

Association of weekend admission and clinical outcomes in hospitalized patients with sepsis

An observational study

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Abstract

Sepsis is associated with impaired clinical outcomes. It requires timely diagnosis and urgent therapeutic management. Because staffing during after-hours is limited, we explored whether after-hour admissions are associated with worse clinical outcomes in patients with sepsis.

In this retrospective cohort study, we analyzed nationwide acute care admissions for a main diagnosis of sepsis in Switzerland between 2006 and 2016 using prospective administrative data. The primary outcome was in-hospital mortality using multivariable logistic regression models. Secondary outcomes were intensive care unit (ICU) admission, intubation, and 30-day readmission.

We included 86,597 hospitalizations for sepsis, 60.1% admitted during routine-hours, 16.8% on weekends and 23.1% during night shift. Compared to routine-hours, we found a higher odds ratio (OR) for in-hospital mortality in patients admitted on weekends (Adjusted OR 1.05, 95% confidence interval [95% CI] 1.01, 1.10, $P = .041$). Also, the OR for ICU admission (OR 1.14, 95% CI 1.10, 1.19, $P < .001$) and intubation (OR 1.18, 95% CI 1.12, 1.25 $P < .001$) was higher for weekends compared to routine-hours. Regarding 30-day readmission, evidence for an association could not be observed. Night shift admission, compared to routine-hours, was associated with a higher OR for ICU admission and intubation (ICU admission: OR 1.28 (1.23, 1.32), $P < .001$; intubation: OR 1.31, 95% CI 1.25, 1.37, $P < .001$) but with a lower OR for in-hospital mortality (OR 0.93, 95% CI 0.89, 0.97, $P = .001$).

Among hospitalizations with a main diagnosis of sepsis, weekend admissions were associated with higher OR for in-hospital mortality, ICU admission, and intubation. Whether these findings can be explained by staffing-level differences needs to be addressed.

Abbreviations: 95% CI = 95% confidence interval, CCI = Charlson Comorbidity Index, ICU = intensive care unit, OR = odds ratio.

Keywords: after-hours care, hospital mortality, intensive care unit, intubation, patient readmission, sepsis

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The data that support the findings of this study are available from a third party, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are available from the authors upon reasonable request and with permission of the third party.

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1. Introduction

Sepsis is one of the major life-threatening conditions defined as organ dysfunctions due to the inflammatory response to an infection.^[1,2] Despite intensive efforts and research, epidemiological data vary due to changing definitions over the past years. Still, the burden of disease is tremendous with an estimated incidence of 15 to 19 million annual cases worldwide.^[3,4] Although overall sepsis-related mortality has been decreasing in the last decades along with the implementation of standardized resuscitation guidelines,^[5,6] it still remains high with 20% to 30%, significantly depending on time to diagnosis and quality of treatment and care.^[7–9]

Increased in-hospital mortality has been observed in patients admitted during after-hours compared to routine-hours.^[10] This so-called “weekend” or “after-hours”-effect has been reported for various conditions requiring prompt management such as acute coronary syndrome, pulmonary embolism, and ruptured aortic abdominal aneurysm.^[10,11] Unfavourable clinical outcome was not only associated with weekend admissions but also with admissions during night shifts.^[12] The “after-hours” effect is mostly found in conditions requiring extensive time and resources, such as interdisciplinary teamwork and specialty procedures that may not be available on weekends or at night.^[11,13] As early administration of appropriate antibiotics, fluids, and invasive procedures with close monitoring are crucial in sepsis patients, clinically trained and available health care professionals, an optimal timeliness, and resource management are indispensable.^[14,15]

Whether there is also a weekend effect for sepsis remains understudied.^[15,16] Using data of a large Swiss-wide database, we explored whether after-hour admissions are associated with a higher risk of adverse clinical outcomes in patients with sepsis.

