2%)	19,177 (7.3%)	112,092 (7.1%)
Total, N =	255,276	259,706	266,778	267,375	264,485	264,264	1,577,884
N per 100,000	314.39	316.04	323.28	322.95	318.58	317.75	
Hemorrhagic							
Younger than 40 y, N (%) =	1,703 (3.3%)	1,709 (3.3%)	1,839 (3.6%)	1,679 (3.3%)	1,628 (3.3%)	1,729 (3.6%)	10,287 (3.4%)
40–49 y, N (%) =	3,460 (6.8%)	3,316 (6.3%)	3,172 (6.2%)	3,109 (6.0%)	2,744 (5.5%)	2,649 (5.5%)	18,450 (6.1%)
50–59 y, N (%) =	6,705 (13.1%)	6,753 (12.9%)	6,770 (13.1%)	6,869 (13.3%)	6,664 (13.3%)	6,340 (13.1%)	40,101 (13.2%)
60–69 y, N (%) =	8,140 (15.9%)	8,335 (15.9%)	8,618 (16.7%)	8,656 (16.8%)	8,578 (17.1%)	8,528 (17.6%)	50,855 (16.7%)
70–79 y, N (%) =	16,471 (32.2%)	16,509 (31.5%)	14,988 (29.1%)	14,630 (28.4%)	13,789 (27.5%)	12,895 (26.6%)	89,282 (29.3%)
80–89 y, N (%) =	12,469 (24.4%)	13,392 (25.6%)	13,683 (26.5%)	13,961 (27.1%)	14,018 (28.0%)	13,756 (28.4%)	81,279 (26.6%)
90 y or older, N (%) =	2,201 (4.3%)	2,332 (4.5%)	2,499 (4.9%)	2,570 (5.0%)	2,659 (5.3%)	2,531 (5.2%)	14,792 (4.9%)
Total, N =	51,149	52,346	51,569	51,474	50,080	48,428	305,046
N per 100,000	62.99	63.70	62.49	62.17	60.32	58.23	
All Stroke							
Total	306,425	312,052	318,347	318,849	314,565	312,692	1,882,930
Total per 100,000	377.38	379.74	385.77	385.12	378.91	375.98	

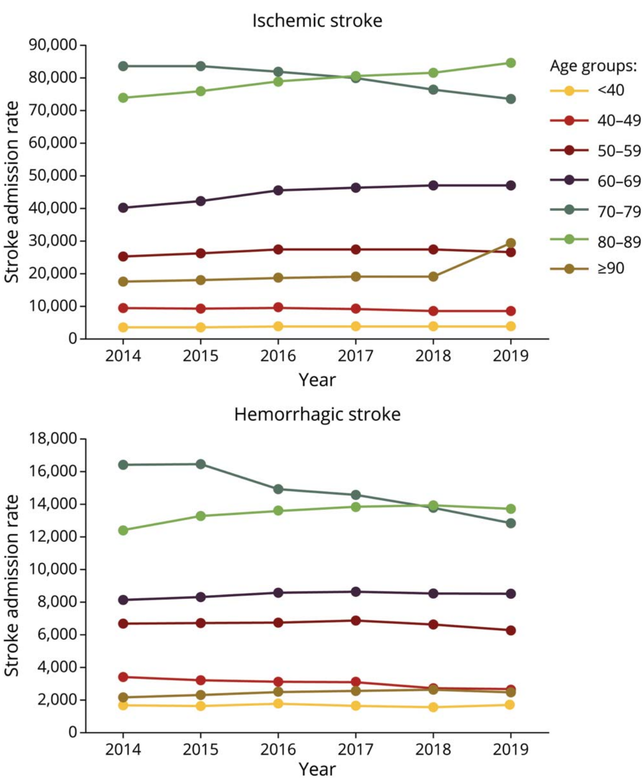
2019 ($p < 0.001$), higher than that of those with ischemic stroke (2.5%; $p < 0.001$). 22% of patients with ICH required mechanical ventilation in comparison with 5% of those with ischemic stroke ($p < 0.001$). The mean length of hospital stay was also greater for patients with ICH at 15.4 days in comparison with 12 days for ischemic stroke patients ($p < 0.001$). The mean charges per case was also nearly double that of their ischemic stroke counterparts at €11,397.59.

Overall, there were 106,007 (6.7%) and 54,469 (17.9%) in-hospital deaths from 2014 to 2019 among the ischemic and hemorrhagic stroke patients, respectively. Death rates remained largely stable for both subtypes throughout this time period (Tables 3 and 4). Predictors of in-hospital mortality for all stroke patients are shown in Figure 2. In a multivariate-adjusted model, hemorrhagic subtype (adjusted OR = 3.06, 95% CI: 3.02–3.10; $p < 0.001$), congestive heart failure (adjusted OR = 1.81, 95% CI: 1.78–1.84; $p < 0.001$), LEAD stages 4–6 (adjusted OR = 1.76, 95% CI: 1.67–1.84; $p < 0.001$), and cancer (adjusted OR = 2.32, 95% CI: 2.25–2.39; $p < 0.001$) were the greatest characteristics and comorbidities predictive of death. For patients with hemorrhagic stroke, premorbid diagnoses of cancer (adjusted OR = 1.68, 1.61–1.76; $p < 0.001$), evacuation of ICH (adjusted OR = 1.86, 1.34–2.59; $p < 0.001$), LEAD stages 4–6 (adjusted OR = 1.53, 1.34–1.74; <0.001), and CHF (adjusted OR = 1.24, 1.20–1.29; <0.001) were all strongly predictive of in-hospital death (Figure 3A). For patients hospitalized with acute ischemic stroke, the greatest predictors of in-hospital death were the presence of cancer (adjusted OR = 2.32, 2.25–2.39; $p < 0.001$), CHF (adjusted OR = 1.81, 1.78–1.84; $p < 0.001$), and LEAD stages 4–6 (adjusted OR = 1.77, 1.68–1.87; $p < 0.001$) (Figure 3B).

