Stroke Incidence and Survival in Ludwigshafen am Rhein, Germany

The Ludwigshafen Stroke Study (LuSSt)

Frederick Palm, MD; Christian Urbanek, MD; Steffen Rose, MD; Florian Buggle, MD; Barbara Bode, MD; Michael G. Hennerici, MD, PhD; Kirsten Schmieder, MD, PhD; Gerhard Inselmann, MD, PhD; Rainer Reiter, MD; Robert Fleischer, MD; Karl-Otto Piplack, MD; Anton Safer, PhD; Heiko Becher, PhD; Armin J. Grau, MD, PhD

Background and Purpose—Considerable locoregional differences in stroke incidence exist even within countries. Based on data from a statewide stroke care quality monitoring project, we hypothesized a high stroke incidence mainly among younger age groups in the industrial city of Ludwigshafen am Rhein, Germany. To test this hypothesis and to provide data on stroke incidence and case-fatality rates, a population-based stroke register was initiated.

Methods—The Ludwigshafen Stroke Study is a prospective ongoing population-based stroke register among the 167,906 inhabitants of Ludwigshafen am Rhein. Starting on January 1, 2006, standard definitions and multiple overlapping methods of case ascertainment were used to identify all patients with incident stroke or transient ischemic attack.

Results—In 2006 and 2007, 1231 cases with stroke or transient ischemic attack including 725 patients with first-ever stroke were identified. The crude annual incidence rate per 1000 for first-ever stroke was 2.16 (95% CI 2.10 to 2.32). After age adjustment to the European population, incidence for first-ever stroke was 1.46 (95% CI 1.35 to 1.57; men: 1.63; 95% CI 1.46 to 1.81; women: 1.29; 95% CI 1.15 to 1.43). Crude annual incidence rates per 1000 were 1.86 for ischemic stroke, 0.19 for intracerebral hemorrhage, 0.05 for subarachnoid hemorrhage, and 0.05 for undetermined stroke. Case-fatality rates for first-ever stroke were 13.6%, 16.4%, and 23.2% at Days 28, 90, and 365, respectively.

Conclusions—High crude incidence rates in our study reflect the rising burden of stroke in our aging population. Age-adjusted incidence rates were somewhat higher than those reported by recent studies from Western Europe, mainly due to higher incidence in subjects <65 years. (Stroke. 2010;41:1865-1870.)

Key Words: case-fatality • population-based stroke register • stroke incidence

Up to half of all stroke survivors have persistent disability requiring help in daily life activities. Because mainly the elderly are affected, stroke represents an increasing social and economical burden given the aging population in Western societies.1,2 There are considerable locoregional differences in stroke incidence rates. To provide optimal treatment, healthcare planning, and stroke-related prevention strategies in each area, regional stroke incidence rates have to be observed.

Data from a statewide quality monitoring project on acute stroke care that has been effective in the state of Rhineland-Palatinate (approximately 4 million inhabitants) since 2001 showed high numbers of patients with stroke/transient ischemic attack (TIA) treated in the Neurology Department of the community hospital Ludwigshafen am Rhein compared with other supraregional stroke units with comparably sized catchment areas. Furthermore, patients aged <45 years have been overrepresented in this department (eg, 8.3% [2002] and 7.1% [2006] of all patients [unpublished data]). Five other hospitals with supraregional stroke units report a mean percentage of 6.1% (2002) and 4.1% (2006). These data might either reflect a higher stroke incidence, particularly among younger age groups in this industrial city and its surroundings, or be the result of differences in patient referral. The Ludwigshafen Stroke Study (LuSSt), an ongoing population-based stroke register, was initiated to investigate whether stroke incidence, particularly in younger age groups, is in fact higher in the city of Ludwigshafen am Rhein than in other areas in Germany and other European countries. If higher incidence is found, the reasons and the potential for

Received June 4, 2010; accepted June 22, 2010.

From the Department of Neurology (F.P., C.U., S.R., F.B., A.J.G.), Klinikum Ludwigshafen, Ludwigshafen, Germany; the Departments of Neurology (M.G.H.) and Neurosurgery (K.S.), University of Heidelberg, Universitätsklinikum Mannheim, Mannheim, Germany; the Department of Internal Medicine (G.I.), Marienkrankenhaus Ludwigshafen, Ludwigshafen, Germany; the Department of Internal Medicine (R.R.), Guter-Hirte Ludwigshafen, Ludwigshafen, Germany; the CNS-Center for Neurology Mannheim (R.F.), Mannheim, Germany; the Local Health Authority (K.-O.P.), Ludwigshafen, Germany; and the Institute of Public Health (A.S., H.B.), University of Heidelberg, Heidelberg, Germany.