2. Methods

2.1. Study design, data source, and participants

For this study, we included all hospitalizations for medical inpatients, presenting with sepsis (Fig. 1). We therefore screened prospective administrative data (“Medizinstatistik”) provided by the Swiss Federal Statistical Office between January 1, 2006, and December 31, 2016 for the principal discharge diagnosis of sepsis according to the International Classification of Diseases, Tenth Revision, German Modification code.

To further qualify for inclusion in this study cohort patients must be aged ≥ 20 years. From the final analysis we excluded non-medical or psychiatric patients, outpatients, and patients transferred to another hospital or treated in post-acute care institutions.

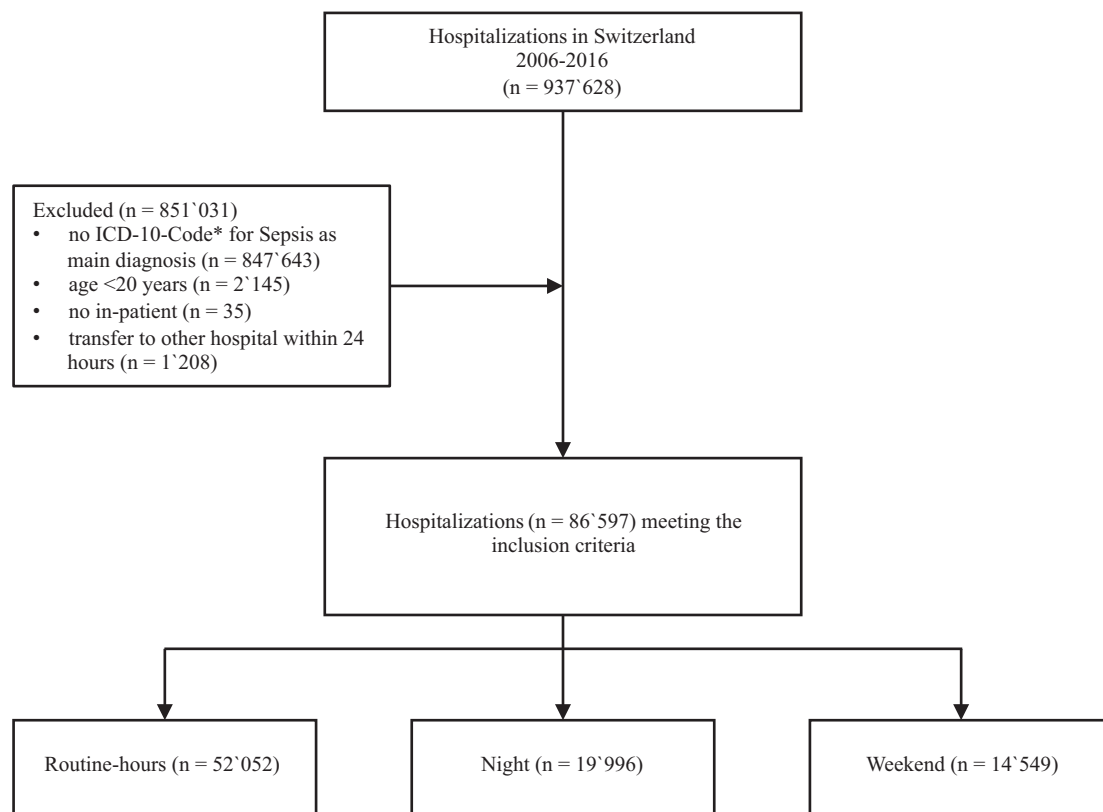
Since the database includes all Swiss inpatient discharge records from acute care-, general-, and specialty hospitals, regardless of payer, it represents almost 100% of inpatient

discharges in Switzerland. As this registry is a national effort, all regions of Switzerland were included in this analysis (Fig. 1).

