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Influence of hospital characteristics on quality of care in patients with community-acquired pneumonia

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Summary

PRINCIPLES: In-hospital care of patients with community-acquired pneumonia (CAP) varies across hospitals. Understanding of the underlying factors is the basis for tailored quality improvements. Using data from a randomised controlled Swiss-wide multicentre trial, we compared length of stay (LOS) and other patient outcomes according to (A) the use of a procalcitonin (PCT)-based antibiotic stewardship protocol, (B) institution type (university vs non-university), and (C) historical time period in relation to the introduction of Diagnosis Related Group (DRG) reimbursement (2012).

Abbreviations

ARDS	acute respiratory distress syndrome
CAP	community-acquired pneumonia
CI	confidence interval
COPD	chronic obstructive pulmonary disease
CRP	C-reactive protein
DRG	Diagnosis Related Group
HR	hazard ratio
IQR	interquartile range
LOS	length of stay
OR	odds ratio
PCT	procalcitonin
PPS	prospective payment system
PSI	Pneumonia Severity Index
SD	standard deviation

METHODS: We included 784 patients hospitalised with CAP from six institutions into this secondary analysis. We used multivariable regression models adjusted for age, comorbidities and disease severity to determine the influence of institution characteristics on LOS and patient outcomes.

FINDINGS: LOS was significantly shorter in the institution using a PCT-based antibiotic stewardship protocol (9.2 vs 5.3 days; adjusted mean difference 3.92 days; 95% confidence interval [CI] 5.16–2.68) with shorter antibiotic treatment. There was no difference in LOS in university vs non-university hospitals, but antibiotic courses in university-type hospitals were longer (11.0 vs 8.3 days; adjusted mean difference 2.59 days; 95% CI, 1.69–3.49). No significant difference in LOS was found when comparing the time period before and after the introduction of the DRG system in Switzerland.

CONCLUSIONS: We found differences in LOS associated with theuse of a PCT-based antibiotic stewardship protocol, which remained robust after multivariable adjustment. Importantly, the type of institution and model of reimbursement did not influence LOS in our CAP cohort. More health services research studies are needed to establish causal effects.

Key words: *community-acquired pneumonia; length of stay; quality of care; practice guidelines; treatment protocol; hospital type; reimbursement system*

Introduction

Healthcare expenses are rising in Switzerland, as in many other countries in Europe and worldwide. During recent years the level of healthcare costs in Switzerland increased although the rate at which costs increased slowed during the 15-year period from 1996 to 2011. Between 2006 and 2011, total health-related costs increased at an average annual rate of about 2.1%, attaining about 65 billion Swiss francs in 2011 [1]. Identifying possible inefficiencies and understanding the underlying sources is thus a core issue of healthcare management to improve the performance of hospitals. Importantly, studies about efficiency of hospitals should focus not only on economic outcome but also on clinical outcome. To assess quality of care, measures such as time to clinical stability and return to daily activity, or low rates of complications and mortality are key comparators. Common diseases with a large economic burden are ideal targets for quality improvement initiatives [2, 3]. In this context, community-acquired pneumonia (CAP) is an important disease affecting 1.6 to 11 per 1000 adults [4–6]. It is still one of the most common acute infections necessitating hospitalisation [7, 8] and it is, according to the World Health Organization, the fourth leading cause of death worldwide and accounts for the leading cause of disability-adjusted life years (DALYs) [9–11]. Rates of in-hospital care for CAP range between 15% and 60%. Importantly, costs for in-hospital care are high and closely related to length of hospital stay (LOS) [12–15].