Correspondence to Frederick Palm, MD, Department of Neurology, Städtisches Klinikum Ludwigshafen, Bremserstr 79, 67063 Ludwigshafen am Rhein, Germany. E-mail: palmf@klilu.de

© 2010 American Heart Association, Inc.

Stroke is available at http://stroke.ahajournals.org DOI: 10.1161/STROKEAHA.110.592642
preventive measures are to be explored. Here, we report incidences and case-fatality rates observed during the first 2 study years, 2006 and 2007.

Subjects and Methods

Study Area, Study Population, and Medical Services

The LuSSt is a prospective population-based stroke register in the population of the city of Ludwigshafen am Rhein that started on January 1, 2006. Ludwigshafen is an industrial city located in the state of Rhineland-Palatinate in West Germany. According to official population statistics at the midpoint of the study period (December 31, 2006), the study population consisted of 167 906 inhabitants (83 017 males and 84 889 females). Ambulatory medical care for patients is performed by general practitioners and internists or, considering neurological illness, by neurologists. Inpatient care is served by hospitals whose access is free and which are open for admission 24 hours all days. In our area, patients with symptoms suggestive of stroke are almost always referred to hospital-based emergency units and the same holds true for TIA unless symptoms had been present for several days. Patients with acute neurological deficits are mostly referred to the Department of Neurology at the Klinikum Ludwigshafen, the only neurology department in the city, comprising 81 neurology beds including 8 beds on a stroke unit. Patients are also admitted to the Departments of Internal Medicine at the Marienkrankenhaus and the Geriatric Department of the "Krankenhaus zum Guten Hirten." Few patients, especially those suggestive for subarachnoid hemorrhage (SAH), are referred to the Departments of Neurology or Neurosurgery at the nearby University Hospital Mannheim.

Study Criteria

Malmgren et al defined criteria for "ideal" population-based stroke studies. Those criteria were updated by Bonita et al, Sudlow and Warlow, and, more recently, by Feigin et al. Our register meets all core and supplementary criteria, including standard definitions, standard methods of case ascertainment, and standard data presentation.

Standard Definitions

According to the definition of the World Health Organization, stroke was defined as a syndrome of "rapidly developing clinical symptoms and/or signs of focal (or at times global) disturbance of cerebral function lasting >24 hours (unless interrupted by surgery) or leading to death, with no apparent cause other than of vascular origin." Clinically asymptomatic acute vascular lesions on neuroimaging and the combination of symptoms lasting <24 hours with acute vascular lesions on neuroimaging were not diagnosed as stroke in this study. Patients who received thrombolysis were diagnosed as stroke even if symptoms completely resolved within 24 hours. Stroke associated with cerebral trauma or brain malignancy was excluded. Patients with no clinical evidence of any previous stroke event were diagnosed as first-ever-in-a-lifetime stroke (FES). Stroke was classified as ischemic stroke (IS), intracerebral hematoma (ICH), or SAH according to results of neuroimaging (or lumbar puncture in SAH). Stroke events that did not undergo brain imaging or autopsy were classified as undetermined strokes. TIA was defined as transient focal cerebral ischemia with symptoms lasting <24 hours independent of neuroimaging results. A patient with a first stroke and a previous TIA was coded as FES. Vital status was assessed at Day 28 and at 3 and 12 months after stroke onset.

Case Ascertainment

Affiliation to the study population was determined by a postal address within the city borders. To achieve complete case ascertainment, multiple overlapping methods of patient identification were used based on cooperation of all providers of in- and outpatient care in and around the city of Ludwigshafen am Rhein.

Patients with stroke were identified by daily screening of the patient list at the Emergency Unit of the Klinikum Ludwigshafen that includes all patients seen with acute neurological problems independent of later hospitalization or outpatient care by the study team (F.P., C.U., B.B., S.R.). The study team daily checked all patients admitted to the Department of Neurology during morning conferences on weekdays, regularly viewed the Discharge Data Base of the Department of Neurology, and contacted consulting neurologists who examined patients who developed neurological symptoms at the time of being treated in other departments. There was a regular check of all patients referred to our hospital for carotid endarterectomy or carotid stenting.

