Baseline characteristics, secondary prevention and outcome after acute is-chaemic stroke in three different socioeconomic environments in Europe

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Abstract:	Background: The differences in vascular risk factors' and stroke burden across Europe are notable, however there is limited understanding of the influence of socioeconomic environ-ment on the quality of secondary prevention and outcome after acute ischaemic stroke. Methods: In this observational multicenter cohort study, we analyzed

	baseline characteris-tics, reperfusion treatment, outcome and secondary prevention in patients with acute is-chaemic stroke from three tertiary-care teaching hospitals with similar service population size in different socioeconomic environments: Bern/CH/n=293 (high-income), Gdansk/PL/n=140 (high-income) and Lutsk/UA/n=188 (lower-middle-income). Results: We analyzed 621 patients (43.2% women, median age=71.4y), admitted between 07-12/2019. Significant differences were observed in median BMI (CH=26/PL=27.7/UA=27.89), stroke severity [(median NIHSS CH=4(0-40)/PL=11(0-33)/UA=7(1-30)], initial neuroimaging (CT:CH=21.6%/PL=50.7%/UA=71.3%), conservative treatment (CH=34.1%/PL=38.6%/UA=95.2%) (each p<0.001), in arterial hypertension (CH=63.8%/PL=72.6%/UA=87.2%), atrial fibrillation (CH=28.3%/PL=41.4%/UA=39.4%), hy-perlipidaemia (CH=84.9%/PL=76.4%/UA=17%) (each p<0.001) and active smoking (CH=32.2%/PL=27.3%/UA=10.2%) (p<0.007). 3-months favourable outcome (mRS=0-2) was seen in CH=63.1%/PL=50%/UA=59% (unad-justed-p=0.01/adjusted-p CH-PL/CH-UA=0.601/0.981), excellent outcome (mRS=0-1) in CH=48.5%PL=32.1%/UA=27% (unadjusted-p<0.001/adjusted-p CH-PL/CH-UA=0.201/0.08 and adjusted-OR CH-UA=2.094). 3-months mortality was similar between groups (CH=17.2%/PL=15.7%/UA=4.8%) (unadjusted-p=0.71/adjusted-p CH-PL/CH-UA=0.087/0.24). 3-months recurrent stroke/TIA occurred in CH=3.1%/PL=10.7%/UA=3.1%, adjusted-p/OR CH-PL=0.038/0.318). 3-months follow-up medication intake rates were the same for antihypertensives. Statin/OAC intake was lowest in UA=67.1%/25.5% (CH=87.3%/39.2%/unadjusted-p<0.001/adjusted-p CH-UA=0.02/0.012/adjusted-OR CH-UA=2.326/2.18). Oral antidiabetics' intake was lowest in CH=10.8% (PL=15.7%/UA=16.1%/unadjusted-p=0.245/adjusted-p CH-PL/CH-UA=0.061/0.002/adjusted-OR CH-UA=0.249). Smoking rates decreased in all groups during follow up. Conclusions: Substantial differences in presentation, treatment and secondary prevention measures, are linked to a twofold difference in adjusted 3-months excellent outcome between Switzerland and Ukraine. This underscores the importance of socioeconomic factors that influence stroke outcomes, emphasizing the necessity for targeted interventions to address disparities in treatment and secondary prevention strategies.

CONTRIBUTIONS

MR Heldner had full access to all the data and take responsibility for the integrity of the data and the accuracy of the data analysis.

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DATA SHARING STATEMENT

Raw data of all patients included in this study can be made available upon request to the corresponding author and after clearance by the local ethics committee.

ETHICAL APPROVAL AND INFORMED CONSENT

The Bernese stroke registry was approved by the local ethics committee (KEK Bern 2016-01905) for quality control and research. Informed consent for study participation was waived by the ethics committee, and patients were informed about the registry and the potential use of their data for research. In accordance with the Swiss law, patients who refused the use of their data for research were excluded from the analysis. For patients from PL and UA, the study protocol and supporting material were approved by the local ethics committee and each patient signed a consent form for the use of their data for research. This study complied with the Declaration of Helsinki and data analyses followed Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

Baseline characteristics, secondary prevention and outcome after acute ischaemic stroke in three different socioeconomic environments in Europe

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ABSTRACT

Background: The differences in vascular risk factors' and stroke burden across Europe are notable, however there is limited understanding of the influence of socioeconomic environment on the quality of secondary prevention and outcome after acute ischaemic stroke.

Methods: In this observational multicenter cohort study, we analyzed baseline characteristics, reperfusion treatment, outcome and secondary prevention in patients with acute ischaemic stroke from three tertiary-care teaching hospitals with similar service population size in different socioeconomic environments: Bern/CH/n=293 (high-income), Gdansk/PL/n=140 (high-income) and Lutsk/UA/n=188 (lower-middle-income).

Results: We analyzed 621 patients (43.2% women, median age=71.4y), admitted between 07-12/2019. Significant differences were observed in median BMI (CH=26/PL=27.7/UA=27.89), stroke severity [(median NIHSS CH=4(0-40)/PL=11(0-33)/UA=7(1-30)], initial neuroimaging (CT:CH=21.6%/PL=50.7%/UA=71.3%), conservative treatment (CH=34.1%/PL=38.6%/UA=95.2%) (each p<0.001), in arterial hypertension (CH=63.8%/PL=72.6%/UA=87.2%), atrial fibrillation (CH=28.3%/PL=41.4%/UA=39.4%), hyperlipidaemia (CH=84.9%/PL=76.4%/UA=17%) (each p<0.001) and active smoking (CH=32.2%/PL=27.3%/UA=10.2%) (p<0.007).

3-months favourable outcome (mRS=0-2) was seen in CH=63.1%/PL=50%/UA=59% (unadjusted-p=0.01/adjusted-p CH-PL/CH-UA=0.601/0.981), excellent outcome (mRS=0-1) in CH=48.5%PL=32.1%/UA=27% (unadjusted-p<0.001/adjusted-p CH-PL/CH-UA=0.201/0.08 and adjusted-OR CH-UA=2.094). 3-months mortality was similar between groups (CH=17.2%/PL=15.7%/UA=4.8%) (unadjusted-p=0.71/adjusted-p CH-PL/CH-UA=0.087/0.24). 3-months recurrent stroke/TIA occurred in CH=3.1%/PL=10.7%/UA=3.1%, adjusted-p/OR CH-PL=0.038/0.318).

3-months follow-up medication intake rates were the same for antihypertensives. Statin/OAC intake was lowest in UA=67.1%/25.5% (CH=87.3%/39.2%/unadjusted-p<0.001/adjusted-p

CH-UA=0.02/0.012/adjusted-OR CH-UA=2.326/2.18). Oral antidiabetics' intake was lowest in CH=10.8% (PL=15.7%/UA=16.1%/unadjusted-p=0.245/adjusted-p CH-PL/CH-UA=0.061/0.002/adjusted-OR CH-UA=0.249). Smoking rates decreased in all groups during follow up.

Conclusions: Substantial differences in presentation, treatment and secondary prevention measures, are linked to a twofold difference in adjusted 3-months excellent outcome between Switzerland and Ukraine. This underscores the importance of socioeconomic factors that influence stroke outcomes, emphasizing the necessity for targeted interventions to address disparities in treatment and secondary prevention strategies.

INTRODUCTION

Stroke is the third-leading cause of death and disability combined in 2019 (measured in disability-adjusted life years (DALYs)) [1], posing a significant global challenge. The aging population contributes to an increased stroke burden [2,3,4], with a projected 31% increase in disability adjusted life-years by 2050 [3]. Despite a decline in age-adjusted stroke incidence rates, particularly in high-income countries [4,5,6,7], about 25% of patients experience recurrent ischaemic strokes within five years [8], leading to poor rehabilitation outcomes and cognitive impairment [9]. While tailored secondary prevention could reduce stroke recurrence risk by up to 80% [2], there remains limited data on the quality of secondary prevention and long-term outcome, particularly in less affluent European countries [2,10].

Differences in stroke burden across Europe are notable, with Eastern European countries facing higher stroke rates and related deaths [2,4], attributed to socioeconomic factors influencing vascular risk factors and healthcare access and quality [2,4,10,11]. Lower-income European countries encounter delays in patient assessment, limited access to interventions, and fewer lifestyle and atrial fibrillation monitoring programs [10]. Despite initiatives like the 2nd Helsingborg declaration having aimed at universal stroke unit access by 2015, significant discrepancies persist, with Eastern European countries lagging behind compared to Western European Countries [2,11]. Furthermore, it has been shown that Gross Domestic Product (GDP) per capita affects specialist care accessibility [10], and income levels impact secondary prevention [12].

The European Stroke Action Plan 2018-2030 [13] aims to address these challenges, necessitating a deeper understanding of care variability across European countries with different history, socioeconomic status and vascular risk. Switzerland, Poland and Ukraine exemplify this diversity, differing significantly in terms of GDP per capita, unemployment rates, and insurance coverage. Switzerland, on the one hand, is a representative of a highly developed Western European country. On the other hand, Poland and Ukraine are countries in Eastern Europe with less developed economic resources. It is worth noting that Poland has

been a member of the EU since 2004, which distinguishes it from Ukraine, a nation facing greater economic challenges and geopolitical complexity. Both countries were classified as high vascular risk countries [14,15,16].

This study aims to elucidate baseline characteristics, secondary prevention and outcome after first acute ischaemic stroke in different socioeconomic environments, i.e. Switzerland, Poland and Ukraine, providing insights into European stroke care.

METHODS

We conducted an observational multicenter cohort study of patients who experienced their first acute ischaemic stroke between July and December 2019 and received treatment at three tertiary care centers. In this study, we focused on AIS patients, excluding those with ICH. AIS represents the majority of strokes, with distinct pathophysiology and treatment approaches compared to ICH. Our study's aim was to investigate specific aspects of AIS, limiting our focus to this subtype. However, we recognize the importance of ICH and its impact on outcome. Future research could explore similar topics related to ICH.

Data for 293 patients from Bern, Switzerland (CH), 140 patients in Gdansk, Poland (PL), and 188 patients in Lutsk, Ukraine (UA) were consecutively collected from three prospective stroke registries. We gathered information on demographics, baseline characteristics, and vascular risk factors, including arterial hypertension, atrial fibrillation, diabetes mellitus, hyperlipidaemia, smoking status, and history of prior myocardial infarction. Vascular risk factors were defined based on a combination of patient records, raw values and medication intake (see supplementary table 2 for further details).

Clinical assessment was performed by a certified neurologist on admission using a standardized acute ischaemic stroke (AIS) protocol based on the AHA/ASA (American Heart Association/ American Stroke Association) 2019 guidelines [17] and included NIHSS (National Institutes of Health Stroke Scale) score in the emergency room and a detailed neurological examination on the ward or in the Stroke Unit [18]. Suspected clinical diagnosis of AIS was

confirmed by Magnetic Resonance Imaging (MRI) or Computed Tomography (CT). The diagnosis was made based on the AHA/ASA 2013 definition of ischaemic stroke [19].

Information in regard to initial therapy (conservative therapy, thrombolysis treatment, mechanical thrombectomy, decompressive craniectomy) and stroke aetiology classification according to the TOAST (Trial of ORG 10172 in Acute Stroke Treatment [20]) was collected from individual patient records. Also, in hospital treatment duration, hospital mortality, disability (measured with modified Rankin scale; mRS [21]) on discharge, discharge destination and discharge medication was assessed.

The follow-up parameters 3 months post-stroke were collected through clinical examinations by a board-certified neurologist, by telephone by a trained study nurse or extracted from external rehabilitation center reports. Data on the primary endpoint, outcome at discharge, were collected. Additionally, data on secondary endpoints, mRS at follow up, dichotomized into excellent (mRS 0-1), favourable (mRS 0-2) outcome, death, intake of secondary preventive medication and reported information on lifestyle behavior (dietary counseling, regular exercise, smoking status) and recurrence of stroke or TIA at 3 months were documented.

Detailed information on the definitions of variables is listed in supplementary table 1.