The variability among hospitals in quality of care in general, and LOS in particular, has many influencing factors [2, 13, 16]. Three main categories may explain this variability including (1) patients' characteristics (mainly severity of disease and comorbidities), (2) physicians' practices and skills, as well as adherence to guidelines for the treatment of CAP [5, 17], and (3) hospital or healthcare system-related characteristics [18]. As patient characteristics cannot directly be influenced, interventions should focus on improvement either of physicians' skills or of hospital processes including in-hospital and discharge management, respectively. Implementation of clinical pathways and prediction rules to standardise care and to facilitate daily work are effective in improving LOS and clinical outcomes [19–21]. The Pneumonia Severity Index (PSI), which stratifies the patients into five categories of risk for 30-day mortality, may help with severity adjustment, triage and improving site-of-care decisions upon emergency department presentation [22, 23]. Similarly, antibiotic stewardship protocols including procalcitonin (PCT) have been found to markedly lower antibiotic consumption and improve care of CAP patients, with positive effects on antibiotic-related side effects and on mortality in the context of critically-ill patients [24–27]. Although PCT has been found effective in safely reducing use and duration of antibiotic treatment, there is insufficient evidence of its real-life impact on relevant social and economic variables such as healthcare-related costs or LOS [28, 29].

Hospital-related characteristics, such as the size or type of a hospital (university vs non-university hospitals), may also influence quality of care and LOS even more than a single procedure such as the implementation of a clinical treatment protocol [2, 13, 16, 20]. The effects may partly relate to patient characteristics as sicker patients tend to be hospitalized to larger public hospitals, but other effects may also exist, and further research to highlight these factors is still in demand.

The reimbursement system may also affect quality of care and influence LOS [30, 31]. In Switzerland, the Swiss Parliament passed a law to introduce a Diagnosis Related Group (DRG)-based hospital financing system, replacing various fee-for-service financing systems in the different cantons (states) on 1 January 2012. The DRG system was expected to create an incentive for hospitals to perform medical care as cheaply as possible, and thus reduce patients' LOS and thereby curtail the increasing costs associated with in-hospital patient care. Whether the quality of care will be affected by the transition of the reimbursement system remains, however, unclear [32–34].

Having access to the database of a large and well-conducted multicentre randomised study in CAP [35], we had a unique opportunity to compare quality of care and patient outcomes in hospital based on (A) the use of a PCT-based antibiotic stewardship protocol, (B) institution type (university vs non-university) and (C) historical time period in relation to the introduction of DRG-based reimbursement (2012).

Methods

Aims

The aim of this analysis was to investigate differences in quality of care, defined as LOS, time to clinical stability, duration of antibiotic treatment, and adverse patient outcomes across hospitals based on three institution characteristics, namely (A) use of a PCT-based antibiotic stewardship protocol, (B) type of institution (university vs non-university) and (C) historical time period in relation to the introduction of DRG reimbursement (1 January 2012).

Study design, setting and patients

This was a secondary analysis of an investigator-initiated, multicentre, randomised, placebo-controlled trial with the primary outcome of time to clinical stability in CAP patients treated with adjunct corticosteroids or placebo [35]. The conduct of the original trial adhered to the declaration of Helsinki and good clinical research practice guidelines, and ethics committees of all participating hospitals approved the study prior to patient recruitment. All patients provided written informed consent. A detailed study protocol has been published previously (ClinicalTrials.gov. number NCT00973154) [36].

In brief, from December 2009 to May 2014, from a total of 2911 potential patients, 802 patients presenting with the diagnosis of a lower respiratory tract infection were consecutively enrolled at emergency departments or medical wards in seven different hospitals in Switzerland, and underwent randomisation. After blinded post-randomisation exclusion of 17 patients retrospectively not meeting eligibility criteria, 392 patients were allocated to adjunct prednisone treatment and 393 patients to placebo.

Inclusion criteria were age of 18 years or older and hospitalisation with CAP defined as a new infiltrate on chest radiograph and the presence of at least one of the following signs and symptoms: cough, sputum production, dyspnoea, core body temperature ≥38.0 °C, auscultatory findings of abnormal breathing sounds or rales, leukocyte count >10.0 or <4.0 G/l [37]. Exclusion criteria were permanent inability to give informed consent, active intravenous drug use, acute burn injury, gastrointestinal bleeding within the past 3 months, known adrenal insufficiency, a condition requiring more than 0.5 mg/kg/d prednisone or equivalent, pregnancy or breast feeding, and severe immunosuppression Severe immunosuppression was defined as one of the following: infection with human immunodeficiency virus and a CD4 cell count below 350 G/l, immunosuppressive therapy after solid organ transplantation, neutropenia <0.5 G/l or neutrophils of 0.5–1 G/l during ongoing chemotherapy with an expected decrease to values below 0.5 G/l, cystic fibrosis, or active tuberculosis [35]. The aim of the initial study was to evaluate whether short-term corticosteroid treatment reduces time to clinical stability in patients hospitalised for CAP.