Physicians of all hospitals in the city of Ludwigshafen (Marienkranchenhaus; Krankenhaus zum Guten Hirten) and in hospitals outside the city boundaries that treat patients with stroke (University Hospital Mannheim, Diakonissen Hospital Mannheim, Hospital Frankfurt) were asked to report patients with stroke or TIA from the study area and were contacted regularly by the study team. Pediatric departments in Ludwigshafen and Mannheim were contacted at larger intervals to assess childhood or juvenile strokes. Patients with SAH are almost always treated at the Department of Neurosurgery at the Klinikum Mannheim. Neurosurgeons were asked to register all patients with SAH or ICH from the study area. Furthermore, regular checkups of patient data were performed there and in larger time intervals also at the more distant Neurosurgery Department of the University of Heidelberg. All cooperating hospitals received intensive informal informations before January 1, 2006.

To identify all nonhospitalized stroke patients, all general practitioners, specialists in internal medicine, and neurologists practicing in Ludwigshafen were extensively informed about the register before study initiation and were contacted every 3 months and asked about patients with stroke or TIA. Nursing and residential homes were contacted 3 to 4 times a year. Death certificates were obtained by the local health authority. Physicians who gave out the certificate were contacted to confirm the diagnosis. Records of the city’s emergency services were reviewed regularly to identify patients who may have died before hospital admission.

All patients received a neurological examination on admission and after 1 day to differentiate between stroke and TIA and were interviewed in a structured way by a member of the study team or a trained physician. In patients unable to communicate, close relatives or legal representatives were interviewed. All diagnoses were made by experienced neurologists of the study team; controversial diagnoses were discussed during study meetings and final adjudication was performed by 1 study member (A.J.G.). All patients with symptoms somewhat suggestive of stroke (disturbed consciousness of unknown origin, vertigo, confusion) were discussed; however, finally, stroke was only acknowledged when a definite diagnosis could be made. Diagnoses and symptoms of previous stroke were assessed in detail and all available medical records were checked to correctly identify recurrent strokes.

Ethical Aspects, Data Protection, and Follow-Up Examinations

The study was approved by the local ethics committee and the data protection commissioner of Rhineland-Palatinate. According to legal requirements, patients could be registered at the data holding center (Neurology Department Klinikum Ludwigshafen) including personal data if written informed consent by themselves or their legal representative was available and with the use of a pseudonymization code that avoids double registration in the absence of written informed consent. In all patients, data were stored in a computerized database separate from any personal data according to the guidelines of the data protection commissioner.

Follow-up investigations were performed by telephone 28 days and 3 and 12 months after symptom onset using a standardized questionnaire in all patients who themselves or their legal representative had given written informed consent according to requirements by the data protection commissioner. In all other patients without statement of consensus, or in case of patients who could not be contacted, information regarding survival had been obtained from
the population registration authority. If patients had died, death certificates were checked. Furthermore, newspapers were regularly checked by a study nurse for obituaries and death announcements.

**Statistical Analyses**

We calculated crude, age-specific, and age-adjusted incidence rates by sex both for all cases and stroke subtypes. Population numbers at the midpoint of the study period (December 31, 2006) multiplied by 2 were used as person-year approximation. Mid-decade age bands were used. The standard European population was used for standardization. Exact 95% CIs for the rates based on the Poisson distribution were calculated. Case-fatality rates for FES and stroke subtypes at Day 28 and after 3 and 12 months after stroke onset and Kaplan–Meier survival curves are provided. The chi-square test was used to compare crude incidence rates between studies. Data were analyzed using the software package SAS 9.1.3.

**Results**

Between January 1, 2006, and December 31, 2007, 1231 patients with stroke or TIA were registered. Mean age was 71.6 (±12.9 SD) years. Among all identified cases, 629 (51.1%) occurred in males and 602 (48.9%) in females. Hospitalization rate was 94.9%. Data on neuroimaging were available in 93.2% of patients.