Based on the Swiss Diagnosis-Related Groups definition of 2012 an “index admission” was defined as every admission to a hospital, unless patients have been readmitted to the same hospital within 18 days after discharge. However, if readmission occurred after 18 days of discharge or to a different hospital, it was evaluated as a new index admission. Thus, a single patient may have more than 1 index admission within the study period. Independent of this, information about readmission was available for all hospitalizations and was always attributed to the discharging hospital.^[17]

The exposure of interest was the time interval related to the patient admission. Routine-hour admission was defined as a time interval from 8 am to 8 pm from Monday through Friday, night shift from 8 pm to 8 am from Monday to Sunday, and weekend admission from 8 am to 8 pm on Saturdays and Sundays. We defined night shift or weekend admission as “after-hours” admission. Definition was done based on national working experience as international consensus on how to define “after-hours” is still debatable.

This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.^[18] Institutional review board approval, including



* To qualify for inclusion in this study cohort, hospitalized patients must have had a principal discharge diagnosis with the following *International Classification of Diseases, Tenth Revision, German Modification* code for sepsis entities: A02.1, A20.7, A22.7, A26.7, A32.7, A39.2, A39.3, A39.4, A40.0, A40.1, A40.2, A40.3, A40.8, A40.9, A41.0, A41.1, A41.2, A41.3, A41.4, A41.51, A41.52, A41.58, A41.8, A41.9, A42.7, B37.7, or R57.2.

Figure 1. Study flow chart ICD-10 codes for sepsis (A02.1, A20.7, A22.7, A26.7, A32.7, A39.2, A39.3, A39.4, A40.0, A40.1, A40.2, A40.3, A40.8, A40.9, A41.0, A41.1, A41.2, A41.3, A41.4, A41.51, A41.52, A41.58, A41.8, A41.9, A42.7, B37.7, or R57.2).

waiver of the requirement of participant informed consent, as the data were de-identified, was provided by the institutional review board of North-Western Switzerland (AG/SO 2009/074 and EKNZ BASEC PB_2017–00449).

2.2. Primary and secondary endpoints

The main outcome was all-cause in-hospital mortality as an increased early mortality during weekends has been reported in earlier studies.^[15] Secondary outcomes were intensive care unit (ICU) admission, intubation, and 30-day readmission. To identify interregional outcome differences, we stratified admissions upon geographical location of the hospitals. We defined 7 geographical regions compliant with the Swiss Federal Statistical Office guidelines (i.e., “Ostschweiz”, “Zuerich”, “Zentralschweiz”, “Nordwestschweiz”, “Espace Mittelland”, “Genferseeregion”, “Tessin”).^[19]

2.3. Statistical analysis

In this study, we explored whether all-cause in-hospital mortality increases in hospitalizations for sepsis during after-hours compared to routine-hours. First, we examined patient and geographical characteristics of the index hospitalization stratified by admission time period. The index hospitalization formed the unit of analysis in these descriptive statistics. For the primary and secondary endpoints, we compared frequencies using a Kruskal–Wallis test and we fitted a multivariable logistic regression model adjusted for age, gender, year and month of admission, geographical region, severity of sepsis, and Charlson Comorbidity Index (CCI).^[20] We reported adjusted odds ratios (OR) and corresponding 95% confidence intervals (95% CIs). Due to a change in the coding policy for sepsis definition by the Swiss Federal Statistical Office in 2013/2014 we did a sensitivity analysis for the year 2006 to 2013 and 2014 to 2016. According

to the new definition, sepsis could only be coded as main diagnosis, if an organ failure related to the infection is recorded, meaning that only former severe sepsis is now coded as sepsis.

The Kaplan–Meier method was used to visualize 30 day in-hospital survival over time by calculating the probability of 30 day in-hospital event-free survival within 30 days of study entry. The Log-rank test was calculated to assess the probability of rejecting the null hypothesis (curves are not different) and estimates of the effect size and corresponding 95% CIs were determined using Cox proportional hazards regression analysis.

In our subgroup analysis, we studied interregional differences of the 7 geographical regions in Switzerland and whether outcomes vary by region by calculating OR, adjusted for age, gender, year and month of admission, and CCI. We first compared the overall OR with the OR of 1 region. To better illustrate the clinical impact of the interregional differences, we calculated the absolute risk differences (ARD) comparing the absolute risk of 1 region with the absolute risk of all regions except for the named region.