Discussion

We present nationwide data regarding the rates of hospitalized stroke in Germany from 2014 to 2019 along with subtype-specific demographics, clinical characteristics, complications, and outcomes. Overall, there were stable rates of

Figure 1 Ischemic and Hemorrhagic Stroke Admission Rates in Germany (2014–2019) According to Age Group and Year



stroke hospitalization during this time period with a small decline observed in recent years. Use of IV thrombolysis and mechanical thrombectomy progressively increased during this period along a parallel increase in the rate of hemorrhagic transformation. However, despite greater therapeutic intervention, in-hospital stroke mortality rates did not improve over this period, with hemorrhagic subtype and several comorbidities including CHF, LEAD, and cancer all predictive of a greater risk of death.

These national data show small decreases in rates of hospitalized stroke for both ischemic and hemorrhagic subtypes in Germany in 2018 and 2019. Our results are in keeping with reductions in stroke hospitalization and severity that have been observed in other developed countries including Israel,[17] Norway,[18] and the United Kingdom.[19] These changes may reflect improved control of cardiovascular risk factors, the availability of high-equality evidence and guidelines on best practices in primary and secondary stroke prevention,[20,21] and more proactive implementation of stroke prevention clinics. Better hypertension control and improved antihypertensive use have also been reported in Germany during this time period.[22] Reassuringly, in contrast to some previous population-based studies, we did not find an increasing stroke admission rate in younger age groups.[23-25] This discrepancy may relate to the more recent time period of this study because those studies that previously reported increases in "young stroke" were generally comparing the 1990s with the early 2000 period, after which this apparent increase appeared to plateau.[24,26] Although one may have expected greater reductions in hospitalization rates by the end of the period, improvements in diagnosis over time could have resulted in more accurate diagnoses in later years, thus affecting rates.

Few studies have looked at recent temporal trends in patient characteristics among acute stroke patients.[27] Overall, the number, median age, and risk factor profile among stroke patients remained stable between 2014 and 2019 in Germany. Ischemic stroke patients were more multimorbid with a greater prevalence of hypertension, atrial fibrillation, coronary heart disease, CKD, diabetes mellitus, dyslipidemia, and dementia compared with hemorrhagic stroke patients. A premorbid diagnosis of cancer was more prevalent in the latter group. These risk factor differences between the major stroke subtypes appear to be consistent over time and with prior literature.[28] Multimorbidity burden in stroke has important implications because it has been associated with an increasing risk of all-cause mortality, with mortality risk more than doubled for those with at least 5 morbidities compared with those with none.[29]

For therapies and complications, there was nearly a three-fold increase in mechanical thrombectomy rates along with a smaller increase in IVT numbers during this time period. However, this was accompanied by increased hemorrhagic transformation. These changes align with the growing evidence during this period that thrombolytic therapy and mechanical thrombectomy among eligible patients were associated with less death and dependency despite a relative increase in symptomatic ICH in those treated with IVT.[5,30] Decompressive craniectomy rates remained stable for both ischemic and hemorrhagic stroke patients. The hemorrhagic stroke group experienced a greater number of poststroke complications with higher rates of bleeding and need for blood transfusion, AKI and requirement for RRT, sepsis, and cardiac arrest. They also had more complex care needs including requirement for mechanical ventilation, longer lengths of stay, and associated higher health care costs. These complications in the acute phase have been shown to worsen brain injury and have been linked to worse outcomes after hemorrhagic stroke.[31,32]

In-hospital mortality rates were higher among patients with ICH compared with those with ischemic stroke. Despite recent improvements in evidence-based therapies[33] and postacute stroke management including stroke units[34] in the past decade, mortality rates did not improve for either subtype during the study time period. For ischemic stroke, these findings somewhat conflict with the improved short-term fatality rates observed in other population-based studies.[12,35] However, this discrepancy may be attributable to the relatively narrow time window of this study or to the crude trends that we present in comparison with some of the former studies. Because only aggregate data were available, we were unable to produce age-standardized rates, where

Table 2 Baseline Characteristics of Patients Hospitalized With Acute Stroke in Germany According to Subtype

	Ischemic	Hemorrhagic	Total	*p* Value
Number of cases–N	1,577,884 (83.8%)	305,046 (16.2%)	1,882,930 (100.0%)	***
Median age—Yr (Q1,Q3)	76 (66, 83)	74 (61, 83)	76 (65, 83)	<0.001
Female sex–n (%)	761,537 (48.3%)	144,130 (47.3%)	905,667 (48.1%)	<0.001
Codiagnoses				
LEAD stages–n (%)[a]				<0.001
LEAD RF 1-3	31,620 (2.0%)	2,663 (0.9%)	34,283 (1.8%)	
LEAD RF 4-6	14,232 (0.9%)	1,347 (0.4%)	15,579 (0.8%)	
Hypertension, n (%)	1,196,720 (75.8%)	203,473 (66.7%)	1,400,193 (74.4%)	<0.001
Atrial fibrillation, n (%)	462,599 (29.3%)	62,254 (20.4%)	524,853 (27.9%)	<0.001
Acute myocardial infarction, n (%)	19,885 (1.3%)	2,327 (0.8%)	22,212 (1.2%)	<0.001
Cancer, n (%)	44,984 (2.9%)	10,511 (3.5%)	55,495 (3.0%)	<0.001
Cerebrovascular disease, n (%)	212,810 (13.5%)	7,739 (2.5%)	220,549 (11.7%)	<0.001
CHD, n (%)	242,481 (15.4%)	31,058 (10.2%)	273,539 (14.5%)	<0.001
Chronic heart failure, n (%)	172,525 (10.9%)	21,013 (6.9%)	193,538 (10.3%)	<0.001
RV-CHF, n (%)	37,582 (2.4%)	4,775 (1.6%)	42,357 (2.3%)	<0.001
LV-CHF, n (%)				<0.001
NYHA I	14,853 (0.9%)	1,256 (0.4%)	16,109 (0.9%)	
NYHA II	41,327 (2.2%)	4,449 (1.5%)	45,776 (2.4%)	
NYHA III	41,550 (2.6%)	5,080 (1.7%)	46,630 (2.5%)	
NYHA IV	30,253 (1.9%)	4,241 (1.4%)	34,494 (1.8%)	
Chronic kidney disease, n (%)	223,498 (14.2%)	28,493 (9.3%)	251,991 (13.4%)	<0.001
Diabetes mellitus, n (%)	442,222 (28.0%)	52,006 (17.1%)	494,228 (26.3%)	<0.001
Dyslipidemia, n (%)	633,558 (40.2%)	39,144 (12.8%)	672,702 (35.7%)	<0.001
Obesity, n (%)	76,731 (4.9%)	10,905 (3.6%)	87,636 (4.7%)	<0.001
Current smoking, n (%)	70,557 (4.5%)	6,037 (2.0%)	76,594 (4.1%)	<0.001
Prev. ischemic stroke, n (%)	110,878 (7.0%)	0 (0.0%)	110,878 (5.9%)	<0.001
Prev. intracranial bleeding, n (%)	8,010 (0.5%)	6,052 (2.0%)	14,062 (0.8%)	<0.001
Ischemic heart disease, n (%)	251,407 (15.9%)	32,376 (10.6%)	283,783 (15.1%)	<0.001
Dementia, n (%)	83,166 (5.3%)	10,975 (3.6%)	94,141 (5.0%)	<0.001
Prev. CABG, n (%)	34,593 (2.2%)	4,632 (1.5%)	39,225 (2.1%)	<0.001
Prev. valve, n (%)	11,101 (0.7%)	2,234 (0.7%)	13,335 (0.7%)	0.082