Statistical analysis

Statistical analysis was performed using SPSS 25.0 (SPSS Inc., Chicago, Illinois, USA). In univariable analysis, the χ2-test was applied for categorical variables and the ANOVA-test for ordinal and continuous variables to compare baseline characteristics and outcomes between patients from Switzerland (CH), Poland (PL) and Ukraine (UA). A 2-tailed p-value <0.05 was considered significant. Binary logistic regression and ordinal and linear regression analysis were performed for outcome analysis where appropriate. Regression analyses got adjusted

for the differences in admission NIHSS, and therapy, which differed significantly in comparison of baseline characteristics.

Standard protocol approvals, registrations, patient consent and reporting

The Bernese stroke registry was approved by the local ethics committee (KEK Bern 2016-01905) for quality control and research. Informed consent for study participation was waived by the ethics committee, and patients were informed about the registry and the potential use of their data for research. In accordance with the Swiss law, patients who refused the use of their data for research were excluded from the analysis. For patients from PL and UA, the study protocol and supporting material were approved by the local ethics committee and each patient signed a consent form for the use of their data for research. This study complied with the Declaration of Helsinki and data analyses followed Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines [22].

RESULTS

We included 293 patients from CH [128 (43.7%) women, median age 74.2 (20-97.4)], 140 from PL [54 (38.8%) women, median age 70 (18-85)] and 188 from UA [86 (45.7%) women, median age 71.4 (18-97.4)]. 19 Swiss and 6 Ukrainian patients were lost to follow-up, none from PL. Ukrainian and Polish patients had significantly higher median Body Mass Index (BMI) than Swiss patients ($p<0.001$). Pre-stroke mRS differed significantly between Polish and Swiss patients ($p<0.001$) (no data available for Ukrainian patients, since not routinely assessed) (Table 3). For socioeconomic and hospital characteristics of the three study centers see table 1 and 2.

Arterial hypertension and atrial fibrillation were found significantly more often in Ukrainian and Polish compared to Swiss patients ($p<0.007$). However, hyperlipidaemia and active/former vs. never smoking was significantly less often found in Ukrainian, compared to Polish and Swiss

patients (17% vs. 76.4% vs. 84.9%, p<0.001 and 40.1% vs. 60.4% vs. 56.7%, p<0.001) (Table 3).

Admission stroke severity differed significantly: Swiss patients had a median admission NIHSS of 4(0-36), Ukrainian 7(1-30), and Polish patients of 11(0-33) (p<0.001). Initial neuroimaging was significantly more often CT vs. MRI or both in UA (71.3%) and PL (50.7%) compared to in CH (21.6%) (p<0.001). Initial conservative vs. reperfusion treatment was applied to 95.2% of Ukrainian, compared to 34.1% of Swiss and 38.6% of Polish patients (p<0.001). Reperfusion treatment was most often mechanical thrombectomy (TBM) compared to intravenous thrombolysis with recombinant tissue Plasminogen Activator (rtPA) and both TBM and rtPA with 30.4% vs. 22.5% vs. 12.3% in Switzerland, 19.6% vs. 17.1% vs. 27.1% in Poland and 0.5% vs. 3.7% vs. 0.5% in Ukraine (p<0.001) (Table 3).

At discharge, excellent outcome was found in 47.1% of Swiss, 33.6% of Polish and 11.7% of Ukrainian patients (unadjusted-p<0.001, adjusted-p CH-PL=0.913, adjusted-p CH-UA<0.001, adjusted-OR CH-UA=6.03). Favourable outcome at discharge was found in 59.9% of Swiss, 51.4% of Polish and 36.7% of Ukrainian patients (unadjusted-p<0.001, adjusted-p CH-PL=0.195 and adjusted-p CH-UA=0.114). Hospital mortality did not differ significantly between groups. Discharge destination was most often home in PL (52.1%) and UA (84.1%) and to another acute care facility in CH (43.5%) (un-/adjusted-p<0.001). Median duration of hospitalization was 3.63 [0-59] days in CH, 8 [3-98] days in PL and 10 [1-32] days in UA (un-/adjusted-p<0.001) (Table 4). Medication prescription at discharge differed as follows: antihypertensive intake was higher in UA than PL and CH (92.6% vs. 81.7% vs. 65.3%, unadjusted-p<0.001, adjusted-p CH-PL/CH-UA=0.378/<0.001, adjusted OR CH-UA=0.149). Statins were significantly more often used in PL (unadjusted-p=0.002, adjusted-p CH-PL<0.001 and adjusted-OR CH-PL=0.186) (Table 4).

At 3 months follow-up, excellent outcome was seen in 48.5% Swiss, 32.1% Polish and 27% Ukrainian patients (unadjusted-p<0.001, adjusted-p CH-PL/CH-UA=0.201/0.008 and adjusted-OR CH-UA=2.094). Favourable outcome was seen in 63.1% Swiss, 50% Polish and

59% Ukrainian patients (unadjusted-p=0.01, adjusted-p CH-PL/CH-UA=0.601/0.981). Mortality did not differ significantly between groups.

Recurrent stroke or TIA occurred in 10.7% of Polish, 5% of Ukrainian and 3.1% of Swiss patients (unadjusted-p=0.152, adjusted-p CH-PL=0.038 and adjusted-OR CH-PL/CH-UA=0.318/0.709). Re-hospitalization for any reason (including causes unrelated to TIA/AIS) occurred in 16.4% of Swiss, 16.1% of Polish and in 4.3% of Ukrainian patients (unadjusted-p<0.001, adjusted-p CH-PL/CH-UA=0.914/<0.001 and adjusted-OR CH-UA=5.24) (Table 5).

At 3 months, follow-up medication intake rates were the same for antihypertensives in UA, CH and PL (89.4% vs. 83.9% vs. 86.4%, unadjusted-p=0.303, adjusted-p CH-PL/CH-UA=0.092/0.217). However, statin and oral anticoagulants (OAC) intake was lower in UA than in CH and PL (67.1% vs. 87.3% vs. 87.3%, unadjusted-p<0.001, adjusted-p CH-PL/CH-UA=0.795/0.02 and adjusted-OR C-UA=2.326 and 25.5% vs. 39.2% vs. 41.5% unadjusted-p=0.006, adjusted-p CH-PL/CH-UA=0.892/0.012 and adjusted-OR CH-UA=2.18). Intake of oral antidiabetics was lowest in CH (10.8% vs. PL=15.7% vs. UA=16.1%, unadjusted-p=0.245, adjusted-p CH-PL/CH-UA=0.061/0.002 and adjusted-OR CH-UA=0.249).

Regular exercise was reported most often in UA at 3 months, but dietary counseling was given to only 19.9% of Ukrainian vs. 86.4% of Polish and 81% of Swiss patients (unadjusted-p<0.001, adjusted-p CH-PL/CH-UA=0.341/<0.001OR=0.046). Smoking rates in comparison to baseline decreased in all groups with 18.7% in CH, 13.7% in PL and 8.2% in UA (unadjusted-p<0.001, adjusted-p CH-PL/CH-UA=0.36/<0.001, adjusted OR CH-UA=8.66) (Table 5).

DISCUSSION

The main finding of this observational cohort study in 2019 shows a more than twofold difference in adjusted 3-months excellent outcome between high-income-country Switzerland and lower-middle-income country Ukraine. Data on acute ischaemic stroke patients in three different socioeconomic environments in teaching hospitals in Bern (Switzerland) (high-

income), Gdansk (Poland) (high-income) and Lutsk (Ukraine) (lower-middle-income) were collected and analyzed. The world bank classification of countries by GDP per capita defined high-income as GDP per capita of over 12'375$ in 2019. While the per capita GDP in Poland was 15'699.91$ in 2019, GDP per capita in Switzerland was more than 5 times higher at 84'121.93$ [23].

While the hospitals share similarities in carrying capacity, guideline compliance (as demonstrated by the prescription of guideline-based drugs at discharge) and research and teaching engagement, this study identified differences in baseline characteristics, reperfusion treatment, secondary prevention and outcome among the three cohorts.

Baseline characteristics

In our analysis, Polish patients had a higher pre-stroke mRS than Swiss patients. Data for Ukrainian patients were not available. This aligns with previous findings associating lower socioeconomic status (SES) with higher pre-stroke comorbidity rates [24,25].

Ukrainian and Polish compared to Swiss patients showed higher BMI, arterial hypertension, and atrial fibrillation prevalence, consistent with higher vascular risk factor burden in Eastern European countries, where these risk factors are often less effectively controlled [2,8,13,25, 26,27]. In contrast, our study revealed a lower prevalence of hyperlipidaemia among Ukrainians (17%) compared to Swiss (84.9%) and Polish (76.4%) patients, potentially due to differences in screening practices, diagnostic approaches, and disease awareness levels, but also underreporting in Ukraine [2,28]. Moreover, we observed a lower smoking prevalence among Ukrainians, particularly in women, possibly attributed to historical smoking patterns and anti-smoking measures implemented in UA since 2006, but also underreporting could have contributed to this observation [29].

Ukrainian patients presented with the highest median NIHSS score on admission, Swiss patients with the lowest. This disparity may be attributed to varying referral practices, as well as a higher prevalence of atrial fibrillation in Polish and Ukrainian patients in our cohorts,

potentially contributing to increased stroke severity [30]. Furthermore, a consistent association exists between lower socioeconomic status (SES) and increased stroke severity [31]. Also, this could be due to discrepancies in demograpics, healthcare structure and limited access to acute medical care for patients with minor stroke [2,10,32].

The initial neuroimaging technique differed significantly, with MRI more often used in CH compared to UA and PL, likely due to factors such as limited accessibility, availability, and the higher cost of MRI compared to CT [33]. Additionally, CT is favored in many places due to its shorter examination time.

Reperfusion treatment

Despite higher stroke severity, Ukrainian patients received intravenous thrombolysis and endovascular treatment less often than Swiss and Polish patients, possibly due to delayed hospital admission [2,29,34]. Delayed hospital admission often results from factors such as delayed stroke symptom recognition, organization of emergency services, and care protocol implementation [29]. Unfortunately, we have not registered time delays from last seen well or first seen sick to hospital arrival and treatment in our study.

Additionally, accessibility and availability of treatment may be have been limited in UA [13]. This was evident in 2019 during the reform of the healthcare system in UA. Insufficient funding and limited state provision led to low rates of intravenous thrombolysis (0.9%) and endovascular treatment (0.2%) in patients with acute ischaemic stroke [13]. Reimbursement initiatives by the National Health Service of UA in 2020 then resulted in an increase in reperfusion treatment, with intravenous thrombolysis rates increasing to 6.4% and of endovascular treatment to 0.7% [35]. Lutsk City Hospital, which participated in this study, reflected a similar trend, with 21.1% and 7.1% of all acute ischaemic stroke patients receiving reperfusion treatment. The substantial changes observed in UA highlight the dependence of stroke reperfusion treatment on SES. Nevertheless, it is still essential to validate the overall effect on mortality and morbidity through comprehensive analyses.

Outcome at discharge and 3 months

Previous studies found poorer functional outcome in patients with lower SES [32]. In our study, functional outcome at discharge showed differences in univariable analysis, but after adjustment for admission NIHSS score and treatment, only excellent outcome remained 6 times more likely in Swiss compared to Ukrainian patients. This could be partly associated with lower vascular risk factor burden in Swiss patients. At 3 months, excellent outcome in CH was around 1.5 times more likely than in PL and almost 1.8 times more likely than in UA, but only the difference between CH and UA was significantly different in the adjusted analysis. Mortality did not differ between groups. Overall, the association with SES and outcome after stroke is to some extent consistent with previous studies [32,36].

Also, recurrent stroke/TIA occurred around 70% less likely in Swiss compared to Polish patients, potentially liked to the higher prevalence of atrial fibrillation and comorbidities in the Polish patient cohort [30]. Feigin et al. (2014) reported a greater stroke burden in Eastern European countries, yet there is limited evidence concerning the association between SES and stroke recurrence [26,37].