We applied a significance level of .05 and did not correct for multiple testing. We conducted all statistical analyses with Stata 15.1 (StataCorp. 2015. Stata Statistical Software: Release 15. College Station, TX: StataCorp LP).

3. Results

During the study time from January 1, 2006 through December 31, 2016, we identified a total of 86,597 admissions meeting our inclusion criteria. Baseline characteristics depending on time of admission are shown in Table 1 and S1 Table, <http://links.lww.com/MD/E429>.

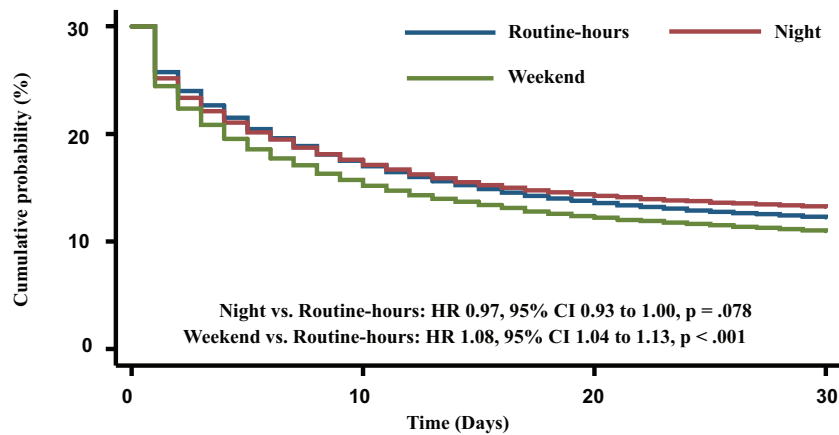
60.1% were admitted during routine-hours, 23.1% during night shifts and 16.8% on weekends. 56.1% were male. 46.6% were between 60 and 80 years old. The mean CCI, representing the severity of comorbidities and sickness of patients, was highest

Table 1
Baseline characteristics depending on time of admission.

Characteristics	Entire cohort 86597 (100.0)	Weekday 52052 (60.1)	Night 19996 (23.1)	Weekend 14549 (16.8)
Age				
≤60 yr	17149 (19.8)	10130 (19.5)	4216 (21.1)	2803 (19.3)
>60 to <80 yr	40359 (46.6)	24278 (46.6)	9393 (47.0)	6688 (46.0)
≥80 years	29089 (33.6)	17644 (33.9)	6387 (31.9)	5058 (34.8)
Gender				
Male	48579 (56.1)	28786 (55.3)	11616 (58.1)	8177 (56.2)
Female	38018 (43.9)	23266 (44.7)	8380 (41.9)	6372 (43.8)
Region				
“Ostschweiz”	8694 (10.0)	5480 (10.5)	1782 (8.9)	1432 (9.8)
“Zuerich”	14132 (16.3)	7819 (15.0)	3992 (20.0)	2321 (16.0)
“Zentralschweiz”	6806 (7.9)	4032 (7.7)	1582 (7.9)	1192 (8.2)
“Nordwestschweiz”	14005 (16.2)	8447 (16.2)	3240 (16.2)	2318 (15.9)
“Espace Mittelland”	22654 (26.2)	13638 (26.2)	5100 (25.5)	3916 (26.9)
“Genferseeregion”	15610 (18.0)	9760 (18.8)	3293 (16.5)	2557 (17.6)
“Tessin”	4696 (5.4)	2876 (5.5)	1007 (5.0)	813 (5.6)
CCI (Charlson Comorbidity Index)				
CCI, mean value	1.87 (2.25)	1.89 (2.26)	1.81 (2.22)	1.87 (2.27)
Severity of infection				
Sepsis	85057 (98.2)	51149 (98.3)	19680 (98.4)	14268 (98.1)
Septic shock	1500 (1.7)	903 (1.7)	316 (1.6)	281 (1.9)

Data are n (%) or mean (SD).

CCI=Charlson Comorbidity Index.