Abbreviations: CABG indicates coronary artery bypass graft; CHD = coronary heart disease; CHF = congestive heart failure; LEAD = lower extremity artery disease; LV = left ventricular; NYHA = New York Heart Association; RV = right ventricular.
[a] LEAD 1-3 represents Rutherford stage 1–3 and indicates intermittent claudication. LEAD 4-6 represents for Rutherford stage 4–6 and indicates critical limb ischemia.

improvement for ischemic stroke mortality has been previously described.[12] In contrast, the high mortality rates that we report after ICH are similarly well-described in other contemporary cohorts,[36,37] likely related to the lack of effective therapeutic options[31] and the high complication rate as described above.[32] There have been no successful phase 3 clinical trials for acute interventions in ICH to date. Therefore, admission to dedicated stroke or neurocritical care units with intensive prevention or early detection of complications has been proposed as the best approach to improve ICH outcomes.[38]

Table 3 Acute Therapies Received by Patients Hospitalized With Acute Ischemic Stroke in Germany According to Year of Event

Year	2014	2015	2016	2017	2018	2019	Total	P for trend
Carotid EA–n (%)	4,061 (1.6%)	4,265 (1.6%)	4,338 (1.6%)	4,691 (1.8%)	4,911 (1.9%)	4,831 (1.8%)	27,097 (1.7%)	<0.001
Carotid stent–n (%)	1,790 (0.7%)	2,271 (0.9%)	2,577 (1.0%)	2,800 (1.0%)	3,514 (1.3%)	3,527 (1.3%)	16,479 (1.0%)	<0.001
Carotid interposition graft n (%)	49 (0.0%)	37 (0.0%)	a	32 (0.0%)	a	34 (0.0%)	a	n.a.
Decompressive hemicraniectomy, n (%)	897 (0.4%)	897 (0.4%)	966 (0.4%)	1,020 (0.4%)	950 (0.4%)	954 (0.4%)	5,684 (0.4%)	0.270
Evacuation of extracranial hemorrhage, n (%)	380 (0.2%)	392 (0.2%)	431 (0.2%)	423 (0.2%)	405 (0.2%)	388 (0.2%)	2,419 (0.2%)	0.901
Evacuation of ICH, n (%)	4 (0.0%)	6 (0.0%)	4 (0.0%)	12 (0.0%)	a	5 (0.0%)	a (0.0%)	n.a.
Thrombectomy, extracranial, n (%)	156 (0.1%)	268 (0.1%)	317 (0.1%)	360 (0.1%)	462 (0.2%)	478 (0.2%)	2,041 (0.1%)	<0.001
Thrombectomy, intracranial–n (%)	4,919 (1.9%)	7,174 (2.8%)	9,837 (3.7%)	12,203 (4.6%)	14,837 (5.6%)	16,217 (6.1%)	65,187 (4.1%)	<0.001
PCI, n (%)	697 (0.3%)	779 (0.3%)	799 (0.3%)	877 (0.3%)	977 (0.4%)	956 (0.4%)	5,085 (0.3%)	<0.001
DES, n (%)	367 (0.1%)	526 (0.2%)	610 (0.2%)	677 (0.3%)	680 (0.3%)	706 (0.3%)	3,566 (0.2%)	<0.001
BMS, only, n (%)	170 (0.1%)	87 (0.0%)	a	a	a	a	319 (0.0%)	n.a.
CABG, n (%)	17 (0.0%)	17 (0.0%)	a	a	16 (0.0%)	31 (0.0%)	113 (0.0%)	n.a.
Renal replacement therapy, n (%)	1,233 (0.5%)	1,272 (0.5%)	1,370 (0.5%)	1,452 (0.5%)	1,354 (0.5%)	1,382 (0.5%)	8,063 (0.5%)	0.012
Systemic thrombolysis, n (%)	28,658 (11.2%)	30,785 (11.9%)	34,036 (12.8%)	36,354 (13.6%)	37,201 (14.1%)	37,121 (14.1%)	204,155 (12.9%)	<0.001
Selective thrombolysis, n (%)	934 (0.4%)	934 (0.4%)	982 (0.4%)	936 (0.4%)	867 (0.3%)	772 (0.3%)	5,425 (0.3%)	<0.001
Intra-arterial thrombolysis, n (%)	55 (0.0%)	63 (0.0%)	47 (0.0%)	57 (0.0%)	53 (0.0%)	57 (0.0%)	332 (0.0%)	0.715
GpIIb/IIIa inhibitor, n (%)	259 (0.1%)	238 (0.1%)	286 (0.1%)	404 (0.2%)	504 (0.2%)	484 (0.2%)	2,175 (0.1%)	<0.001
Any minor or major bleeding event, n (%)	3,202 (1.3%)	3,592 (1.4%)	3,937 (1.5%)	4,090 (1.5%)	4,337 (1.6%)	4,299 (1.6%)	23,457 (1.5%)	<0.001
Haemorrhagic transformation, n (%)	7,119 (2.8%)	7,466 (2.9%)	8,338 (3.1%)	8,880 (3.3%)	9,336 (3.5%)	13,553 (5.1%)	54,692 (3.5%)	<0.001
Blood transfusion, n (%)	5,525 (2.2%)	5,221 (2.0%)	5,408 (2.0%)	5,444 (2.0%)	5,572 (2.1%)	5,540 (2.1%)	32,710 (2.1%)	0.899
Blood transfusion or bleeding event, n (%)	7,922 (3.1%)	7,920 (3.1%)	8,409 (3.2%)	8,568 (3.2%)	8,868 (3.4%)	8,813 (3.3%)	50,500 (3.2%)	<0.001
AKI, n (%)	3,491 (1.4%)	4,654 (1.8%)	5,679 (2.1%)	6,372 (2.4%)	6,893 (2.6%)	7,152 (2.7%)	34,241 (2.2%)	<0.001
Sepsis, n (%)	2,937 (1.2%)	3,184 (1.2%)	3,569 (1.3%)	3,743 (1.4%)	3,846 (1.5%)	3,899 (1.5%)	21,178 (1.3%)	<0.001
AKI or need for dialysis, n (%)	4,388 (1.7%)	5,568 (2.1%)	6,607 (2.5%)	7,377 (2.8%)	7,778 (2.9%)	8,062 (3.1%)	39,780 (2.5%)	<0.001
Cardiac arrest–n (%)	1,191 (0.5%)	1,283 (0.5%)	1,411 (0.5%)	1,391 (0.5%)	1,444 (0.6%)	1,376 (0.5%)	8,096 (0.5%)	<0.001
Mechanical ventilation, n (%)	11,441 (4.5%)	12,123 (4.7%)	13,216 (5.0%)	13,939 (5.2%)	14,410 (5.5%)	14,252 (5.4%)	79,381 (5.0%)	<0.001
Median duration of ventilation, h (Q1,Q3)	106 (23, 315)	96 (23,306)	97 (24,307)	95 (22,307)	89 (21,302)	81 (21,280)	93 (22,302)	<0.001
Mean length of hospital stay, days (SD)	12.3 (13.2)	12.1 (13.3)	11.9 (13.1)	12.0 (13.6)	12.0 (13.8)	11.9 (14.2)	12.0 (13.5)	<0.001
Mean charges per case, EUR (SD)	6,352.35 (8,870.30)	6,352.35 (8,870.30)	6,726.25 (9,354.69)	7,062.29 (10217.47)	7,358.41 (10,431.05)	7,634.42 (10,843.74)	6,946.17 (9,921.42)	<0.001
In-hospital death, n (%)	17,032 (6.7%)	17,578 (6.8%)	17,624 (6.6%)	17,908 (6.7%)	17,890 (6.8%)	17,975 (6.8%)	106,007 (6.7%)	0.074