In PL and UA, patients were most often discharged home, while in CH, they were transferred to another acute care facility. Some evidence suggests that higher SES serves as a determinant of postacute stroke rehabilitation, potentially explaining this variation [37]. Swiss patients experienced the shortest median first hospital stay, possibly attributed to efficient healthcare systems, streamlined processes, and prompt access to necessary post-acute stroke care services. However, despite a lower vascular risk factor burden, rehospitalization for any reason (including causes unrelated to TIA/AIS) within 3 months was approximately five times more frequent in Swiss patients compared to Ukrainian patients. This increased rate of rehospitalization may be influenced by factors such as closer post-acute monitoring or a higher threshold for readmission to ensure comprehensive medical care [10,28,32].

Secondary prevention

In our study, secondary prevention measures were implemented to a considerable extent across all three groups, with high intake rates of guideline-recommended medications. Statin intake at discharge were 80% less likely in CH than in PL, and antihypertensive intake was 70% less likely in CH than in UA. After 3 months, statin and OAC intake was twice as common, while oral antidiabetics' intake were 75% less likely in CH compared to UA. Some of these differences can only partly be explained by differences in vascular risk factor burden between cohorts. Previous research in UA indicated lower intake until follow-up to statins and OACs after vascular events, potentially influenced by socioeconomic factors such as income per capita, reimbursement, and insurance coverage [12]. Antihypertensive intake rates were high in all cohorts, showing no significant differences between groups.

At 3 months, regular exercise was reported most often in UA. However, dietary counseling was least frequently provided to Ukrainian compared to Polish and Swiss patients. Smoking rates decreased in all groups compared to baseline but remained around 9 times more likely in Swiss compared to Ukrainian patients. These differences could be linked to factors like differences in reporting and wage definition (e.g. of regular exercise), in cultural practices (e.g. of lifestyle), in healthcare infrastructure and in disease awareness levels (e.g. of hyperlipidaemia and unhealthy diet) [2,38,39].

Strengths

This study's primary strength lies in its type of multicenter data collection, enabling a direct comparison between hospitals with comparable service population and research engagement in three different socioeconomic environments. The comprehensive assessment of numerous parameters allowed not only the evaluation of outcome differences but also an exploration of distinctions between the tree populations, primarily influenced by socioeconomic factors. Beyond acute clinical practice, this study underscores the significance of such factors for secondary prevention and health outcomes. It aligns with the European Stroke Action Plan

2018-2030's framework for healthcare policy, research, and stroke services development, highlighting the need for a deeper understanding of the current state and diversity across European countries.

Limitations

The study's main limitation arises from patients not providing consent or being lost to follow-up or from missing variables , particularly regarding incomplete data on secondary prevention measures such as dietary counseling, smoking status and medication at 3 months. In addition, caution is required when extrapolating results from individual hospitals to entire European countries. The stroke centers participating in the study stand out in terms of quality compared to the national average. It can therefore be assumed that the national average for each country might be worse and these differences are likely to be greater the less affluent a country is. Furthermore, socioeconomic factors were not assessed at the individual patient level.

Also, the data collected in 2019 may not reflect current realities given the widespread adoption of therapies and socioeconomic changes due to the Covid-19 pandemic and the war in Ukraine. Future research should compare these data with current data to assess the evolution of stroke care amid these global events.

Conclusion

Substantial differences in presentation, treatment and secondary prevention measures, are linked to a twofold difference in adjusted 3-months excellent outcome between high and lower-middle-income countries. This underscores the importance of targeted interventions to address treatment and secondary prevention disparities.

The Stroke Alliance for Europe (SAFE) projects a 35% increase in stroke cases by 2035, necessitating comprehensive investment in primary and secondary prevention beyond acute care. The lack of comprehensive data, as seen in Ukrainian patients in our study [2], underscores the need for standardized pan-European data collection to guide intervention.

Addressing these socioeconomic disparities should be central to policy programmes aimed at reducing the burden of stroke in Europe and promote a more equitable healthcare system

CONTRIBUTIONS

MR Heldner had full access to all the data and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Interpretation of data: All co-authors.

Drafting of the manuscript: C Berger, H Hammer and MR Heldner.

Critical revision of the manuscript for important intellectual content: All co-authors.

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CONFLICTS OF INTEREST/ DISCLOSURES

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All other co-authors report no disclosures directly related to this manuscript.

DATA SHARING STATEMENT

Raw data of all patients included in this study can be made available upon request to the corresponding author and after clearance by the local ethics committee.

ETHICAL APPROVAL AND INFORMED CONSENT

The Bernese stroke registry was approved by the local ethics committee (KEK Bern 2016-01905) for quality control and research. Informed consent for study participation was waived by the ethics committee, and patients were informed about the registry and the potential use of their data for research. In accordance with the Swiss law, patients who refused the use of their data for research were excluded from the analysis. For patients from PL and UA, the study protocol and supporting material were approved by the local ethics committee and each patient signed a consent form for the use of their data for research. This study complied with the Declaration of Helsinki and data analyses followed Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

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TABLES

Table 1: Socioeconomic situation in Bern (Switzerland), Gdansk (Poland), Lutsk (Ukraine) in 2019

	Switzerland	Poland	Ukraine
GDP per capita	84'121 USD	15'699.91 USD	3'661.46 USD
Unemployment rate	4.39%	3.28%	8.19%
Rate of stroke units per million inhabitants	2.21	4.59	0.14

Data sources: Swiss Federal Statistical Office (www.bfs.admin.ch), Central Statistical Office of Poland (www.stat.gov.pl) and Ukraine Government Website (), Aguiar de Sousa et.al 2019 [40].

Table 2: Hospital characteristics and services of three different study centers in Bern (Switzerland), Gdansk (Poland), Lutsk (Ukraine) in 2019

	Bern (Switzerland)	Gdansk (Poland)	Lutsk (Ukraine)
Total number of beds	926	1200	715
Number of beds of the neurology department	132	50	65
Total no of acute stroke patients	1313	621	625
Catchment area	1.5 Million people	500'000 people	216'887 people

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Number of beds of the neurology department	132	50	65
Total no of acute stroke patients	1313	621	625
Hospital population area	1.5 Million people	500'000 people	216'887 people

Data sources: Swiss Federal Statistical Office (www.bfs.admin.ch), Central Statistical Office of Poland (www.stat.gov.pl) and Ukraine Government Website (www.lutsk.ukrstat.gov.ua).

Table 3: Baseline characteristics, Risk factors, Diagnostics and reperfusion treatment [n (%)]

	Bern (Switzerland) , n=293	Gdansk (Poland), n=140	Lutsk (Ukraine), n=188	p-value (Pearson)
Sex [n (%)]				0.45
Male	165 (56.3%)	85 (61.2%) †	102 (54.3%)	
Female	128 (43.7%)	54 (38.8%)†	86 (45.7%)	
BMI [median (range)]	26.01 (15.92-46.9)	27.68 (19.53-42.52)	27.79 (17.99-49.9)	<0.001
Age [y] [median (range)]	74.2 (20-97.4)	70 (18-85)	71.4 (18-97.4)	0.060
Time of the day [n (%)]				0.534
Day	227 (77.5%)	102 (72.9 %)	140 (74.5%)	
Wake up stroke	66 (22.5%)	38 (27.1 %)	48 (25.5%)	
Pre mRS [n (%)]			No data collected	<0.001
0	179 (62.8%)†	61 (43.6%)	No data collected	
1	47 (16.5%)†	42 (30%)	No data collected	
2	17 (6.0%)†	26 (18.6%)	No data collected	
3	27 (9.5%)†	9 (6.4%)	No data collected	
4	14 (4.9%)†	2 (1.4%)	No data collected	
5	1 (0.4%)†	0 (0%)	No data collected	
Atrial fibrillation	83 (28.3%)	58 (41.4%)	74 (39.4%)	0.007
Diabetes mellitus	66 (22.6%)	26 (18.6%)	37 (19.7%)	0.578
Arterial hypertension	187 (63.8%)	102 (72.6%)	164 (87.2%)	<0.001
Hyperlipidaemia	248 (84.9%)	107 (76.4%)	32 (17.0%)	<0.001
Post myocardial infarction	24 (8.2%)	21 (15%)	26 (13.8%)	0.057
Smoking status				<0.001
Never smoker	101 (43.3%)†	55 (39.6%)†	106 (59.9%)†	
Active smoker	75 (32.2%)%)†	38 (27.3%)†	18 (10.2%)†	
Former smoker	57 (24.5%)†	46 (33.1%)†	53 (29.9%)†	
NIHSS initial [median (range)]	4 (0-36)	11 (0-33)	7 (1-30)	<0.001
0-9 (mild stroke)	202 (70.9%)	65 (46.4%)	113 (62%)	<0.001

≥ 10 (moderate/severe stroke)	75 (29.1%)	75 (53.6%)	75 (39.9%)	<0.001
Initial neuroimaging				<0.001
MRI	145 (51.1%)†	22 (15.7%)	31 (16.5%)	
CT	74 (26.1%)†	71 (50.7%)	134 (71.3%)	
Both	65 (22.9%)	47 (33.6%)	23 (12.2%)	
Etiology TOAST				0.37
Cardioembolism	107 (36.6%)	61 (43.6%)	71 (37.8%%)	
No Cardioembolism	185 (48.6%)	79 (56.4%)	117 (62.2%)	
Therapy				<0.001
Conservative	100 (34.1%)	54 (38.6%)	179 (95.2%)	
Intravenous thrombolysis with rtPA only	66 (22.5%)	24(17.1%)	7 (3.7%)	
TBM only	89 (30.4%)	22 (19.6%)	1 (0.5%)	
Craniectomy only	2 (0.7%)	2 (1.4%)	0 (0%)	
Both rtPA and TBM	36 (12.3%)	38 (27.1%)	1 (0.5%)	
rtPA, TBM and Craniectomy	0 (0%)	1 (0.7%)	0 (0%)	

†*Note: Sex n=139, data on 1 Polish patient missing, Pre-mRS n=285, data of 8 Swiss patients missing, Smoking status CH n=233, data of 60 Swiss patients missing, PL n= 139, data of 1 Polish patient missing, UA=177, data of 11 Ukrainian patients missing, Initial Neuroimaging n=284, data of 9 Swiss patients missing*

Table 4: Outcome at discharge and medication at discharge

	Bern (Switzerland), n=293	Gdansk (Poland), n=140	Lutsk (Ukraine), n=188	p-value (Pearson)	p-value (controlled CH PL)	Odds ratio, CH PL 95%CI	p-value (controlled CH UA)	Odds ratio, CH UA 95%CI
mRS discharge								
Excellent 0-1	126 (47.1%)†	47 (33.6%)	22 (11.7%)	<0.001	0.913	1.029 (0.61-1.73)	<0.001	6.03 (3.19-11.4)
Favourable 0-2	158 (59.9%)†	72 (51.4%)	69 (36.7%)	<0.001	0.195	0.707 (0.42-1.2)	0.114	1.611 (0.89-2.91)
Dead 6	24 (9.1%)†	16 (11.4%)	12 (6.4%)	0.454	0.785	1.105 (0.54-2.27)	0.857	0.894 (0.26-3.05)
Mortality in hospital	24 (8.2%)	16 (11.4%)	12 (6.4%)	0.261	0.861	0.938 (0.46-1.91)	0.645	0.754 (0.23-2.51)

Discharge destination				<0.001	<0.001		<0.001	<0.001
Home	66 (22.6%)†	73 (52.1%)	148 (84.1%)					
Rehabilitation	71 (24.3%)†	38 (27.1%)	28 (15.9%)					
Nursing facility	4 (1.4%)†	13 (9.3%)	0 (0%)					
Other acute care hospital	127 (43.5%)†	0 (0%)	0 (0%)					
Dead	24 (8.2%)†	16 (11.4%)	12 (6.4%)					
Duration first hospital [days] [median (range)]	3.63 days (0-59 days)	8 days (3-98 days)	10 days (1-32)	<0.001	<0.001	NA	<0.001	NA
Antihypertensives	173 (65.3%)†	102 (81.7%)	163 (92.6%)	<0.001	0.378	0.903 (0.72-1.13)	<0.001	0.149 (0.07-0.3)
OAC	83 (30.8%)†	41 (32.8%)	56 (31.8%)	0.925	0.969	0.991 (0.62-1.59)	0.748	1.901 (0.64-1.86)
Antiplatelets	181 (67.3%)†	89 (71.2%)	115 (65.3%)	0.560	0.267	0.762 (0.47-1.23)	0.581	1.159 (0.69-1.96)
Statin	224 (86.2%)†	120 (96%)	152 (86.9%)	0.002	<0.001	0.186 (0.07-0.49)	0.686	0.865 (0.43-1.75)
Oral antidiabetics	31 (11.5%)†	18 (14.4%)	29 (16.5%)	0.312	0.152	0.616 (0.32-1.2)	0.826	0.394 (0.19-8.3)
Insulin	25 (9.6%)†	10 (8%)	8 (4.5%)	0.178	0.549	1.274 (0.58-2.82)	0.11	2.27 (0.83-6.22)