Number at risk				
Routine-hours	52052	45552	43604	42838
Night	19996	17519	16875	16653
Weekend	14549	12470	11984	11790

Figure 2. Kaplan–Meier survival estimates show 30-day in-hospital event-free survival stratified by time of admission, comparing night shift and routine-hours admission and weekend and routine-hours admission. HR=hazard ratio, 95% CI = 95% confidence interval.

in routine-hours admissions (1.89 points, standard deviation 2.26) and lowest during night-shifts (1.81 points, standard deviation 2.22). 98.2% were admitted with sepsis and 1.7% with septic shock. The most common comorbidities were arterial hypertension (42.2%), renal insufficiency (33.4%), and diabetes mellitus (21.7%) (S1 Table, <http://links.lww.com/MD/E429>). The overall all-cause in-hospital mortality was 19.0%, 29.6% of hospitalizations were admitted to the ICU, 13.9% were intubated, and 10.3% were readmitted for any cause within 30 days after discharge.

Compared to routine-hour admissions, adjusted all-cause in-hospital mortality was higher in patients admitted on weekends with multivariable regression analyses revealing a 5% higher

in-hospital mortality (OR 1.05, 95% CI 1.01,1.10, $P = .041$) for admissions on weekends. The Kaplan–Meier plot shows that there were more deaths in hospitals within 30 days amongst weekend compared to routine-hours admissions (Log-rank test $P < .001$, Fig. 2).

The adjusted OR for ICU admission (OR 1.14, 95% CI 1.10, 1.19, $P < .001$) and intubation (OR 1.18, 95% CI 1.12, 1.25, $P < .001$) was higher on weekends compared with routine-hour admissions, whereas 30-day readmission rates showed no significant difference (Table 2). The sensitivity analysis comparing the years 2006 to 2013 and 2014 to 2016 is further supporting our main findings, that weekend admissions have a higher OR for in-hospital mortality when sepsis cases are more severe (S2 Table, <http://links.lww.com/MD/E429> and S1 Fig, <http://links.lww.com/MD/E429>).

Admissions during night shifts were associated with lower adjusted all-cause in-hospital mortality compared to routine-hour admissions with a 7.0% lower in-hospital mortality during night shifts (OR 0.93, 95% CI 0.89, 0.97, $P = .001$) in the multivariable regression analysis. This association of a lower 30-day in-hospital mortality with night shift admission is also illustrated in the Kaplan–Meier plot, though with a higher rate of deaths in the early days (early vs late effect, Fig. 2). Compared to routine-hour admissions, hospitalizations for sepsis during night shifts faced a higher OR for ICU admission (OR 1.28, 95% CI 1.23, 1.32, $P < .001$) and intubation (OR 1.31, 95% CI 1.25, 1.37, $P < .001$). We found no significant differences regarding 30-day readmission rates between routine-hours and night shifts (Table 2).

Detailed incidences for the primary and secondary outcomes in different pre-defined regions of Switzerland are shown in S3 Figure, <http://links.lww.com/MD/E429>.

3.1. Subgroup analysis

For interregional differences, we compared the OR of 1 region during after-hours with the overall OR during routine-hours. We found, that the OR for in-hospital mortality was highest in the

Table 2
Association of time of admission with primary and secondary outcomes.

	No. Events by TOA, n (%)	Multivariable regression	
		OR (95% CI)	P-value
In-hospital mortality	16448 (19.0)	–	–
Weekday	9985 (19.2)	ref	ref
Night	3549 (17.7)	0.93 (0.89–0.97)	.001
Weekend	2914 (20.0)	1.05 (1.01–1.10)	.041
ICU admission	25617 (29.6)	–	–
Weekday	14568 (28.0)	ref	ref
Night	6606 (33.0)	1.28 (1.23–1.32)	<.001
Weekend	4443 (30.5)	1.14 (1.10–1.19)	<.001
Intubation	11995 (13.9)	–	–
Weekday	6691 (12.9)	ref	ref
Night	3172 (15.9)	1.31 (1.25–1.37)	<.001
Weekend	2132 (14.7)	1.18 (1.12–1.25)	<.001
30-d readmission	8950 (10.3)	–	–
Weekday	5426 (10.4)	ref	ref
Night	2068 (10.3)	0.99 (0.93–1.04)	.615
Weekend	1456 (10.0)	0.96 (0.90–1.02)	.186