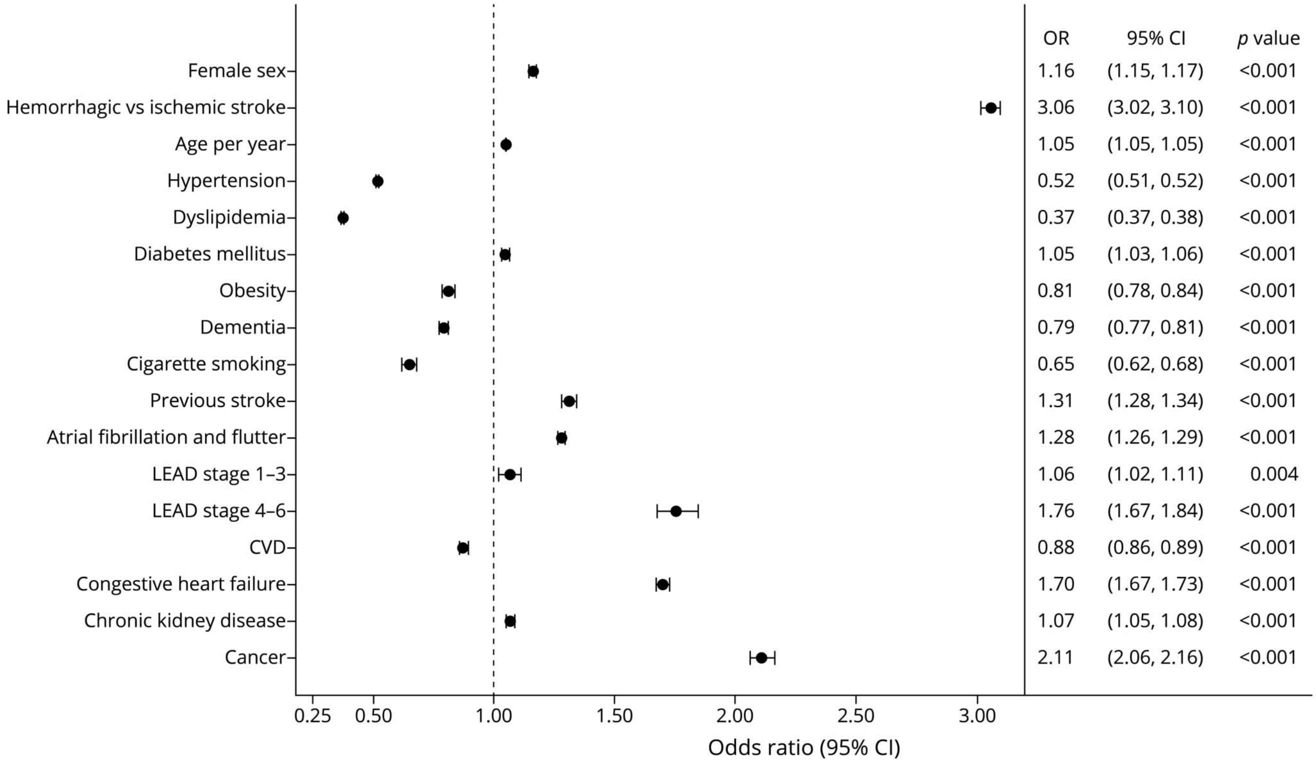
Abbreviations: AKI indicates acute kidney injury; BMS = bare metal stent; CABG OP = coronary artery bypass graft off pump; DES = drug-eluting stent; EA = endarterectomy; ICH = intracerebral hemorrhage; IQR = interquartile range; PCI = percutaneous coronary intervention; SD = standard deviation.
[a] This number was removed from the destatis because of data protection, that is, cell number was smaller than 3.