Note: For 18 Swiss patients, 15 Polish patients and for 12 Ukrainian patients, who died during in hospital care no medication was assessed.
†mRS discharge n=264, data of 39 Swiss patients missing, Discharge destination n=292, data of 1 Swiss patient missing, Antihypertensives n=265, data of 10 Swiss patients missing, OAC, Antiplatelets, Statin, Oral antidiabetics, Insulin n=270, data of 5 Swiss patients missing

Table 5: Follow-up at 3 months

Follow-up 3 months [n (%)]	Bern (Switzerland), n=293	Gdansk (Poland), n=140	Lutsk (Ukraine), n=188	p-value (Pearson)	p-value (controlled CH PL)	Odds ratio, CH PL 95%CI	p-value (controlled CH UA)	Odds ratio, CH UA 95%CI
mRS								
Excellent 0-1	133 (48.5%)†	45 (32.1%)	48 (27%)†	<0.001	0.201	1.369 (0.85-2.21)	0.008	2.094 (1.209-3.627)
Favourable 0-2	173 (63.1%)†	70 (50%)	105 (59%)†	0.01	0.601	1.137 (0.70-1.84)	0.981	1.007 (0.548-1.853)

Dead 6	47 (17.2%)†	22 (15.7%)	9 (4.8%)	0.71	0.087	1.703 (0.93-3.14)	0.24	1.837 (0.666-5.069)
Stroke/TIA	7 (3.1%)†	13 (10.7%)†	8 (5%)†	0.152	0.038	0.318 (0.108-0.938)	0.709	0.747 (0.162-3.441)
Re-Hospitalization	35 (16.4%)	19 (16.1%)	7 (4.3%)	<0.001	0.914	0.965 (0.51-1.84)	<0.001	5.24 (1.96-14.02)
Medication			n=161					
Antihypertensives	177 (83.9%)†	102 (86.4%),	144 (89.4%)†	0.303	0.092	0.755 (0.55-1.05)	0.217	0.601 (0.27-1.35)
OAC	83 (39.2%)†	49 (41.5%)	41 (25.5%)†	0.006	0.892	0.967 (0.6-1.57)	0.012	2.18 (1.91-3.99)
Antiplatelets	134 (63.5%)†	66 (55.9%)	109 (67.7%)†	0.130	0.261	1.322 (0.81-2.15)	0.668	0.879 (0.49-1.59)
Statin	185 (87.3%)†	103 (87.3%)	108 (67.1%)†	<0.001	0.795	1.1 (0.54-2.26)	0.02	2.326 (1.14-4.73)
Oral antidiabetics	23 (10.8%)†	19 (15.7%)	26 (16.1%)†	0.245	0.061	0.508 (0.25-1.03)	0.002	0.249 (0.10-0.61)
Insulin	11 (5.2%)†	7 (6.3%)	4 (2.5%)†	0.310	0.902	0.937 (0.33-2.64)	0.8	1.23 (0.24-6.27)
Regular Exercise 3m				<0.001	0.028		0.057	
Yes	53 (38.4%)†	62 (53%)†	100 (62.1%)†					
No	39 (28.3%)†	37 (31.6%)†	61 (37.9%)†					
Disability	46 (33.3%)†	18 (15.4%)†	0 (0%)†					
Dietary counseling	124 (81.0%)†	101 (86.3%)†	32 (19.9%)†	<0.001	0.341	1.405 (0.7-2.83)	<0.001	0.046 (0.02-0.10)
Active smoking	29 (18.7%)†	16 (13.7%)†	4 (8.2%)†	<0.001	0.36	1.387 (0.69-2.8)	<0.001	8.663 (2.51-29.85)

Note: for 47 patients from Switzerland and for 22 from Poland and 9 from Ukraine, who had died until the follow-up, no data besides mRS was assessed.
†mRS-3months CH n=274, data of 19 Swiss patients missing, UA n=178, data from 10 Ukrainian patients missing, Stroke/TIA CH n=225, data of 21 Swiss patients missing, PL n=108, data of 10 Polish patients missing, UA n=161, data of 19 Ukrainian patients missing, Re-Hospitalization CH n=214, data of 32 Swiss patients missing, UA n=161, data of 19 Ukrainian patients missing, Medication UA n=161, data of 18 Ukrainian patients missing, Antihypertensives CH n=211, data of 35 Swiss patients missing, OAC CH n=212, data of 34 Swiss patients missing, Antiplatelets CH n=211, data of 35 Swiss patients missing, Statin, Oral Antidiabetics CH n=212, data of 34 Swiss patients missing, Insulin CH n=211, data of 35 Swiss patients missing, Regular exercise CH n=117, data of 129 Swiss patients missing, PL n=117, data of 1 Polish patient missing , UA n=161, data of 19 Ukrainian patients missing, Dietary counseling CH n=152, data of 94 Swiss patients missing, PL n= 117, data of 1 Polish patient missing, UA n=161, data of 19 Ukrainian patients missing, Active smoking CH n=155, data of 91 Swiss patients missing, PL n=117, data of 1 Polish patient missing, UA n=161, data of 19 Ukrainian patients missing.

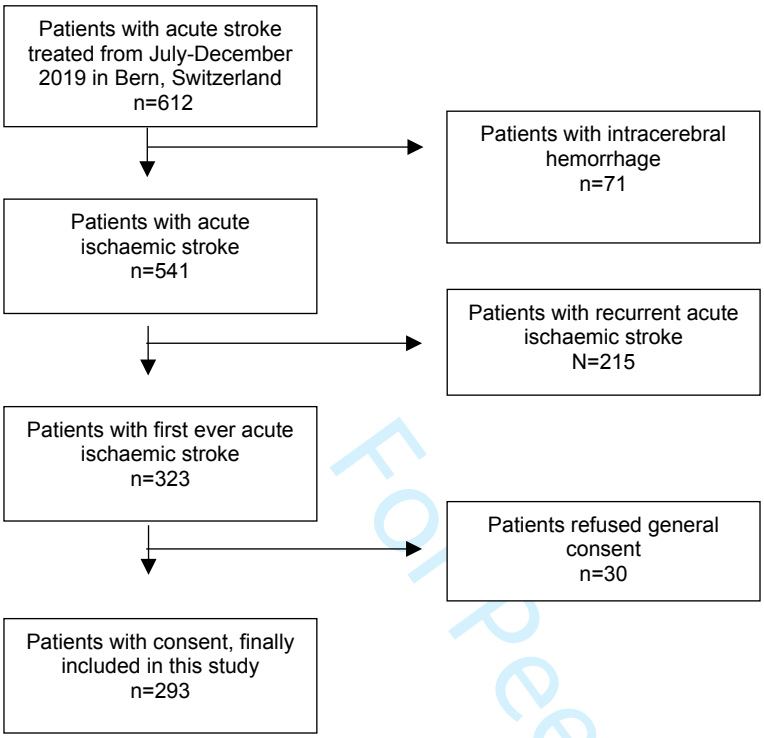
Supplementary file 1: table 1: Definitions of variables

Variable	Definition
Country	1=Poland, 2=Switzerland, 3=Ukraine
Age	In years
Sex	0=male, 1=female
Time of the day	1=7:00-22:00, 0=22:01-6:59
BMI	Weight [m]/(height [kg])^2
Pre mRS	0-6
Pre mRS excellent	mRS 0-1=1, mRS 2-6=0
Pre mRS favourable 0-2	mRS 0-2=1, mRS 3-6=0
Pre mRS dead	mRS 6=1, 1-5=0
NIHSS	0-42, assessed by a certified neurologist on admission
Stoke Severity	NIHSS 0-9=1, >9=0
Atrial Fibrillation	0=no, 1=yes, based on patient records, raw values (based on 12 lead ECG) and medication intake (OAC)
Diabetes Mellitus	0=no, 1=yes, based on patient records; raw values (fasting blood-glucose level of 126 mg/dl (7 mmol/L) or higher and/or random blood glucose level of 200 mg/dl (11.1 mmol/L) or higher); and medication intake (insulin and/or oral antidiabetics)
Arterial Hypertension	0=no, 1=yes, based on patient records, raw values (systolic blood-pressure of 140 mmHg and higher and/or diastolic blood-pressure of 90 mmHg or higher) and medication intake (antihypertensives)
Hyperlipidaemia	0=no, 1=yes, based on patient records, raw values (total cholesterol of 240 mg/dL (6.2 mmol/L) or higher and/or low-density-lipoprotein LDL of 160 mg/dL (4.1 mmol/L) or higher) and medication intake (lipid lowering drugs)
Post myocardial infarction	0=no, 1=yes, based on patient records
Smoker active	0=no, 1=yes (current smoking or stopped <2 years ago), based on patient records and raw values
Smoker former	0=no, 1=yes (stopped smoking $\geq$ 2 years ago), based on patient records and raw values
Never smoker	0=no, 1=yes, based on patient records and raw values
Initial neuroimaging	1=MRI, 2=CT, 3=both
Therapy	1=conservative, 2= Intravenous thrombolysis with rtPA only, 3= Mechanical Thrombectomy (TBM) only, 4= Craniectomy only, 5= Both rtPA and TBM, 6= rtPA, TBM and Craniectomy

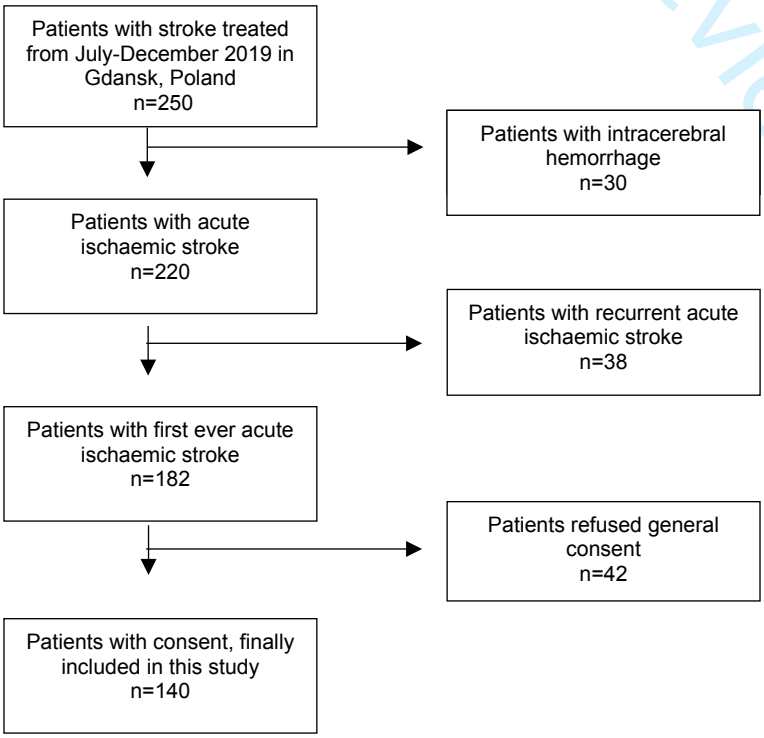
Etiology TOAST	0= no cardioembolism, 1= cardioembolism
mRS discharge	0-6
mRs discharge excellent	mRS 0-1=1, mRS 2-6=0
mRS discharge favourable	mRS 0-2=1, mRS 3-6=0
mRS discharge mortality	mRS 6=1, 1-5=0
Mortality in hospital	0=no, 1=yes
Duration first hospital	In days
Discharge destination	1=home, 2=rehabilitation, 3= nursing home, 4=other, 5=dead
OAC discharge	0=no, 1=yes
Antiplatelets discharge	0=no, 1=yes
Antihypertensives discharge	0=no, 1=yes
Statin discharge	0=no, 1=yes
Oral antidiabetics discharge	0=no, 1=yes
Insulin discharge	0=no, 1=yes
mRS 3months	0-6
mRS 3months excellent	mRS 0-1=1, mRS 2-6=0
mRS 3months favourable	mRS 0-2=1, mRS 3-6=0
mRS 3months mortality	mRS 6=1, 1-5=0
Stroke/TIA 3 months	0=no, 1=yes
Re-Hospitalisation 3 months	0=no, 1=yes
OAC 3 months	0=no, 1=yes
Antiplatelets 3 months	0=no, 1=yes
Antihypertensives 3 months	0=no, 1=yes
Statins 3 months	0=no, 1=yes
Oral antidiabetics 3 months	0=no, 1=yes
Insulin 3 months	0=no, 1=yes
Regular Exercise 3 months	0=no, 1=yes, 2=disability
Dietary counseling 3 months	0=no, 1=yes
Active smoking 3 months	0=no, 1=yes