Risk adjustment was made for age, sex, Charlson Comorbidity Index (CCI), year, month, and region of admission and Severity of Sepsis (Sepsis vs Septic Shock). 95% CI = 95% confidence interval, ICU = intensive care unit, OR = odds ratio, ref = reference.

region “Tessin: (OR 1.24, 95% CI 1.04, 1.48, $P=.019$) during weekend admissions and highest in the region “Nordwestschweiz” (OR 1.06, 95% CI 0.95, 1.18, $P=.284$) during night shifts. We found the lowest OR per region during after-hours in the region “Zuerich” (OR 0.90, 95% CI 0.80, 1.01, $P=.085$) for weekend admissions and in the region “Espace Mittelland” (OR 0.89, 95% CI 0.81, 0.97, $P=.009$) during night shifts.

Regarding ICU admission, the OR was highest in the region “Tessin” at night (OR 1.53, 95% CI 1.32, 1.78, $P<.001$). We found the highest OR for intubation in the region “Tessin” (OR 1.67, 95% CI 1.35, 2.07, $P<.001$) during night shifts. And, we found the highest 30-day re-admission rate in the region “Zentralschweiz” (OR 1.17, 95% CI 0.97, 1.42, $P=.099$) during night shifts. Detailed results are illustrated in S3 Table, <http://links.lww.com/MD/E429>, S2 Figure, <http://links.lww.com/MD/E429> and S3 Figure, <http://links.lww.com/MD/E429>.

On the subject of the absolute adjusted risk (AAR) stratified by different regions of Switzerland we found the highest overall in-hospital mortality in the region “Tessin” (Absolute risk difference [ARD] 6.24%, 95% CI 4.88, 7.60, $P<.001$) and lowest in the region “Espace Mittelland: (ARD -2.22%, 95% CI -2.82, -1.63, $P<.001$) compared to all other regions. The absolute adjusted risk [AAR] for overall ICU admission was highest in the region “Tessin” (ARD 6.21%, 95% CI 4.70, 7.71, $P<.001$). Regarding intubation, the absolute adjusted risk [AAR] was highest in the region “Zuerich” (ARD 4.12%, 95% CI 3.32, 4.92, $P<.001$). Comparing all different regions of Switzerland, we found the highest absolute risk [AAR] for overall 30-day readmission in the region “Tessin” (ARD 4.05%, 95% CI 2.88, 5.23, $P<.001$). Detailed results are shown in S4 Table, <http://links.lww.com/MD/E429>, AARs stratified by region and time of admission are listed in S5 Table, <http://links.lww.com/MD/E429>.

4. Discussion

The aim of this study was to investigate an association between clinical outcomes and after-hours admission in patients with sepsis. Using administrative data of patients admitted for all-cause sepsis the key findings are fourfold. First, a hospitalization for sepsis during the weekend compared to routine-hours was associated with a higher in-hospital mortality. Second, after-hour admissions including weekends and night shifts were associated with a higher OR of ICU admission and intubations. Third, night shift admissions were associated with lower in-hospital mortality and fourth, 30-day readmission rates did not differ significantly.

The so-called “after-hours” effect, referring to impaired outcomes associated with admission during after-hours, was first described in 2001.^[10] Up to date, results in the literature are mixed investigating conditions requiring prompt management, with various studies proclaiming differences in outcomes depending on time of admission,^[11,16,21] whereas other studies did not find such associations.^[22,23] Few studies discuss whether outcome differences are rather related to time trends over the week, other than after-hour duties.^[12,23] Changing the time boundaries between routine hours and after-hours (e.g., 7 AM to 7 PM instead of 8 AM to 8 PM) in a sensitivity analysis did not relevantly alter the results.