Table 4 Acute Therapies Received by Patients Hospitalized With Acute Hemorrhagic Stroke in Germany According to Year of Event

Year	2014	2015	2016	2017	2018	2019	Total	P For trend
Carotid EA, n (%)	5 (0.0%)	a	a	a	3 (0.0%)	4 (0.0%)	26 (0.0%)	n.a.
Carotid stent, n (%)	11 (0.0%)	18 (0.0%)	10 (0.0%)	15 (0.0%)	12 (0.0%)	8 (0.0%)	74 (0.0%)	0.430
Carotid interposition graft, n (%)	a	0 (0.0%)	a	0 (0.0%)	a	0 (0.0%)	a	n.a.
Decompressive craniectomy, n (%)	891 (1.7%)	971 (1.9%)	996 (1.9%)	963 (1.9%)	950 (1.9%)	892 (1.8%)	5,663 (1.9%)	0.252
Evacuation of extracranial hemorrhage, n (%)	4,899 (9.6%)	5,131 (9.8%)	5,104 (9.9%)	5,120 (9.9%)	5,441 (10.9%)	4,696 (9.7%)	30,391 (10.0%)	<0.001
Evacuation of ICH, n (%)	34 (0.1%)	56 (0.1%)	35 (0.1%)	35 (0.1%)	20 (0.0%)	31 (0.1%)	211 (0.1%)	0.027
Thrombectomy, extracranial, n (%)	a	0 (0.0%)	a	0 (0.0%)	a	0 (0.0%)	5 (0.0%)	n.a.
Thrombectomy, intracranial, n (%)	32 (0.1%)	36 (0.1%)	50 (0.1%)	64 (0.1%)	77 (0.2%)	97 (0.2%)	356 (0.1%)	<0.001
PCI, n (%)	30 (0.1%)	55 (0.1%)	42 (0.1%)	40 (0.1%)	47 (0.1%)	44 (0.1%)	258 (0.1%)	0.260
DES, n (%)	10 (0.0%)	28 (0.1%)	31 (0.1%)	23 (0.0%)	28 (0.1%)	26 (0.1%)	146 (0.1%)	0.046
BMS, only, n (%)	10 (0.0%)	10 (0.0%)	a	a	a	a	25 (0.0%)	n.a.
CABG, n (%)	a	0 (0.0%)	a	a	3 (0.0%)	0 (0.0%)	8 (0.0%)	n.a.
Renal replacement therapy, n (%)	450 (0.9%)	470 (0.9%)	447 (0.9%)	518 (1.0%)	438 (0.9%)	391 (0.8%)	2,714 (0.9%)	0.434
Systemic thrombolysis, n (%)	110 (0.2%)	108 (0.2%)	120 (0.2%)	115 (0.2%)	119 (0.2%)	91 (0.2%)	663 (0.2%)	0.797
Selective thrombolysis, n (%)	90 (0.2%)	79 (0.2%)	87 (0.2%)	90 (0.2%)	99 (0.2%)	93 (0.2%)	538 (0.2%)	0.147
Intra-arterial thrombolysis, n (%)	264 (0.5%)	269 (0.5%)	262 (0.5%)	253 (0.5%)	231 (0.5%)	255 (0.5%)	1,534 (0.5%)	0.624
GpIIb/IIIa inhibitor, n (%)	66 (0.1%)	69 (0.1%)	102 (0.2%)	104 (0.2%)	113 (0.2%)	120 (0.2%)	574 (0.2%)	<0.001
Any minor or major bleeding event, n (%)	953 (1.9%)	1,039 (2.0%)	1,026 (2.0%)	1,112 (2.2%)	1,135 (2.3%)	1,062 (2.2%)	6,327 (2.1%)	<0.001
Blood transfusion, n (%)	2,972 (5.8%)	2,740 (5.2%)	2,678 (5.2%)	2,590 (5.0%)	2,410 (4.8%)	2,262 (4.7%)	15,652 (5.1%)	<0.001
Blood transfusion or bleeding event, n (%)	3,601 (7.0%)	3,447 (6.6%)	3,359 (6.5%)	3,359 (6.5%)	3,198 (6.4%)	3,035 (6.3%)	19,999 (6.6%)	<0.001
AKI, n (%)	1,051 (2.1%)	1,264 (2.4%)	1,516 (2.9%)	1,596 (3.1%)	1,655 (3.3%)	1,628 (3.4%)	8,710 (2.9%)	<0.001
Sepsis, n (%)	1,320 (2.6%)	1,377 (2.6%)	1,446 (2.8%)	1,521 (3.0%)	1,427 (2.9%)	1,355 (2.8%)	8,446 (2.8%)	0.002
AKI or need for dialysis, n (%)	1,286 (2.5%)	1,517 (2.9%)	1,734 (3.4%)	1,851 (3.6%)	1,849 (3.7%)	1,824 (3.8%)	10,061 (3.3%)	<0.001
Cardiac arrest, n (%)	562 (1.1%)	589 (1.1%)	543 (1.1%)	537 (1.0%)	565 (1.1%)	515 (1.1%)	3,311 (1.1%)	0.641
Mechanical ventilation, n (%)	11,354 (22.2%)	11,616 (22.2%)	11,350 (22.0%)	11,275 (21.9%)	10,839 (21.6%)	10,727 (22.2%)	67,161 (22.0%)	0.186
Median duration of ventilation, h (IQR)	75 (16,305)	73 (17, 314)	81 (16,316)	83 (17,318)	86 (19,328)	91 (19,329)	82 (17,318)	<0.001
Mean length of hospital stay, days (SD)	15.2 (20.1)	15.3 (20.3)	15.3 (20.3)	15.3 (20.3)	15.7 (21.5)	15.8 (21.4)	15.4 (20.7)	0.030
Mean charges per case, EUR (SD)	10,523.73 (18,194.01)	10,796.90 (19,371.56)	11,063.82 (19,152.13)	11,492.44 (19,378.23)	12,001.94 (20,444.18)	12,610.17 (21,197.79)	11,397.59 (19,637.89)	<0.001
In-hospital death, n (%)	8,905 (17.4%)	9,333 (17.8%)	9,062 (17.6%)	9,212 (17.9%)	8,966 (17.9%)	8,991 (18.6%)	54,469 (17.9%)	<0.001

Abbreviations: AKI indicates acute kidney injury; BMS = bare metal stent; CABG OP = coronary artery bypass graft off pump; DES = drug-eluting stent; EA = endarterectomy; ICH = intracerebral hemorrhage; IQR = interquartile range; PCI = percutaneous coronary intervention; SD = standard deviation.
[a] This number was removed from the destatis because of data protection, that is, cell number was smaller than 3.