Supplementary table 2: flow chart of in- and exclusion process

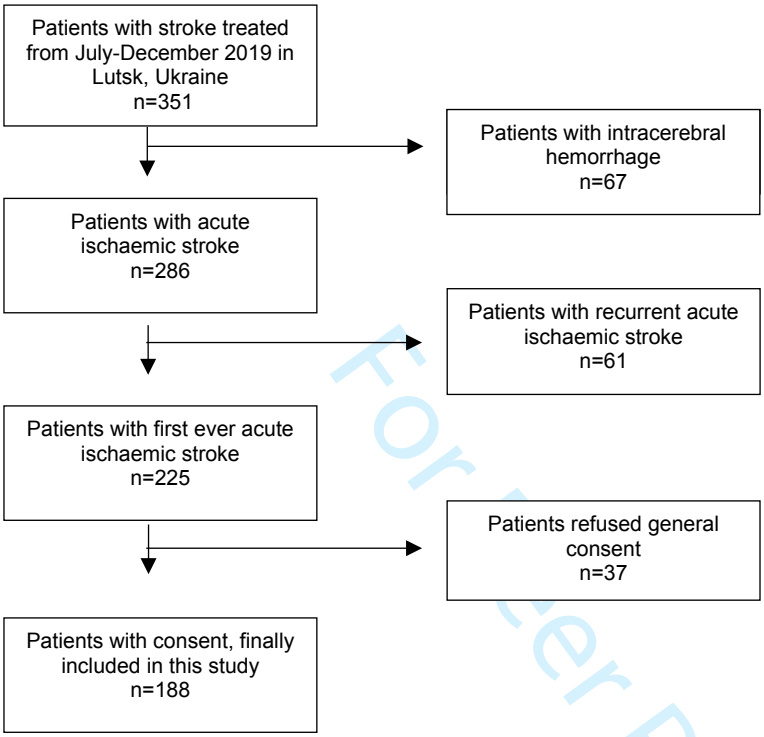
Bern, Switzerland



Gdansk, Poland



Lutsk, Ukraine



Baseline characteristics, secondary prevention and outcome after acute ischaemic stroke in three different socioeconomic environments in Europe

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Subject terms: Cerebrovascular disease/Stroke

ABSTRACT

Background: The differences in vascular risk factors' and stroke burden across Europe are notable, however there is limited understanding of the influence of socioeconomic environment on the quality of secondary prevention and outcome after acute ischaemic stroke.

Methods: In this observational multicenter cohort study, we analyzed baseline characteristics, reperfusion treatment, outcome and secondary prevention in patients with acute ischaemic stroke from three tertiary-care teaching hospitals with similar service population size in different socioeconomic environments: Bern/CH/n=293 (high-income), Gdansk/PL/n=140 (high-income) and Lutsk/UA/n=188 (lower-middle-income).

Results: We analyzed 621 patients (43.2% women, median age=71.4y), admitted between 07-12/2019. Significant differences were observed in median BMI (CH=26/PL=27.7/UA=27.89), stroke severity [(median NIHSS CH=4(0-40)/PL=11(0-33)/UA=7(1-30)], initial neuroimaging (CT:CH=21.6%/PL=50.7%/UA=71.3%), conservative treatment (CH=34.1%/PL=38.6%/UA=95.2%) (each p<0.001), in arterial hypertension (CH=63.8%/PL=72.6%/UA=87.2%), atrial fibrillation (CH=28.3%/PL=41.4%/UA=39.4%), hyperlipidaemia (CH=84.9%/PL=76.4%/UA=17%) (each p<0.001) and active smoking (CH=32.2%/PL=27.3%/UA=10.2%) (p<0.007).

3-months favourable outcome (mRS=0-2) was seen in CH=63.1%/PL=50%/UA=59% (unadjusted-p=0.01/adjusted-p CH-PL/CH-UA=0.601/0.981), excellent outcome (mRS=0-1) in CH=48.5%PL=32.1%/UA=27% (unadjusted-p<0.001/adjusted-p CH-PL/CH-UA=0.201/0.08 and adjusted-OR CH-UA=2.094). 3-months mortality was similar between groups (CH=17.2%/PL=15.7%/UA=4.8%) (unadjusted-p=0.71/adjusted-p CH-PL/CH-UA=0.087/0.24). 3-months recurrent stroke/TIA occurred in CH=3.1%/PL=10.7%/UA=3.1%, adjusted-p/OR CH-PL=0.038/0.318).

3-months follow-up medication intake rates were the same for antihypertensives. Statin/OAC intake was lowest in UA=67.1%/25.5% (CH=87.3%/39.2%/unadjusted-p<0.001/adjusted-p

CH-UA=0.02/0.012/adjusted-OR CH-UA=2.326/2.18). Oral antidiabetics' intake was lowest in CH=10.8% (PL=15.7%/UA=16.1%/unadjusted-p=0.245/adjusted-p CH-PL/CH-UA=0.061/0.002/adjusted-OR CH-UA=0.249). Smoking rates decreased in all groups during follow up.

Conclusions: Substantial differences in presentation, treatment and secondary prevention measures, ~~, based on socioeconomic factors,~~ are linked to a twofold difference in adjusted 3-months excellent outcome between Switzerland and Ukraine. This underscores the importance of socioeconomic factors that influence stroke outcomes, emphasizing the necessity for targeted interventions to address disparities in treatment and secondary prevention strategies.

INTRODUCTION

Stroke is the third-leading cause of death and disability combined in 2019 (measured in disability-adjusted life years (DALYs)) [1], posing a significant global challenge. The aging population contributes to an increased stroke burden [2,3,4], with a projected 31% increase in disability adjusted life-years by 2050 [3]. Despite a decline in age-adjusted stroke incidence rates, particularly in high-income countries [4,5,6,7], about 25% of patients experience recurrent ischaemic strokes within five years [8], leading to poor rehabilitation outcomes and cognitive impairment [9]. While tailored secondary prevention could reduce stroke recurrence risk by up to 80% [2], there remains limited data on the quality of secondary prevention and long-term outcome, particularly in less affluent European countries [2,10].

Differences in stroke burden across Europe are notable, with Eastern European countries facing higher stroke rates and related deaths [2,4], attributed to socioeconomic factors influencing vascular risk factors and healthcare access and quality [2,4,10,11]. Lower-income European countries encounter delays in patient assessment, limited access to interventions, and fewer lifestyle and atrial fibrillation monitoring programs [10]. Despite initiatives like the 2nd Helsingborg declaration having aimed at universal stroke unit access by 2015, significant discrepancies persist, with Eastern European countries lagging behind compared to Western European Countries [2,11]. Furthermore, it has been shown that Gross Domestic Product (GDP) per capita affects specialist care accessibility [10], and income levels impact secondary prevention [12].

The European Stroke Action Plan 2018-2030 [13] aims to address these challenges, necessitating a deeper understanding of care variability across European countries with different history, socioeconomic status and vascular risk. Switzerland, Poland and Ukraine exemplify this diversity, differing significantly in terms of GDP per capita, unemployment rates, and insurance coverage. Switzerland, on the one hand, is a representative of a highly developed Western European country. On the other hand, Poland and Ukraine are countries in Eastern Europe with less developed economic resources. It is worth noting that Poland has

been a member of the EU since 2004, which distinguishes it from Ukraine, a nation facing greater economic challenges and geopolitical complexity. Both countries were classified as high vascular risk countries [14,15,16].

This study aims to elucidate baseline characteristics, secondary prevention and outcome after first acute ischaemic stroke in different socioeconomic environments, i.e. Switzerland, Poland and Ukraine, providing insights into European stroke care.~~This study aims to elucidate the association of socioeconomic environment on baseline characteristics, outcome and secondary prevention after first acute ischaemic stroke in Switzerland, Poland and Ukraine, providing insights into European stroke care.~~

METHODS

We conducted an observational multicenter cohort study of patients who experienced their first acute ischaemic stroke between July and December 2019 and received treatment at three tertiary care centers. In this study, we focused on AIS patients, excluding those with ICH. AIS represents the majority of strokes, with distinct pathophysiology and treatment approaches compared to ICH. Our study's aim was to investigate specific aspects of AIS, limiting our focus to this subtype. However, we recognize the importance of ICH and its impact on outcome. Future research could explore similar topics related to ICH.

Data for 293 patients from Bern, Switzerland (CH), 140 patients in Gdansk, Poland (PL), and 188 patients in Lutsk, Ukraine (UA) were consecutively collected from three prospective stroke registries. We gathered information on demographics, baseline characteristics, and vascular risk factors, including arterial hypertension, atrial fibrillation, diabetes mellitus, hyperlipidaemia, smoking status, and history of prior myocardial infarction. Vascular risk factors were defined based on a combination of patient records, raw values and medication intake (see supplementary table 2 for further details).

Clinical assessment was performed by a certified neurologist on admission using a standardized acute ischaemic stroke (AIS) protocol based on the AHA/ASA (American Heart Association/ American Stroke Association) 2019 guidelines [17] and included NIHSS (National Institutes of Health Stroke Scale) score in the emergency room and a detailed neurological examination on the ward or in the Stroke Unit [18]. Suspected clinical diagnosis of AIS was confirmed by Magnetic Resonance Imaging (MRI) or Computed Tomography (CT). The diagnosis was made based on the AHA/ASA 2013 definition of ischaemic stroke [19].

Information in regard to initial therapy (conservative therapy, thrombolysis treatment, mechanical thrombectomy, decompressive craniectomy) and stroke aetiology classification according to the TOAST (Trial of ORG 10172 in Acute Stroke Treatment [20]) was collected from individual patient records. Also, in hospital treatment duration, hospital mortality, disability (measured with modified Rankin scale; mRS [21]) on discharge, discharge destination and discharge medication was assessed.

The follow-up parameters 3 months post-stroke were collected through clinical examinations by a board-certified neurologist, by telephone by a trained study nurse or extracted from external rehabilitation center reports. Data on the primary endpoint, outcome at discharge, were collected. Additionally, data on secondary endpoints, mRS at follow up, dichotomized into excellent (mRS 0-1), favourable (mRS 0-2) outcome, death, intake of secondary preventive medication and reported information on lifestyle behavior (dietary counseling, regular exercise, smoking status) and recurrence of stroke or TIA at 3 months were documented.

Detailed information on the definitions of variables is listed in supplementary table 1.

Statistical analysis

Statistical analysis was performed using SPSS 25.0 (SPSS Inc., Chicago, Illinois, USA). In univariable analysis, the $\chi 2$-test was applied for categorical variables and the ANOVA-test for

ordinal and continuous variables to compare baseline characteristics and outcomes between patients from Switzerland (CH), Poland (PL) and Ukraine (UA). A 2-tailed p-value <0.05 was considered significant. Binary logistic regression and ordinal and linear regression analysis were performed for outcome analysis where appropriate. Regression analyses got adjusted for the differences in admission NIHSS, and therapy, which differed significantly in comparison of baseline characteristics.