Among all recorded patients, 269 (21.7%) had a TIA and 237 patients (19.3%) had a recurrent stroke. A FES was diagnosed in 725 (58.9%) patients (age 71.5±13.1 years; range 26 to 102 years). FES occurred in 350 men (48.3%; age 69.5±12.2 years) and 375 women (51.7%, age 73.4±13.5 years). In FES, brain imaging was performed in 97.7% of patients and the hospitalization rate was 95.3%.

Age- and sex-specific, crude- and age-adjusted incidence rates for FES are presented in Table 1 and Figure 1. Age-specific incidence rates showed a significant increase with age in males and females. Incidence rates were lower in women than in men except from the group between 45 and 54 years of age. Crude annual incidence rate for FES was 2.16 (95% CI 2.00 to 2.32) for both sexes combined, 2.11 (95% CI 1.90 to 2.35) in men, and 2.21 (95% CI 1.99 to 2.45) in women. After age adjustment to the European population, the incidence rate per 1000 person-years for FES was 1.46 (95% CI 1.35 to 1.57) for both sexes combined, 1.63 for men (95% CI 1.46 to 1.81), and 1.29 for women (95% CI 1.15 to 1.43).

Crude incidence rates for subtypes of FES are shown in Table 2. Among patients with FES, 626 (86.3%) had IS, ICH was diagnosed in 65 patients (9.0%), and SAH in 17 patients (2.3%). Stroke subtype could not be determined in 17 patients (2.3%). Age-adjusted incidence rates were 1.25 (95% CI 1.14 to 1.35) for IS, 0.14 (95% CI 0.10 to 0.17) for ICH, 0.04 (95% CI 0.01 to 0.10) for SAH, and 1.63 (95% CI 1.56 to 1.70) for both sexes combined.

**Table 1. Age- and Sex-Specific, Crude- and Age-Adjusted Incidence Rates of FES/1000 Person-Years, 2006 to 2007**

<table>
<thead>
<tr>
<th>Age Group, Years</th>
<th>Cases (Population)</th>
<th>Rate (95% CI)</th>
<th>Cases (Population)</th>
<th>Rate (95% CI)</th>
<th>Cases (Population)</th>
<th>Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–24</td>
<td>0 (21 985)</td>
<td>...</td>
<td>0 (21 545)</td>
<td>...</td>
<td>0 (43 530)</td>
<td>...</td>
</tr>
<tr>
<td>25–34</td>
<td>2 (11 193)</td>
<td>0.09 (0.01–0.32)</td>
<td>2 (11 068)</td>
<td>0.09 (0.01–0.32)</td>
<td>4 (22 261)</td>
<td>0.09 (0.02–0.23)</td>
</tr>
<tr>
<td>35–44</td>
<td>8 (14 744)</td>
<td>0.27 (0.12–0.53)</td>
<td>6 (13 065)</td>
<td>0.23 (0.08–0.5)</td>
<td>14 (27 809)</td>
<td>0.25 (0.14–0.42)</td>
</tr>
<tr>
<td>45–54</td>
<td>32 (12 370)</td>
<td>1.29 (0.88–1.82)</td>
<td>34 (11 571)</td>
<td>1.47 (1.02–2.09)</td>
<td>66 (23 941)</td>
<td>1.38 (1.08–1.78)</td>
</tr>
<tr>
<td>55–64</td>
<td>68 (9232)</td>
<td>3.68 (2.88–4.75)</td>
<td>44 (9180)</td>
<td>2.40 (1.74–3.26)</td>
<td>112 (18 412)</td>
<td>3.04 (2.51–3.68)</td>
</tr>
<tr>
<td>65–74</td>
<td>101 (8723)</td>
<td>5.79 (4.74–6.95)</td>
<td>93 (9661)</td>
<td>4.80 (3.90–5.90)</td>
<td>194 (18 404)</td>
<td>5.27 (4.56–6.10)</td>
</tr>
<tr>
<td>75–84</td>
<td>110 (4040)</td>
<td>13.61 (11.24–16.47)</td>
<td>122 (6429)</td>
<td>9.49 (7.91–11.26)</td>
<td>232 (10 469)</td>
<td>11.08 (9.72–12.67)</td>
</tr>
<tr>
<td>&gt;85</td>
<td>29 (730)</td>
<td>19.86 (13.31–28.60)</td>
<td>74 (2350)</td>
<td>15.74 (12.43–19.83)</td>
<td>103 (3080)</td>
<td>16.72 (13.71–20.06)</td>
</tr>
<tr>
<td>Total</td>
<td>350 (83 017)</td>
<td>2.11 (1.90–2.35)</td>
<td>375 (84 889)</td>
<td>2.21 (1.99–2.45)</td>
<td>725 (167 906)</td>
<td>2.16 (2.00–2.32)</td>
</tr>
<tr>
<td>ASR</td>
<td>1.63 (1.46–1.81)</td>
<td>1.29 (1.15–1.43)</td>
<td>1.46 (1.35–1.57)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ASR indicates age-standardized rates adjusted to the European population.