Figure 2 Predictors of In-Hospital Death for All Hospitalized Patients With Acute Stroke



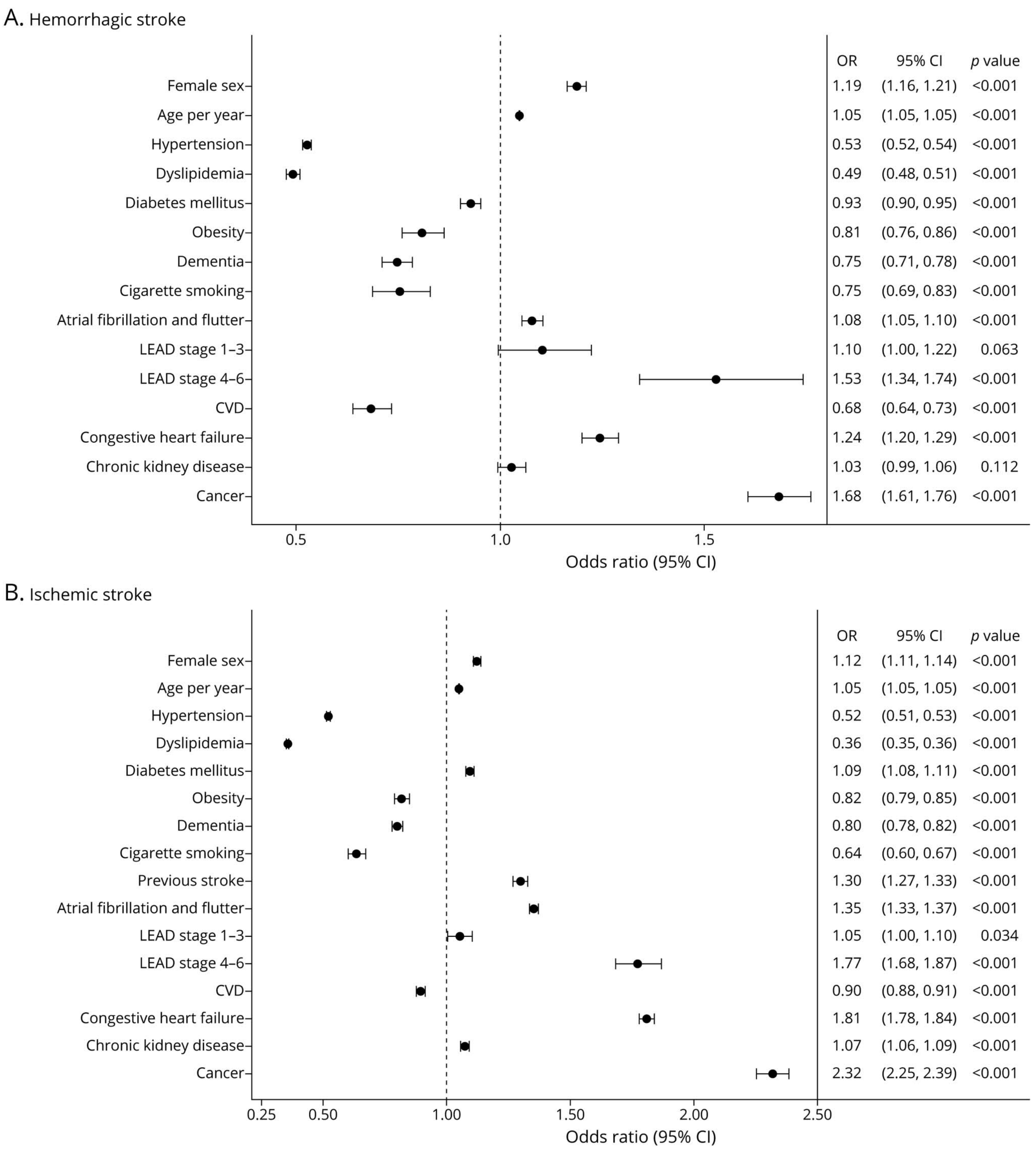
Multivariate-adjusted ORs presented with final model including all other variables. CI = confidence interval; CVD, cardiovascular disease; LEAD, lower extremity arterial disease*; OR, odds ratio. *LEAD 1-3 represents Rutherford stage 1–3 and indicates intermittent claudication; LEAD 4-6 represents for Rutherford stage 4–6 and indicates critical limb ischemia.

Cancer, LEAD, and CHF were all strongly predictive of in-hospital mortality in both groups of patients. The association of cancer with poor survival after stroke has been well-described,[39] particularly in the setting of cryptogenic mechanisms, lung cancer, and systemic metastasis.[40] These factors are closely linked to hypercoagulability[41] and correction of coagulopathy in the setting of cancer appears to be protective for stroke survival.[42] Similarly, the presence of LEAD is known to increase the risk of secondary cardiovascular death and events,[43] including both ischemic and hemorrhagic stroke,[44] particularly if severe–that is, baseline ankle-brachial index (ABI) < 0.60 or history of amputation.[45] There is emerging evidence for the role of dual hemostatic blockade (aspirin and low-dose rivaroxaban) in such patients with polyvascular disease as it was associated with a lower risk of the composite outcome of cardiovascular death, stroke, or myocardial infarction in the COMPASS trial.[46] Stroke in patients with CHF has also previously been reported to be associated with worse outcomes and higher mortality,[47] underscoring the need for better prevention and treatment strategies in this vulnerable group.