Standard protocol approvals, registrations, patient consent and reporting

The Bernese stroke registry was approved by the local ethics committee (KEK Bern 2016-01905) for quality control and research. Informed consent for study participation was waived by the ethics committee, and patients were informed about the registry and the potential use of their data for research. In accordance with the Swiss law, patients who refused the use of their data for research were excluded from the analysis. For patients from PL and UA, the study protocol and supporting material were approved by the local ethics committee and each patient signed a consent form for the use of their data for research. This study complied with the Declaration of Helsinki and data analyses followed Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines [22].

RESULTS

We included 293 patients from CH [128 (43.7%) women, median age 74.2 (20-97.4)], 140 from PL [54 (38.8%) women, median age 70 (18-85)] and 188 from UA [86 (45.7%) women, median age 71.4 (18-97.4)]. 19 Swiss and 6 Ukrainian patients were lost to follow-up, none from PL. Ukrainian and Polish patients had significantly higher median Body Mass Index (BMI) than Swiss patients ($p<0.001$). Pre-stroke mRS differed significantly between Polish and Swiss patients ($p<0.001$) (no data available for Ukrainian patients, since not routinely assessed)

(Table 3). For socioeconomic and hospital characteristics of the three study centers see table 1 and 2.

Arterial hypertension and atrial fibrillation were found significantly more often in Ukrainian and Polish compared to Swiss patients (p<0.007). However, hyperlipidaemia and active/former vs. never smoking was significantly less often found in Ukrainian, compared to Polish and Swiss patients (17% vs. 76.4% vs. 84.9%, p<0.001 and 40.1% vs. 60.4% vs. 56.7%, p<0.001) (Table 3).

Admission stroke severity differed significantly: Swiss patients had a median admission NIHSS of 4(0-36), Ukrainian 7(1-30), and Polish patients of 11(0-33) (p<0.001). Initial neuroimaging was significantly more often CT vs. MRI or both in UA (71.3%) and PL (50.7%) compared to in CH (21.6%) (p<0.001). Initial conservative vs. reperfusion treatment was applied to 95.2% of Ukrainian, compared to 34.1% of Swiss and 38.6% of Polish patients (p<0.001). Reperfusion treatment was most often mechanical thrombectomy (TBM) compared to intravenous thrombolysis with recombinant tissue Plasminogen Activator (rtPA) and both TBM and rtPA with 30.4% vs. 22.5% vs. 12.3% in Switzerland, 19.6% vs. 17.1% vs. 27.1% in Poland and 0.5% vs. 3.7% vs. 0.5% in Ukraine (p<0.001) (Table 3).

At discharge, excellent outcome was found in 47.1% of Swiss, 33.6% of Polish and 11.7% of Ukrainian patients (unadjusted-p<0.001, adjusted-p CH-PL=0.913, adjusted-p CH-UA<0.001, adjusted-OR CH-UA=6.03). Favourable outcome at discharge was found in 59.9% of Swiss, 51.4% of Polish and 36.7% of Ukrainian patients (unadjusted-p<0.001, adjusted-p CH-PL=0.195 and adjusted-p CH-UA=0.114). Hospital mortality did not differ significantly between groups. Discharge destination was most often home in PL (52.1%) and UA (84.1%) and to another acute care facility in CH (43.5%) (un-/adjusted-p<0.001). Median duration of hospitalization was 3.63 [0-59] days in CH, 8 [3-98] days in PL and 10 [1-32] days in UA (un-/adjusted-p<0.001) (Table 4). Medication prescription at discharge differed as follows: antihypertensive intake was higher in UA than PL and CH (92.6% vs. 81.7% vs. 65.3%, unadjusted-p<0.001, adjusted-p CH-PL/CH-UA=0.378/<0.001, adjusted OR CH-UA=0.149).

Statins were significantly more often used in PL (unadjusted-p=0.002, adjusted-p CH-PL<0.001 and adjusted-OR CH-PL=0.186) (Table 4).

At 3 months~~,~~ follow-up, excellent outcome was seen in 48.5% Swiss, 32.1% Polish and 27% Ukrainian patients (unadjusted-p<0.001, adjusted-p CH-PL/CH-UA=0.201/0.008 and adjusted-OR CH-UA=2.094). Favourable outcome was seen in 63.1% Swiss, 50% Polish and 59% Ukrainian patients (unadjusted-p=0.01, adjusted-p CH-PL/CH-UA=0.601/0.981). Mortality did not differ significantly between groups.

Recurrent stroke or TIA occurred in 10.7% of Polish, 5% of Ukrainian and 3.1% of Swiss patients (unadjusted-p=0.152, adjusted-p CH-PL=0.038 and adjusted-OR CH-PL/CH-UA=0.318/0.709). Re-hospitalization for any reason (including causes unrelated to TIA/AIS) occurred in 16.4% of Swiss, 16.1% of Polish and in 4.3% of Ukrainian patients (unadjusted-p<0.001, adjusted-p CH-PL/CH-UA=0.914/<0.001 and adjusted-OR CH-UA=5.24) (Table 5).

At 3 months, follow-up medication intake rates were the same for antihypertensives in UA, CH and PL (89.4% vs. 83.9% vs. 86.4%, unadjusted-p=0.303, adjusted-p CH-PL/CH-UA=0.092/0.217). However, statin and oral anticoagulants (OAC) intake was lower in UA than in CH and PL (67.1% vs. 87.3% vs. 87.3%, unadjusted-p<0.001, adjusted-p CH-PL/CH-UA=0.795/0.02 and adjusted-OR C-UA=2.326 and 25.5% vs. 39.2% vs. 41.5% unadjusted-p=0.006, adjusted-p CH-PL/CH-UA=0.892/0.012 and adjusted-OR CH-UA=2.18). Intake of oral antidiabetics was lowest in CH (10.8% vs. PL=15.7% vs. UA=16.1%, unadjusted-p=0.245, adjusted-p CH-PL/CH-UA=0.061/0.002 and adjusted-OR CH-UA=0.249).

Regular exercise was reported most often in UA at 3 months, but dietary counseling was given to only 19.9% of Ukrainian vs. 86.4% of Polish and 81% of Swiss patients (unadjusted-p<0.001, adjusted-p CH-PL/CH-UA=0.341/<0.001OR=0.046). Smoking rates in comparison to baseline decreased in all groups with 18.7% in CH, 13.7% in PL and 8.2% in UA (unadjusted-p<0.001, adjusted-p CH-PL/CH-UA=0.36/<0.001, adjusted OR CH-UA=8.66) (Table 5).

DISCUSSION

The main finding of this observational cohort study in 2019 shows a more than twofold difference in adjusted 3-months excellent outcome between high-income-country Switzerland and lower-middle-income country Ukraine. Data on acute ischaemic stroke patients in three different socioeconomic environments in teaching hospitals in Bern (Switzerland) (high-income), Gdansk (Poland) (high-income) and Lutsk (Ukraine) (lower-middle-income) were collected and analyzed. The world bank classification of countries by GDP per capita defined high-income as GDP per capita of over 12'375$ in 2019. While the per capita GDP in Poland was 15'699.91$ in 2019, GDP per capita in Switzerland was more than 5 times higher at 84'121.93$ [23].

While the hospitals share similarities in carrying capacity, guideline compliance (as demonstrated by the prescription of guideline-based drugs at discharge) and research and teaching engagement, this study identified differences in baseline characteristics, reperfusion treatment, secondary prevention and outcome among the three cohorts.

~~In this manuscript, we focused on AIS patients and excluded patients with intracerebral haemorrhage (ICH) for several reasons. First, AIS represents the majority of strokes and is associated with different pathophysiological mechanisms and treatment approaches than ICH. Secondly, our study aimed to investigate specific aspects or interventions related to AIS, which limited our focus to this subtype. However, we recognize the importance of ICH and its significant impact on outcome. Future research could explore similar topics related to ICH.~~

Baseline characteristics

In our analysis, Polish patients had a higher pre-stroke mRS than Swiss patients. Data for Ukrainian patients were not available. This aligns with previous findings associating lower socioeconomic status (SES) with higher pre-stroke comorbidity rates [24,25].

Ukrainian and Polish compared to Swiss patients showed higher BMI, arterial hypertension, and atrial fibrillation prevalence, consistent with higher vascular risk factor burden in Eastern European countries, where these risk factors are often less effectively controlled [2,8,13,25, 26,27]. In contrast, our study revealed a lower prevalence of hyperlipidaemia among Ukrainians (17%) compared to Swiss (84.9%) and Polish (76.4%) patients, potentially due to differences in screening practices, diagnostic approaches, and disease awareness levels, but also underreporting in Ukraine [2,28]. Moreover, we observed a lower smoking prevalence among Ukrainians, particularly in women, possibly attributed to historical smoking patterns and anti-smoking measures implemented in UA since 2006, but also underreporting could have contributed to this observation [29].

Ukrainian patients presented with the highest median NIHSS score on admission, Swiss patients with the lowest. This disparity may be attributed to varying referral practices, as well as a higher prevalence of atrial fibrillation in Polish and Ukrainian patients in our cohorts, potentially contributing to increased stroke severity [30]. Furthermore, a consistent association exists between lower socioeconomic status (SES) and increased stroke severity [31]. Also, this could be due to discrepancies in demograpics, healthcare structure and limited access to acute medical care for patients with minor stroke [2,10,32].

The initial neuroimaging technique differed significantly, with MRI more often used in CH compared to UA and PL, likely due to factors such as limited accessibility, availability, and the higher cost of MRI compared to CT [33]. Additionally, CT is favored in many places due to its shorter examination time.

Reperfusion treatment

Despite higher stroke severity, Ukrainian patients received intravenous thrombolysis and endovascular treatment less often than Swiss and Polish patients, possibly due to delayed hospital admission [2,29,34]. Delayed hospital admission often results from factors such as delayed stroke symptom recognition, organization of emergency services, and care protocol

implementation [29]. Unfortunately, we have not registered time delays from last seen well or first seen sick to hospital arrival and treatment in our study.

Additionally, accessibility and availability of treatment may be have been limited in UA [13]. This was evident in 2019 during the reform of the healthcare system in UA. Insufficient funding and limited state provision led to low rates of intravenous thrombolysis (0.9%) and endovascular treatment (0.2%) in patients with acute ischaemic stroke [13]. Reimbursement initiatives by the National Health Service of UA in 2020 then resulted in an increase in reperfusion treatment, with intravenous thrombolysis rates increasing to 6.4% and of endovascular treatment to 0.7% [35]. Lutsk City Hospital, which participated in this study, reflected a similar trend, with 21.1% and 7.1% of all acute ischaemic stroke patients receiving reperfusion treatment. The substantial changes observed in UA highlight the dependence of stroke reperfusion treatment on SES. Nevertheless, it is still essential to validate the overall effect on mortality and morbidity through comprehensive analyses.

Outcome at discharge and 3 months

Previous studies found poorer functional outcome in patients with lower SES [32]. In our study, functional outcome at discharge showed differences in univariable analysis, but after adjustment for admission NIHSS score and treatment, only excellent outcome remained 6 times more likely in Swiss compared to Ukrainian patients. This could be partly associated with lower vascular risk factor burden in Swiss patients. At 3 months, excellent outcome in CH was around 1.5 times more likely than in PL and almost 1.8 times more likely than in UA, but only the difference between CH and UA was significantly different in the adjusted analysis. Mortality did not differ between groups. Overall, the association with SES and outcome after stroke is to some extent consistent with previous studies [32,36].

Also, recurrent stroke/TIA occurred around 70% less likely in Swiss compared to Polish patients, potentially liked to the higher prevalence of atrial fibrillation and comorbidities in the Polish patient cohort [30]. Feigin et al. (2014) reported a greater stroke burden in Eastern

European countries, yet there is limited evidence concerning the association between SES and stroke recurrence [26,37].