All patients were treated according to current CAP guidelines [38, 39]. Within the study, the decision of the type and duration of intravenous or total antibiotic treatment, as well as the decision to discharge patients, was left to the discretion of the treating physicians without interference by the study team. However, all of the treating physicians had access to the study flow chart, which suggested objective discharge criteria (possible oral intake of food, liquids and drugs, stable vital signs >24 hours, recovery from CAP-related worsening of mental status, no evidence of acute serious CAP or related comorbidity that necessitated further hospitalisation).

Patient outcomes

Baseline data contained medical history items, relevant comorbidities, clinical items relating to pneumonia, and all parameters required for the calculation of the PSI [22].

Study nurses evaluated patients every 12 hours during hospitalisation for clinical stability (primary endpoint in the original study). Clinical stability was defined as time (days) until stable vital signs (including temperature of 37.8 °C or lower, heart rate of 100 beats per minute or lower, spontaneous respiratory rate of 24 breaths per min or lower, systolic blood pressure of 90 mm Hg or higher, mental status back to level, ability to intake orally, and adequate oxygenation on room air) for 24 hours or longer [35]. In addition, duration of total and intravenous antibiotic treatment was recorded, as was time to discharge from hospital, all-cause mortality and incidence of CAP complications (i.e. acute respiratory distress syndrome [ARDS], empyema, persistence of pneumonia) within 30 days. Structured follow-up telephone interviews for secondary outcomes after discharge were performed on day 30 and included assessment of adverse events such as recurrence of pneumonia, or re-hospitalisation.

In this secondary analysis we examined quality of care and patient outcomes defined as follows: length of stay (LOS: time from hospitalisation to effective hospital discharge measured in days) as our main endpoint; time to clinical stability (as defined in the initial trial), total duration and duration of intravenous antibiotic treatment (details on dosing of all prescribed antimicrobials during the study period were recorded by study nurses and reassessed every 12 hours), death from any cause within 30 days, re-hospitalisation and CAP complications such as ARDS, empyema, persistence of pneumonia, as well as respiratory failure or CAP-associated mortality, which was defined as death from CAP or CAP complications, until day 30 as further endpoints.

Statistical analysis

We used descriptive statistics including means and standard deviations (SDs), medians and interquartile ranges (IQRs; 25th–75th percentiles), or natural frequencies and percentages to summarise data. Two-group comparison was done by chi-square tests and the student's t test or Mann-Whitney U test as appropriate. Our main research question was to compare quality of care and patient outcomes according to three institution characteristics: (A) use of a PCT-based antibiotic stewardship protocol, (B) type of institution (university vs non-university) and (C) historical time period in relation to the introduction of DRG reimbursement. Accordingly, we performed three separate statistical analyses using univariable and multivariable regression analysis. For our first analysis (A), we compared one centre that had the PCT stewardship algorithm routinely implemented, and continuously promoted its use (PCT-enforced) to all other centres, in which the algorithm was not promoted in the same manner (non-PCT-enforced). For the second analysis (B), we divided the institutions based on the characterisation made by the Federal Statistical Office and the Federal Office of Public Health into university type (K111) and non-university type (K112) [40]. One hospital did not meet either definition, and was thus excluded (characterised as a basic hospital, K121). The above-mentioned PCT-enforced centre was secondarily excluded although it met the definition of a type K112 hospital. For the third analysis (C), we compared patients included up to December 2011 with patients enrolled from 1 January 2012 until the end of the study in May 2014. The cantons of two of the involved hospitals (Aargau and Solothurn) introduced an AP-DRG reimbursement system based on the German G-DRG system before SwissDRG was implemented nationwide in 2012. These two hospitals were excluded from that analysis.