This present study has many strengths resulting from the rigorous methodology applied to nationwide data, including consistency across cases. This is also a large and comprehensive sample of unselected participants who are also unbiased by insurance status, geographic location, or providing institution, and, therefore, the observed trends are high applicable to daily practice. High-quality, country-specific epidemiologic data such as these are an important way to monitor the global stroke burden.[13]

However, our study has several limitations. First, our analysis of administrative data may be subject to miscoding of ICD codes and despite rigorous abstraction processes, variation in reporting may still be present. Second, data acquisition was case-based rather than patient-based and, therefore, there could have led to a certain number of double-counted patients, for example, by hospital transfer. Third, hospital-based data has some inherent limitations including selection bias related to the indication for admission which is influenced by stroke severity and prognosis, and variable access to specialized stroke units and center-specific services. As such, hospitalization data may not reflect the full burden of stroke in the population. However, because Germany has a health care system with a very high admittance rate for transient ischemic attack and minor stroke, this national data set is very inclusive and representative of all cases of acute stroke. Fourth, because data were limited to ICD codes, no medication, laboratory or imaging data were available for analysis. For this reason, we were also unable to capture discharge disposition information (i.e., home, rehabilitation

Figure 3 Predictors of In-Hospital Death for All Hospitalized Patients With (A) Hemorrhagic Stroke and (B) Ischemic Stroke



Multivariate-adjusted ORs presented with final model including all other variables. CI = confidence interval; CVD, cardiovascular disease; LEAD, lower extremity arterial disease*; OR, odds ratio. *LEAD 1-3 represents Rutherford stage 1–3 and indicates intermittent claudication; LEAD 4-6 represents for Rutherford stage 4–6 and indicates critical limb ischemia.

hospital, or nursing facility) which would have enhanced the richness of this report. Finally, we were unable to distinguish first from recurrent strokes because of the case-based nature of the data.

In conclusion, we have presented a nationwide, administrative data analysis of all patients hospitalized with acute stroke in Germany from 2014 to 2019. There were favorable trends toward improved rates of hospitalization in recent years although these were still accompanied by high in-hospital mortality rates, particularly for patients with ICH, who require research prioritization to identify novel therapeutic tools and optimal strategies to prevent and treat early complications. Our study also highlighted the impact of multimorbidity on short-term stroke survival and the need to personalize management strategies to these comorbidities.

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Disclosure

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Jannik Feld, MSc	Institute of Biostatistics and Clinical Research, University of Muenster, Germany	Analysis or interpretation of data
Peter M. Rothwell, MD, PhD, FMedSci	Wolfson Centre for the Prevention of Stroke and Dementia, Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital, University of Oxford, United Kingdom	Drafting/revision of the manuscript for content, including medical writing for content; Analysis or interpretation of data
Holger Reinecke, MD, PhD	Department of Cardiology I: Coronary and Peripheral Vascular Disease, Heart Failure, University Hospital Muenster, Germany	Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data
Jeanette Koeppe, PhD	Institute of Biostatistics and Clinical Research, University of Muenster, Germany	Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data

References

1. Global, regional, and national burden of stroke and its risk factors, 1990-2019: a systematic analysis for the global burden of disease study 2019. *Lancet Neurol.* 2021;20(10):795-820.
2. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the global burden of disease study 2019. *Lancet.* 2020;396:1223-1249.
3. Spence JD, Azarpazhooh MR, Larsson SC, Bogiatzi C, Hankey GJ. Stroke prevention in older adults: recent advances. *Stroke.* 2020;51:3770-3777.
4. Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med.* 2015;372:11-20.
5. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Eng J Med.* 2015;372(11):1019-1030.
6. Thomalla G, Simonsen CZ, Boutitie F, et al. MRI-guided thrombolysis for stroke with unknown time of onset. *N Engl J Med.* 2018;379:611-622.
7. Ma H, Campbell BCV, Parsons MW, et al. Thrombolysis guided by perfusion imaging up to 9 hours after onset of stroke. *N Engl J Med.* 2019;380:1795-1803.
8. Moullaali TJ, Wang X, Martin RH, et al. Blood pressure control and clinical outcomes in acute intracerebral haemorrhage: a preplanned pooled analysis of individual participant data. *Lancet Neurol.* 2019;18(9):857-864.
9. Edwards JD, Kapral MK, Fang J, Swartz RH. Trends in long-term mortality and morbidity in patients with no early complications after stroke and transient ischemic attack. *J Stroke Cerebrovasc Dis.* 2017;26(7):1641-1645.
10. Wang Y, Rudd AG, Wolfe CD. Trends and survival between ethnic groups after stroke: the South London stroke register. *Stroke.* 2013;44:380-387.
11. Kazlauskas HA, Raskauskiene N, Radziuviene R, Janusonis V. Twenty years trends in mortality rates from stroke in Klaipeda. *Brain Behav.* 2016;6:e00499.
12. Kamal N, Lindsay MP, Côté R, Fang J, Kapral MK, Hill MD. Ten-year trends in stroke admissions and outcomes in Canada. *Can J Neurol Sci.* 2015;42:168-175.
13. Nichols M, Townsend N, Scarborough P, Rayner M. Cardiovascular disease in europe: epidemiological update. *Eur Heart J.* 2013;34:3028-3034.
14. Steinbeck G, Sinner MF, Lutz M, Müller-Nurasyid M, Kääb S, Reinecke H. Incidence of complications related to catheter ablation of atrial fibrillation and atrial flutter: a nationwide in-hospital analysis of administrative data for Germany in 2014. *Eur Heart J.* 2018;39(45):4020-4029.
15. Kuehnemund L, Koeppe J, Feld J, et al. Gender differences in acute myocardial infarction-a nationwide German real-life analysis from 2014 to 2017. *Clin Cardiol.* 2021;44(7):890-898.
16. Hatano S. Experience from a multicentre stroke register: a preliminary report. *Bull World Health Organ.* 1976;54(5):541-553.
17. Koton S, Geva D, Streifler JY, et al. Declining rate and severity of hospitalized stroke from 2004 to 2013: the national acute stroke Israeli registry. *Stroke.* 2018;49(6):1348-1354.
18. Rand K, Dahl FA, Viana J, Rønning OM, Faiz KW, Barra M. Fewer ischemic strokes, despite an ageing population: stroke models from observed incidence in Norway 2010-2015. *BMC Health Serv Res.* 2019;19(1):705.
19. Rothwell PM, Coull AJ, Giles MF, et al. Change in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxfordshire, UK from 1981 to 2004 (Oxford Vascular Study). *Lancet.* 2004;363(9425):1925-1933.