---

**Figure 1. Age-specific incidence of FES in 3 population-based stroke registers in patients <75 years of age.**
CI 0.02 to 0.07) for SAH, and 0.04 (95% CI 0.02 to 0.07) for undetermined strokes.

Data on case-fatality could be obtained in 98.2% of all FES. Case-fatality rate was 13.6% (95% CI 12.6 to 14.7) at 28 days, 16.4% (95% CI 15.2 to 17.7) at 3 months, and 23.2% (95% CI 21.6 to 25.0) at 12 months. According to stroke subtype, case-fatality rates for IS were 9.7% (95% CI 9.0 to 10.5) at 28 days, 12.1% (95% CI 11.2 to 13.1) at 3 months, and 19.8% (95% CI 18.3 to 21.4) at 12 months. Case-fatality rates for ICH were 29.7% (95% CI 23.0 to 38.2) at 28 days, 37.5% (95% CI 29.1 to 40.3) at 3 months, and 39.1% (95% CI 30.3 to 50.3) at 12 months. In patients with SAH, the case-fatality rate was 31.3% (95% CI 17.9 to 50.6) at 28 days and remained the same at 3 and 12 months. The case-fatality rate for undetermined strokes was 86.7% (95% CI 48.5 to 100.0) at 28 days and 3 and 12 months (Figure 2).

Discussion

Epidemiological data on stroke in Germany are scarce and this study is only the second population-based stroke register without any age restriction in our country. LuSSt was initiated to provide up-to-date information on stroke incidence and case-fatality rates and to test the hypothesis of a relatively high stroke incidence, particularly among younger age groups, in the industrial city of Ludwigshafen am Rhein. The register should furthermore represent the basis for studies on the cause of any increased incidence. We used a hot-pursuit approach and prospectively assessed all patients suspected of having a TIA or stroke in a defined and stable population for 2 complete years. Finally, only those patients with a definite diagnosis of stroke or TIA were included. Patients with TIA were registered not to miss patients with mild strokes. Diagnosis of stroke was based on the World Health Organization definition and therefore on clinical data. We are aware of recent changes in tissue-based definition of stroke and TIA. However, the availability of imaging resources varies between different epidemiological studies and incidence rates have to be comparable between studies. We only deviated from the aforementioned definitions in patients treated with thrombolysis and diagnosed a stroke in

### Table 2. Crude Annual Incidence/1000 Person-Years for Pathological Subtypes of FES, 2006 to 2007

<table>
<thead>
<tr>
<th>Stroke Subtype</th>
<th>Men</th>
<th>Women</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>IS</td>
<td>299/83 017 1.80 (1.61–2.02)</td>
<td>327/84 889 1.93 (1.73–2.16)</td>
<td>626/167 906 1.86 (1.72–2.01)</td>
</tr>
<tr>
<td>ICH</td>
<td>36/83 017 0.22 (0.15–0.31)</td>
<td>29/84 889 0.17 (0.11–0.24)</td>
<td>65/167 906 0.19 (0.15–0.24)</td>
</tr>
<tr>
<td>SAH</td>
<td>7/83 017 0.04 (0.02–0.08)</td>
<td>10/84 889 0.06 (0.03–0.11)</td>
<td>17/167 906 0.05 (0.03–0.08)</td>
</tr>
<tr>
<td>UND</td>
<td>8/83 017 0.05 (0.02–0.10)</td>
<td>9/84 889 0.05 (0.02–0.10)</td>
<td>17/167 906 0.05 (0.03–0.08)</td>
</tr>
<tr>
<td>Total</td>
<td>350/83 017 2.11 (1.90–2.35)</td>
<td>375/84 889 2.21 (1.99–2.45)</td>
<td>725/167 906 2.16 (2.00–2.32)</td>
</tr>
</tbody>
</table>

ASR indicates age-standardized rates adjusted to the European population; UND, undetermined stroke.
these patients even if symptoms completely resolved within 24 hours. Because symptoms did not completely resolve in any of the patients with thrombolysis (8.3% of first-ever ischemic strokes) within 24 hours, this modification did not relevantly influence the incidence rates.