In PL and UA, patients were most often discharged home, while in CH, they were transferred to another acute care facility. Some evidence suggests that higher SES serves as a determinant of postacute stroke rehabilitation, potentially explaining this variation [37]. Swiss patients experienced the shortest median first hospital stay, possibly attributed to efficient healthcare systems, streamlined processes, and prompt access to necessary post-acute stroke care services. However, despite a lower vascular risk factor burden, rehospitalization for any reason (including causes unrelated to TIA/AIS) within 3 months was approximately five times more frequent in Swiss patients compared to Ukrainian patients. This increased rate of rehospitalization may be influenced by factors such as closer post-acute monitoring or a higher threshold for readmission to ensure comprehensive medical care [10,28,32].

Secondary prevention

In our study, secondary prevention measures were implemented to a considerable extent across all three groups, with high intake rates of guideline-recommended medications. Statin intake at discharge were 80% less likely in CH than in PL, and antihypertensive intake was 70% less likely in CH than in UA. After 3 months, statin and OAC intake was twice as common, while oral antidiabetics' intake were 75% less likely in CH compared to UA. Some of these differences can only partly be explained by differences in vascular risk factor burden between cohorts. Previous research in UA indicated lower intake until follow-up to statins and OACs after vascular events, potentially influenced by socioeconomic factors such as income per capita, reimbursement, and insurance coverage [12]. Antihypertensive intake rates were high in all cohorts, showing no significant differences between groups.

At 3 months, regular exercise was reported most often in UA. However, dietary counseling was least frequently provided to Ukrainian compared to Polish and Swiss patients. Smoking rates

decreased in all groups compared to baseline but remained around 9 times more likely in Swiss compared to Ukrainian patients. These differences could be linked to factors like differences in reporting and wage definition (e.g. of regular exercise), in cultural practices (e.g. of lifestyle), in healthcare infrastructure and in disease awareness levels (e.g. of hyperlipidaemia and unhealthy diet) [2,38,39].

Strengths

This study's primary strength lies in its type of multicenter data collection, enabling a direct comparison between hospitals with comparable service population and research engagement in three different socioeconomic environments. The comprehensive assessment of numerous parameters allowed not only the evaluation of outcome differences but also an exploration of distinctions between the tree populations, primarily influenced by socioeconomic factors. Beyond acute clinical practice, this study underscores the significance of such factors for secondary prevention and health outcomes. It aligns with the European Stroke Action Plan 2018-2030's framework for healthcare policy, research, and stroke services development, highlighting the need for a deeper understanding of the current state and diversity across European countries.

Limitations

The study's main limitation arises from patients not providing consent or being lost to follow-up or from missing variables ~~arises from patients being lost to follow-up or missing variables~~, particularly regarding incomplete data on secondary prevention measures such as dietary counseling, smoking status and medication at 3 months. In addition, caution is required when extrapolating results from individual hospitals to entire European countries. The stroke centers participating in the study stand out in terms of quality compared to the national average. It can therefore be assumed that the national average for each country might be worse and these differences are likely to be greater the less affluent a country is. Furthermore, socioeconomic factors were not assessed at the individual patient level.

Also, the data collected in 2019 may not reflect current realities given the widespread adoption of therapies and socioeconomic changes due to the Covid-19 pandemic and the war in Ukraine. Future research should compare these data with current data to assess the evolution of stroke care amid these global events.

Conclusion

Substantial differences in presentation, treatment and secondary prevention measures~~, based on socioeconomic factors~~, are linked to a twofold difference in adjusted 3-months excellent outcome between high and lower-middle-income countries. This underscores the importance of targeted interventions to address treatment and secondary prevention disparities.

The Stroke Alliance for Europe (SAFE) projects a 35% increase in stroke cases by 2035, necessitating comprehensive investment in primary and secondary prevention beyond acute care. The lack of comprehensive data, as seen in Ukrainian patients in our study [2], underscores the need for standardized pan-European data collection to guide intervention. Addressing these socioeconomic disparities should be central to policy programmes aimed at reducing the burden of stroke in Europe and promote a more equitable healthcare system

CONTRIBUTIONS

MR Heldner had full access to all the data and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Critical revision of the manuscript for important intellectual content: All co-authors.

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CONFLICTS OF INTEREST/ DISCLOSURES

MRH reports grants from SITEM Research Funds and the. Swiss Heart Foundation, outside the sumbitted work and grants from the Swiss National Science Foundation partly related to the submitted work

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All other co-authors report no disclosures directly related to this manuscript.

DATA SHARING STATEMENT

Raw data of all patients included in this study can be made available upon request to the corresponding author and after clearance by the local ethics committee.

ETHICAL APPROVAL AND INFORMED CONSENT

The Bernese stroke registry was approved by the local ethics committee (KEK Bern 2016-01905) for quality control and research. Informed consent for study participation was waived by the ethics committee, and patients were informed about the registry and the potential use of their data for research. In accordance with the Swiss law, patients who refused the use of their data for research were excluded from the analysis. For patients from PL and UA, the study protocol and supporting material were approved by the local ethics committee and each patient signed a consent form for the use of their data for research. This study complied with the Declaration of Helsinki and data analyses followed Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

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TABLES

Table 1: Socioeconomic situation in Bern (Switzerland), Gdansk (Poland), Lutsk (Ukraine) in 2019

	Switzerland	Poland	Ukraine
GDP per capita	84’121 USD	15’699.91 USD	3'661.46 USD
Unemployment rate	4.39%	3.28%	8.19%
Rate of stroke units per million inhabitants	2.21	4.59	0.14

Data sources: Swiss Federal Statistical Office (www.bfs.admin.ch), Central Statistical Office of Poland (www.stat.gov.pl) and Ukraine Government Website (), Aguiar de Sousa et.al 2019 [40].

Table 2: Hospital characteristics and services of three different study centers in Bern (Switzerland), Gdansk (Poland), Lutsk (Ukraine) in 2019

	Bern (Switzerland)	Gdansk (Poland)	Lutsk (Ukraine)
Total number of beds	926	1200	715
Number of beds of the neurology department	132	50	65
Total no of acute stroke patients	1313	621	625
Catchment area	1.5 Million people	500’000 people	216’887 people
~~Bern (Switzerland)~~	~~Gdansk (Poland)~~	~~Lutsk (Ukraine)~~	

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Hospital population area	1.5 Million people	500'000 people	216'887 people			
~~Carrying capacity~~				~~926~~	~~1200~~	~~715~~
~~Carrying capacity of the neurology department~~				~~132~~	~~50~~	~~65~~
~~Total no of acute stroke patients~~				~~1313~~	~~621~~	~~625~~
~~Hospital population area~~				~~1.5 Million people~~	~~500'000 people~~	~~216'887 people~~

Data sources: Swiss Federal Statistical Office (www.bfs.admin.ch), Central Statistical Office of Poland (www.stat.gov.pl) and Ukraine Government Website (www.lutsk.ukrstat.gov.ua).

Table 3: Baseline characteristics, Risk factors, Diagnostics and reperfusion treatment [n (%)]

	Bern (Switzerland) , n=293	Gdansk (Poland), n=140	Lutsk (Ukraine), n=188	p-value (Pearson)
Sex [n (%)]				0.45
Male	165 (56.3%)	85 (61.2%) †	102 (54.3%)	
Female	128 (43.7%)	54 (38.8%)†	86 (45.7%)	
BMI [median (range)]	26.01 (15.92-46.9)	27.68 (19.53-42.52)	27.79 (17.99-49.9)	<0.001
Age [y] [median (range)]	74.2 (20-97.4)	70 (18-85)	71.4 (18-97.4)	0.060
Time of the day [n (%)]				0.534
Day	227 (77.5%)	102 (72.9 %)	140 (74.5%)	
Wake up stroke	66 (22.5%)	38 (27.1 %)	48 (25.5%)	
Pre mRS [n (%)]			No data collected	<0.001
0	179 (62.8%)†	61 (43.6%)	No data collected	

1	47 (16.5%)†	42 (30%)	No data collected	
2	17 (6.0%)†	26 (18.6%)	No data collected	
3	27 (9.5%)†	9 (6.4%)	No data collected	
4	14 (4.9%)†	2 (1.4%)	No data collected	
5	1 (0.4%)†	0 (0%)	No data collected	
Atrial fibrillation	83 (28.3%)	58 (41.4%)	74 (39.4%)	0.007
Diabetes mellitus	66 (22.6%)	26 (18.6%)	37 (19.7%)	0.578
Arterial hypertension	187 (63.8%)	102 (72.6%)	164 (87.2%)	<0.001
Hyperlipidaemia	248 (84.9%)	107 (76.4%)	32 (17.0%)	<0.001
Post myocardial infarction	24 (8.2%)	21 (15%)	26 (13.8%)	0.057
Smoking status				<0.001
Never smoker	101 (43.3%)†	55 (39.6%)†	106 (59.9%)†	
Active smoker	75 (32.2%)%)†	38 (27.3%)†	18 (10.2%)†	
Former smoker	57 (24.5%)†	46 (33.1%)†	53 (29.9%)†	
NIHSS initial [median (range)]	4 (0-36)	11 (0-33)	7 (1-30)	<0.001
0-9 (mild stroke)	202 (70.9%)	65 (46.4%)	113 (62%)	<0.001
≥ 10 (moderate/severe stroke)	75 (29.1%)	75 (53.6%)	75 (39.9%)	<0.001
Initial neuroimaging				<0.001
MRI	145 (51.1%)†	22 (15.7%)	31 (16.5%)	
CT	74 (26.1%)†	71 (50.7%)	134 (71.3%)	
Both	65 (22.9%)	47 (33.6%)	23 (12.2%)	
Etiology TOAST				0.37
Cardioembolism	107 (36.6%)	61 (43.6%)	71 (37.8%%)	
No Cardioembolism	185 (48.6%)	79 (56.4%)	117 (62.2%)	
Therapy				<0.001
Conservative	100 (34.1%)	54 (38.6%)	179 (95.2%)	
Intravenous thrombolysis with rtPA only	66 (22.5%)	24(17.1%)	7 (3.7%)	
TBM only	89 (30.4%)	22 (19.6%)	1 (0.5%)	
Craniectomy only	2 (0.7%)	2 (1.4%)	0 (0%)	

Both rtPA and TBM	36 (12.3%)	38 (27.1%)	1 (0.5%)	
rtPA, TBM and Craniectomy	0 (0%)	1 (0.7%)	0 (0%)	

†*Note: Sex n=139, data on 1 Polish patient missing, Pre-mRS n=285, data of 8 Swiss patients missing, Smoking status CH n=233, data of 60 Swiss patients missing, PL n= 139, data of 1 Polish patient missing, UA=177, data of 11 Ukrainian patients missing, Initial Neuroimaging n=284, data of 9 Swiss patients missing*

Table 4: Outcome at discharge and medication at discharge

	Bern (Switzerland), n=293	Gdansk (Poland), n=140	Lutsk (Ukraine), n=188	p-value (Pearson)	p-value (controlled CH PL)	Odds ratio, CH PL 95%CI	p-value (controlled CH UA)	Odds ratio, CH UA 95%CI
mRS discharge								
Excellent 0-1	126 (47.1%)†	47 (33.6%)	22 (11.7%)	<0.001	0.913	1.029 (0.61-1.73)	<0.001	6.03 (3.19-11.4)
Favourable 0-2	158 (59.9%)†	72 (51.4%)	69 (36.7%)	<0.001	0.195	0.707 (0.42-1.2)	0.114	1.611 (0.89-2.91)
Dead 6	24 (9.1%)†	16 (11.4%)	12 (6.4%)	0.454	0.785	1.105 (0.54-2.27)	0.857	0.894 (0.26-3.05)
Mortality in hospital	24 (8.2%)	16 (11.4%)	12 (6.4%)	0.261	0.861	0.938 (0.46-1.91)	0.645	0.754 (0.23-2.51)
Discharge destination				<0.001	<0.001		<0.001	<0.001
Home	66 (22.6%)†	73 (52.1%)	148 (84.1%)					
Rehabilitation	71 (24.3%)†	38 (27.1%)	28 (15.9%)					
Nursing facility	4 (1.4%)†	13 (9.3%)	0 (0%)					
Other acute care hospital	127 (43.5%)†	0 (0%)	0 (0%)					
Dead	24 (8.2%)†	16 (11.4%)	12 (6.4%)					
Duration first hospital [days] [median (range)]	3.63 days (0-59 days)	8 days (3-98 days)	10 days (1-32)	<0.001	<0.001	NA	<0.001	NA
Antihypertensives	173 (65.3%)†	102 (81.7%)	163 (92.6%)	<0.001	0.378	0.903 (0.72-1.13)	<0.001	0.149 (0.07-0.3)
OAC	83 (30.8%)†	41 (32.8%)	56 (31.8%)	0.925	0.969	0.991 (0.62-1.59)	0.748	1.901 (0.64-1.86)