20. Arnett DK, Blumenthal RS, Albert MA, et al. ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the american college of cardiology/american heart association task force on clinical practice guidelines. *J Am Coll Cardiol.* 2019;74(11):e177-e232.
21. Meschia JF, Bushnell C, Boden-Albala B, et al. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2014;45(17):3754-3832.
22. Sarganas G, Knopf H, Grams D, Neuhauser HK. Trends in antihypertensive medication use and blood pressure control among adults with hypertension in Germany. *Am J Hypertens.* 2016;29(10304):104-113.
23. Madsen TE, Khoury JC, Leppert M, et al. Temporal trends in stroke incidence over time by sex and age in the GCNKSS. *Stroke.* 2020;51(4):1070-1076.
24. Ekker MS, Verhoeven JI, Vaartjes I, van Nieuwenhuizen KM, Klijn CJM, de Leeuw FE. Stroke incidence in young adults according to age, subtype, sex, and time trends. *Neurology.* 2019;92(21):e2444–e2454.
25. George MG, Tong X, Bowman BA. Prevalence of cardiovascular risk factors and strokes in younger adults. *JAMA Neurol.* 2017;74(10):695-703.
26. Béjot Y, Duloquin G, Thomas Q, et al. Temporal trends in the incidence of ischemic stroke in young adults: dijon stroke registry. *Neuroepidemiology.* 2021;55(3):239-244.
27. Appelros P, Jonsson F, Asplund K, et al. Trends in baseline patient characteristics during the years 1995-2008: observations from riks-stroke, the Swedish stroke register. *Cerebrovasc Dis.* 2010;30(2):114-119.
28. Andersen KK, Olsen TS, Dehlendorff C, Kammersgaard LP. Hemorrhagic and ischemic strokes compared: stroke severity, mortality, and risk factors. *Stroke* 2009;40(2):2068-2072.
29. Gallacher KI, McQueenie R, Nicholl B, Jani BD, Lee D, Mair FS. Risk factors and mortality associated with multimorbidity in people with stroke or transient ischaemic attack: a study of 8,751 UK biobank participants. *J Comorb* 2018;8(1):1-8.
30. Wardlaw JM, Murray V, Berge E, del Zoppo GJ. Thrombolysis for acute ischaemic stroke. *Cochrane Database Syst Rev.* 2014;2014(10):Cd000213.
31. Keep RF, Hua Y, Xi G. Intracerebral haemorrhage: mechanisms of injury and therapeutic targets. *Lancet Neurol.* 2012;11(8):720-731.
32. Balami JS, Buchan AM. Complications of intracerebral haemorrhage. *Lancet Neurol.* 2012;11(10154):101-118.
33. Jahan R, Saver JL, Schwamm LH, et al. Association between time to treatment with endovascular reperfusion therapy and outcomes in patients with acute ischemic stroke treated in clinical practice. *JAMA.* 2019;322(3):252-263.
34. Langhorne P, Lewsey JD, Jhund PS, et al. Estimating the impact of stroke unit care in a whole population: an epidemiological study using routine data. *J Neurol Neurosurg Psychiatry.* 2010;81(12):1301-1305.
35. Joundi RA, Smith EE, Yu AYX, Rashid M, Fang J, Kapral MK. Temporal trends in case fatality, discharge destination, and admission to long-term care after acute stroke. *Neurology.* 2021;96(16):e2037–e2047.
36. Waziry R, Heshmatollah A, Bos D, et al. Time trends in survival following first hemorrhagic or ischemic stroke between 1991 and 2015 in the Rotterdam study. *Stroke.* 2020;51(3):Strokeaha119027198.
37. Andaluz N, Zuccarello M. Recent trends in the treatment of spontaneous intracerebral hemorrhage: analysis of a nationwide inpatient database. *J Neurosurg.* 2009;110(3):403-410.
38. Hemphill JC III, Greenberg SM, Anderson CS, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2015;46(7):2032-2060.
39. Cestari DM, Weine DM, Panageas KS, Segal AZ, DeAngelis LM. Stroke in patients with cancer: incidence and etiology. *Neurology.* 2004;62(11):2025-2030.
40. Navi BB, Singer S, Merkler AE, et al. Cryptogenic subtype predicts reduced survival among cancer patients with ischemic stroke. *Stroke.* 2014;45(8):2292-2297.
41. Buccheri G, Ferrigno D, Ginardi C, Zuliani C. Haemostatic abnormalities in lung cancer: prognostic implications. *Eur J Cancer.* 1997;33(1):50-55.
42. Lee MJ, Chung JW, Ahn MJ, et al. Hypercoagulability and mortality of patients with stroke and active cancer: the OASIS-CANCER study. *J Stroke* 2017;19(1):77-87.
43. Sprengers RW, Janssen KJ, Moll FL, Verhaar MC, van der Graaf Y. Prediction rule for cardiovascular events and mortality in peripheral arterial disease patients: data from the prospective second manifestations of arterial disease (SMART) cohort study. *J Vasc Surg.* 2009;50(6):1369-1376.
44. Meves SH, Diehm C, Berger K, et al. Peripheral arterial disease as an independent predictor for excess stroke morbidity and mortality in primary-care patients: 5-year results of the getABI study. *Cerebrovas Dis.* 2010;29(6):546-554.
45. Kolls BJ, Sapp S, Rockhold FW, et al. Stroke in patients with peripheral artery disease. *Stroke.* 2019;50:1356-1363.
46. Eikelboom JW, Connolly SJ, Bosch J, et al. Rivaroxaban with or without aspirin in stable cardiovascular disease. *N Engl J Med.* 2017;377(14):1319-1330.
47. Witt BJ, Brown RD Jr., Jacobsen SJ, et al. Ischemic stroke after heart failure: a community-based study. *Am Heart J.* 2006;152(1):102-109.

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