We made strong efforts to ensure completeness of case ascertainment and used multiple overlapping sources of information, including reviews of hospital admission and discharge data, regular contacts to hospitals outside of the city limit, general practitioners, cardiologists, and neurologists, nursing and residential homes, and emergency services and evaluated death certificates. Our study adhered to the criteria for "ideal" population-based stroke studies with the exception that no screening was performed among nonhospital-based radiologists. Basic data (eg, hospitalization rate, rate of neuroimaging) are in line with those of other stroke registers, specifically those operating in the same healthcare system.\textsuperscript{10,12} We are confident to have achieved almost complete case ascertainment. However, the possibility of underassessment, especially of nonhospitalized patients, cannot be completely ruled out.

Differences in total stroke incidence can be observed between countries and even within the same country.\textsuperscript{13} The higher crude stroke incidence in LuSSt (2.16/1000) as compared with the only previous German study (Erlangen Stroke Project [ESPro] 1994 to 1996; 1.74/1000) is largely explained by the increasing age in the population between the observation periods and reflects the growing burden of stroke in our societies.

Compared with other recently published registers in Central, Northern, and Western Europe, incidence rates were significantly higher or tended to be higher in the age groups between 45 and 54 years (LuSSt 2006 to 2007: 1.38, 95% CI 1.08 to 1.78; Oxford Vascular StudyOXVASC; 2002 to 2004: 0.64, 95% CI 0.36 to 1.05, P = 0.006 as compared with LuSSt; Lund [Lund Stroke Register; 2001 to 2002]: 0.70, 95% CI 0.46 to 1.06, P < 0.001; Erlangen [ESPro: 1994 to 1996]; 1.05, 95% CI 0.73 to 1.45, P = 0.27) and between 55 and 64 years (LuSSt: 3.04, 95% CI 2.51 to 3.68; Oxford: 1.76, 95% CI 1.21 to 2.47, \textit{P} = 0.006; Lund: 2.33, 95% CI 1.80 to 2.97, P < 0.001; Erlangen: 1.96, 95% CI 1.50 to 2.52, P = 0.002; Figure 1).\textsuperscript{8,10,13} Incidence rates were similar compared with those studies for the other age groups.

Regarding data from Eastern Europe, incidence rates are similar to those from Tartu, Estonia (2001 to 2003; 45 to 64 years: 1.18, 95% CI 0.77 to 1.73, \textit{P} = 0.49; 55 to 64 years: 2.78, 95% CI 2.11 to 3.59, \textit{P} = 0.57) and tend to be lower than those observed in Uzhgorod, Ukraine (1999 to 2000; 45 to 54 years: 3.78, 95% CI 2.97 to 4.8, \textit{P} = 0.07; 55 to 64 years: 7.44, 95% CI 5.94 to 9.3, \textit{P} = 0.16).\textsuperscript{14,15} In all comparisons, the different study periods need to be observed.

Recent European stroke registers showed relatively low age-adjusted stroke incidence rates in Western Europe but higher rates in Eastern Europe.\textsuperscript{16,17} Incidence rates in Ludwigshafen am Rhein were higher or tended to be higher compared with those recently observed in Western and Central Europe (eg, 0.99, 95% CI 0.92 to 1.06 in Dijon, France, 2000 to 2004; 1.34 95% CI 0.99 to 1.68 in Erlangen, Germany).\textsuperscript{10,18} They were similar to those in Northern Europe (1.44, 95% CI 1.30 to 1.58 in Lund, Sweden)\textsuperscript{13} and tended to be lower than those from Eastern Europe (1.64, 95% CI 1.44 to 1.85 in Tartu, Estonia).\textsuperscript{14} These results support our initial hypothesis of a relatively high stroke incidence in the city of Ludwigshafen compared with other Central and Western European registers, particularly among younger age groups. Variations in stroke incidence between countries and regions are influenced by many factors, including lifestyle and socioeconomic variables, differences in healthcare systems, and genetic factors.\textsuperscript{19} Ludwigshafen am Rhein is an industrial city with the world’s largest chemical plant and several other plants within its city area. Age and sex distribution of its population (mean age 42.2 years; 50.5% female) is representative for the German population (mean age 43.7 years; 51.0% female). The unemployment rate (2006 [mean percentage] Ludwigshafen 11.4%; whole Germany 9.6%) and the rate of non-German residents (2006: Ludwigshafen 19.7%; whole Germany 8.8%) is higher and the percentage of highly qualified professionals is lower here than on German average.\textsuperscript{20} Certainly, these data are rather typical for many industrial cities in Germany. We hypothesize that socioeconomic and associated lifestyle factors are dominant in contributing to the relatively high local stroke incidence mainly among younger age groups. However, further analyses are required to test this hypothesis.