Antiplatelets	181 (67.3%)†	89 (71.2%)	115 (65.3%)	0.560	0.267	0.762 (0.47-1.23)	0.581	1.159 (0.69-1.96)
Statin	224 (86.2%)†	120 (96%)	152 (86.9%)	0.002	<0.001	0.186 (0.07-0.49)	0.686	0.865 (0.43-1.75)
Oral antidiabetics	31 (11.5%)†	18 (14.4%)	29 (16.5%)	0.312	0.152	0.616 (0.32-1.2)	0.826	0.394 (0.19-8.3)
Insulin	25 (9.6%)†	10 (8%)	8 (4.5%)	0.178	0.549	1.274 (0.58-2.82)	0.11	2.27 (0.83-6.22)

Note: For 18 Swiss patients, 15 Polish patients and for 12 Ukrainian patients, who died during in hospital care no medication was assessed.
†mRS discharge n=264, data of 39 Swiss patients missing, Discharge destination n=292, data of 1 Swiss patient missing, Antihypertensives n=265, data of 10 Swiss patients missing, OAC, Antiplatelets, Statin, Oral antidiabetics, Insulin n=270, data of 5 Swiss patients missing

Table 5: Follow-up at 3 months

Follow-up 3 months [n (%)]	Bern (Switzerland), n=293	Gdansk (Poland), n=140	Lutsk (Ukraine), n=188	p-value (Pearson)	p-value (controlled CH PL)	Odds ratio, CH PL 95%CI	p-value (controlled CH UA)	Odds ratio, CH UA 95%CI
mRS								
Excellent 0-1	133 (48.5%)†	45 (32.1%)	48 (27%)†	<0.001	0.201	1.369 (0.85-2.21)	0.008	2.094 (1.209-3.627)
Favourable 0-2	173 (63.1%)†	70 (50%)	105 (59%)†	0.01	0.601	1.137 (0.70-1.84)	0.981	1.007 (0.548-1.853)
Dead 6	47 (17.2%)†	22 (15.7%)	9 (4.8%)	0.71	0.087	1.703 (0.93-3.14)	0.24	1.837 (0.666-5.069)
Stroke/TIA	7 (3.1%)†	13 (10.7%)†	8 (5%)†	0.152	0.038	0.318 (0.108-0.938)	0.709	0.747 (0.162-3.441)
Re-Hospitalization	35 (16.4%)	19 (16.1%)	7 (4.3%)	<0.001	0.914	0.965 (0.51-1.84)	<0.001	5.24 (1.96-14.02)
Medication			n=161					
Antihypertensives	177 (83.9%)†	102 (86.4%),	144 (89.4%)†	0.303	0.092	0.755 (0.55-1.05)	0.217	0.601 (0.27-1.35)
OAC	83 (39.2%)†	49 (41.5%)	41 (25.5%)†	0.006	0.892	0.967 (0.6-1.57)	0.012	2.18 (1.91-3.99)
Antiplatelets	134 (63.5%)†	66 (55.9%)	109 (67.7%)†	0.130	0.261	1.322 (0.81-2.15)	0.668	0.879 (0.49-1.59)
Statin	185 (87.3%)†	103 (87.3%)	108 (67.1%)†	<0.001	0.795	1.1 (0.54-2.26)	0.02	2.326 (1.14-4.73)
Oral antidiabetics	23 (10.8%)†	19 (15.7%)	26 (16.1%)†	0.245	0.061	0.508 (0.25-1.03)	0.002	0.249 (0.10-0.61)
Insulin	11 (5.2%)†	7 (6.3%)	4 (2.5%)†	0.310	0.902	0.937 (0.33-2.64)	0.8	1.23 (0.24-6.27)

Regular Exercise 3m				<0.001	0.028		0.057	
Yes	53 (38.4%)†	62 (53%)†	100 (62.1%)†					
No	39 (28.3%)†	37 (31.6%)†	61 (37.9%)†					
Disability	46 (33.3%)†	18 (15.4%)†	0 (0%)†					
Dietary counseling	124 (81.0%)†	101 (86.3%)†	32 (19.9%)†	<0.001	0.341	1.405 (0.7-2.83)	<0.001	0.046 (0.02-0.10)
Active smoking	29 (18.7%)†	16 (13.7%)†	4 (8.2%)†	<0.001	0.36	1.387 (0.69-2.8)	<0.001	8.663 (2.51-29.85)

Note: for 47 patients from Switzerland and for 22 from Poland and 9 from Ukraine, who had died until the follow-up, no data besides mRS was assessed.
†mRS-3months CH n=274, data of 19 Swiss patients missing, UA n=178, data from 10 Ukrainian patients missing, Stroke/TIA CH n=225, data of 21 Swiss patients missing, PL n=108, data of 10 Polish patients missing, UA n=161, data of 19 Ukrainian patients missing, Re-Hospitalization CH n=214, data of 32 Swiss patients missing, UA n=161, data of 19 Ukrainian patients missing, Medication UA n=161, data of 18 Ukrainian patients missing, Antihypertensives CH n=211, data of 35 Swiss patients missing, OAC CH n=212, data of 34 Swiss patients missing, Antiplatelets CH n=211, data of 35 Swiss patients missing, Statin, Oral Antidiabetics CH n=212, data of 34 Swiss patients missing, Insulin CH n=211, data of 35 Swiss patients missing, Regular exercise CH n=117, data of 129 Swiss patients missing, PL n=117, data of 1 Polish patient missing , UA n=161, data of 19 Ukrainian patients missing, Dietary counseling CH n=152, data of 94 Swiss patients missing, PL n= 117, data of 1 Polish patient missing, UA n=161, data of 19 Ukrainian patients missing, Active smoking CH n=155, data of 91 Swiss patients missing, PL n=117, data of 1 Polish patient missing, UA n=161, data of 19 Ukrainian patients missing.

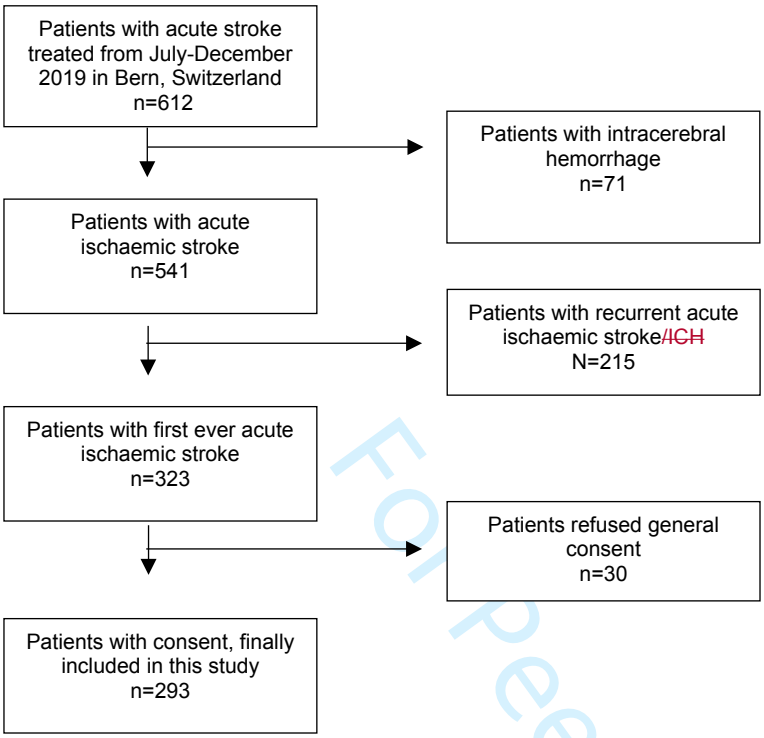
Supplementary file 1: table 1: Definitions of variables

Variable	Definition
Country	1=Poland, 2=Switzerland, 3=Ukraine
Age	In years
Sex	0=male, 1=female
Time of the day	1=7:00-22:00, 0=22:01-6:59
BMI	Weight [m]/(height [kg])^2
Pre mRS	0-6
Pre mRS excellent	mRS 0-1=1, mRS 2-6=0
Pre mRS favourable 0-2	mRS 0-2=1, mRS 3-6=0
Pre mRS dead	mRS 6=1, 1-5=0
NIHSS	0-42, assessed by a certified neurologist on admission
Stoke Severity	NIHSS 0-9=1, >9=0
Atrial Fibrillation	0=no, 1=yes, based on patient records, raw values (based on 12 lead ECG) and medication intake (OAC)
Diabetes Mellitus	0=no, 1=yes, based on patient records; raw values (fasting blood-glucose level of 126 mg/dl (7 mmol/L) or higher and/or random blood glucose level of 200 mg/dl (11.1 mmol/L) or higher); and medication intake (insulin and/or oral antidiabetics)
Arterial Hypertension	0=no, 1=yes, based on patient records, raw values (systolic blood-pressure of 140 mmHg and higher and/or diastolic blood-pressure of 90 mmHg or higher) and medication intake (antihypertensives)
Hyperlipidaemia	0=no, 1=yes, based on patient records, raw values (total cholesterol of 240 mg/dL (6.2 mmol/L) or higher and/or low-density-lipoprotein LDL of 160 mg/dL (4.1 mmol/L) or higher) and medication intake (lipid lowering drugs)
Post myocardial infarction	0=no, 1=yes, based on patient records
Smoker active	0=no, 1=yes (current smoking or stopped <2 years ago), based on patient records and raw values
Smoker former	0=no, 1=yes (stopped smoking $\geq$ 2 years ago), based on patient records and raw values
Never smoker	0=no, 1=yes, based on patient records and raw values
Initial neuroimaging	1=MRI, 2=CT, 3=both
Therapy	1=conservative, 2= Intravenous thrombolysis with rtPA only, 3= Mechanical Thrombectomy (TBM) only, 4= Craniectomy only, 5= Both rtPA and TBM, 6= rtPA, TBM and Craniectomy

Etiology TOAST	0= no cardioembolism, 1= cardioembolism
mRS discharge	0-6
mRs discharge excellent	mRS 0-1=1, mRS 2-6=0
mRS discharge favourable	mRS 0-2=1, mRS 3-6=0
mRS discharge mortality	mRS 6=1, 1-5=0
Mortality in hospital	0=no, 1=yes
Duration first hospital	In days
Discharge destination	1=home, 2=rehabilitation, 3= nursing home, 4=other, 5=dead
OAC discharge	0=no, 1=yes
Antiplatelets discharge	0=no, 1=yes
Antihypertensives discharge	0=no, 1=yes
Statin discharge	0=no, 1=yes
Oral antidiabetics discharge	0=no, 1=yes
Insulin discharge	0=no, 1=yes
mRS 3months	0-6
mRS 3months excellent	mRS 0-1=1, mRS 2-6=0
mRS 3months favourable	mRS 0-2=1, mRS 3-6=0
mRS 3months mortality	mRS 6=1, 1-5=0
Stroke/TIA 3 months	0=no, 1=yes
Re-Hospitalisation 3 months	0=no, 1=yes
OAC 3 months	0=no, 1=yes
Antiplatelets 3 months	0=no, 1=yes
Antihypertensives 3 months	0=no, 1=yes
Statins 3 months	0=no, 1=yes
Oral antidiabetics 3 months	0=no, 1=yes
Insulin 3 months	0=no, 1=yes
Regular Exercise 3 months	0=no, 1=yes, 2=disability
Dietary counseling 3 months	0=no, 1=yes
Active smoking 3 months	0=no, 1=yes

Supplementary table 2: flow chart of in- and exclusion process

Bern, Switzerland



Gdansk, Poland