Various explanations for this effect have been described. Mostly and controversially discussed are the reduced level of staffing and physician fatigue^[10,16,22,24] during after-hour shifts. Supporting, we found an association between weekend admissions and higher in-hospital mortality, an increased ICU

admission-, and intubation in septic patients.^[25,26] However, in-hospital mortality was lower in admissions during the night compared to routine-hour admissions.

These findings are also in line with previous results from recent studies involving different acute care conditions.^[27] A possible explanation is that professionals working during night shifts are more experienced, whereas staff during weekend shifts have lower experience than those working during routine-hours.^[10,16] Importantly, we did not find any change in in-hospital mortality comparing Saturdays and Sundays (data not shown). The clinical presentation of sepsis is diverse and, in fact, sometimes misleading, thus requiring clinical experience. Therefore, the teaching level and skills of the staff involved is of utmost importance.^[7,14,15,28]

There are also arguments that the weekend effect may be caused by the fact that patients are sicker when admitting during after-hours.^[26] We could not confirm this hypothesis, as CCI scores were higher during routine-hours compared to after-hours. However, our findings were congruent with lower CCI scores and all-cause in-hospital mortality during night shifts. Nonetheless, we are aware that the CCI is questionable to serve as a good measure of illness severity on admission.^[29]

Further possible reasons for impaired outcomes during after-hours, such as lower adherence to protocol, time to interventions and availability of specialists is still debatable and was not investigated in our study.^[30]

The clinical relevance of the described differences in in-hospital mortality is unclear, even though statistically significant. The validity of in-hospital mortality as a quality parameter has been questioned by physicians, yet, overall 30-day mortality was not available in our dataset. In line with previous studies, after-hour admissions were associated with higher ICU admission- and intubation-rates, while 30-day readmission rates did not vary significantly.^[25–27,31]

Analysing patient outcomes between different geographical regions we found a substantial interregional heterogeneity. Interestingly, areas with a higher absolute proportion of in-hospital mortality, ICU-admission, and intubation rate, also showed a higher OR for impaired outcomes in after-hours compared to routine-hour hospitalization. Possible explanations may be different adherence to bundled care approaches and different staffing level. Especially in the southern part of Switzerland we found a stronger association of being intubated or admitted to the ICU during night shifts and on weekends. Whether staffing and medical resources are reduced in this region or systematic differences such as variations in ethnicity, health care funding or community services may influence these disparities remains to be investigated.

This study has limitations. First, using administrative data is prone to confounding as hospitalizations were selected according to the ICD-10 classification with the risk of misclassification. Further, the non-experimental design of our study limits the ability to draw a firm causal link between admission times and outcomes of interest. Second, changes in coding and definition of sepsis (in 2014 definition was changed from an organ-infection without organ dysfunction (sepsis) to one with organ dysfunction [former severe sepsis]), could have led to an altered data collection, however, this should not have affected our interpretation. Third, we did not include national holidays in our data analysis, possibly blurring some of the observed effects. Fourth, we had no data about patient history, clinical appearance, laboratory parameters that plays an important role in the severity of acute illness and the outcome of sepsis patients. Fifth, since we

do not have information about time to treatment and its type, we could not adjust our analyses for these factors.^[7] Sixth, we did not adjust for the reduced number of admissions during after-hours compared to routine-hours, possibly influencing the results. Seventh, by excluding surgical patients a selection bias regarding the focus of infection may be present. Eighth, as this is an observational study, we cannot exclude residual confounding although having adjusted for the main potential confounders. And last, since we had no information about hospital size, staffing and teaching status in the available dataset we were unable to analyze if these factors may influence the outcome differences of the admission times, as indicated by previous studies.^[10,28]

In conclusion, among hospitalizations with a main diagnosis of sepsis, weekend admissions were associated with higher odds risk for in-hospital mortality, ICU admission, and intubation. Whether these findings can be explained by staffing-level differences needs to be investigated.

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