Regarding stroke subtypes, age-adjusted rates for ICH (0.14, 95% CI 0.10 to 0.17) were in range with those previously reported by other European Stroke Registers (Erlangen: 0.19, 95% CI 0.15 to 0.24; South London: 0.16, 95% CI 0.13 to 0.19; Dijon: 0.07, 95% CI 0.04 to 0.09).\textsuperscript{10,12,17,18} Results in IS mainly contributed to relatively high age-adjusted incidence rates for FES in our study (1.25 95% CI 1.14 to 1.35; Erlangen: 1.06 95% CI 0.95 to 1.16; South London: 0.86 95% CI 0.79 to 0.93; Dijon: 0.87 95% CI 0.79 to 0.92).\textsuperscript{17} A recent comparative study also showed that variations in stroke incidence between different European regions were mainly related to differences in incidence of IS.\textsuperscript{16}

Crude case-fatality rates for FES were clearly lower than those reported by the German stroke register from Erlangen approximately 10 years ago (13.6%, 16.4%, 23.2% [28 days, 3 months, 1 year]; Ludwigshafen 2006 to 2007) versus 19.4%, 28.5%, and 37.3% (Erlangen 1994 to 1996).\textsuperscript{10} This difference reflects improvements in stroke care during the last decade, mainly due to the establishment of stroke units. More recent studies showed similar (Lund 2001 to 2002: Day 28: 14.3%, 1 year: 23.7%)\textsuperscript{13} or even somewhat lower case-fatality rates (Dijon 2000 to 2004: Day 28: 10.0%).\textsuperscript{18} In particular, a strong decline can be seen in ICH mortality (LuSSt 2006 to 2007: Day 28 29.7% versus ESPRO 1994 to 1996 41.6%; Dijon 1985 to 1989 42.6% versus 2000 to 2004 24.5%).\textsuperscript{10,18} As mentioned, we found higher incidence rates mainly in younger patients with stroke, a group of patients with usually lower mortality rates after stroke.\textsuperscript{18} This might also have influenced case-fatality rates in our study.

Conclusions

The incidence of first-ever stroke in the city of Ludwigshafen is slightly higher than in other recently published registers from Central and Western Europe, particularly regarding IS.
High incidences were mainly found in the age groups from 45 to 54 and 55 to 64 years in our register. The cause of this increased incidence has to be elucidated by further studies. Case-fatality rates were in line with those from recently published population-based stroke studies.

**Acknowledgments**

We gratefully acknowledge the very valuable help by Evelyn Kyak who participated as study nurse in this study.

**Sources of Funding**

The Ludwigshafener Stroke Register received unrestricted funding by Boehringer Ingelheim, Sanofi-Aventis, and BASF. Data analysis was supported by a grant from the Deutsche Forschungsgemeinschaft (DFG; GR1102/6-1). LuSSt is part of the German Competence Network Stroke.

**Disclosures**

None.

**References**

Stroke Incidence and Survival in Ludwigshafen am Rhein, Germany: The Ludwigshafen Stroke Study (LuSSt)
Frederick Palm, Christian Urbanek, Steffen Rose, Florian Buggle, Barbara Bode, Michael G. Hennerici, Kirsten Schmieder, Gerhard Inselmann, Rainer Reiter, Robert Fleischer, Karl-Otto Piplack, Anton Safer, Heiko Becher and Armin J. Grau

Stroke. 2010;41:1865-1870; originally published online August 5, 2010;
doi: 10.1161/STROKEAHA.110.592642

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/41/9/1865