For all outcomes, unadjusted and adjusted effect estimates were calculated together with corresponding 95% confidence intervals (CIs) using linear, logistic, or Cox proportional hazards regression (as appropriate). Regression models were adjusted for the following possible predefined confounders: Total PSI, maximum level of C-reactive protein (CRP), age, initial randomisation, current smoking status, and presence of chronic obstructive pulmonary disease (COPD), diabetes mellitus, cerebrovascular disease, congestive heart failure, malignancy or renal insufficiency. In the third analysis investigating the influence of the reimbursement system we additionally adjusted for the treating centre because some centres joined the trial late and recruitment was thus uneven in the different centres over time. The variables for multivariable adjustment were preplanned on the basis of biological plausibility and the cur-

rent literature [2, 41, 42]. We also performed several sensitivity analyses additionally adjusting for time to clinical stability and presence of bacteraemia.

All statistical tests were two-sided and carried out at a significance level of 5%. Analyses were performed with STATA 12.1 (Stata Corp, College Station, Texas, USA).

Results

Baseline characteristics

This secondary analysis included 784 patients with a definite diagnosis of CAP, whose data were collected during the original study from December 2009 to May 2014. The mean age of the patients was 69.8 years, and 38% were women. Patients had a high burden of comorbidities including diabetes, congestive heart failure, COPD and chronic renal insufficiency. The majority of patients were in high-risk PSI classes IV and V.

Baseline characteristics of the population overall and stratified by (A) the use of a PCT-based antibiotic stewardship protocol (PCT-enforced centre vs non-PCT-enforced centres), (B) the type of institution (university vs non-university) and (C) historical time period in relation to the introduction of the DRG reimbursement are shown in table 1.

For our first analysis (A), patient characteristics in terms of age and gender were similar, as were most baseline data except for neoplastic disease (10.8% vs 6.0%), history of chills (28.4% vs 43.6%), body temperature (37.4 °C vs 37.7 °C), and creatinine levels (114.3 µmol/l vs 101.0 µmol/l).

For the analysis according the type of institution (B) we had an older population in university hospitals. Also, there were significantly more patients with congestive heart failure and renal failure in university hospitals. Total PSI score in university hospitals was higher than in non-university hospitals (94.9 points vs 86.2 points) and we had significantly more patients in higher PSI classes in university hospitals than in non-university hospitals. Further, there were differences in clinical signs and laboratory findings such as a history of chills, mean body temperature, and CRP and albumin levels.

In the third analysis (C), the patient population in the time before implementation of DRGs had fewer current smokers (20.3% vs 27.9%) but more chronic renal failure (35.3% vs 27.1%) compared with the time after the implementation of DRGs.

Differences in quality of care

In our first analysis (A) comparing the PCT-enforced centre to non-PCT-enforced centres, mean LOS was significantly shorter in the PCT-enforced centre (5.3 vs 9.2 days, mean difference 3.92 days, 95% CI 2.6-5.24, p <0.001). This result was confirmed in multivariate linear regression models (mean difference [MD] 3.92, 95% CI 5.16–2.68) adjusted for age, initial randomisation, severity (PSI score) and comorbidities. We also performed a sensitivity analysis additionally adjusting for time to stability and bacteraemia (see appendix), which showed robust results. Median time to clinical stability (3.0 vs 4.0 days; adjusted hazard ratio [HR] 1.41, 95% CI 1.16–1.70, p <0.001), total duration of antibiotic treatment (MD –1.85 days, 95% CI –2.77 to –0.95, p <0.001), and intravenous antibiotic treatment (MD –2.10 days, 95% CI –2.96 to –1.25, p <0.001) were all significantly shorter in the PCT-enforced centre. There was a significant difference in 30-day mortality in the univariate analysis (6.76% vs 2.99%, p = 0.033), which was no longer significant after multivariable adjustment (adjusted odds ratio [OR] 2.07, 95% CI 0.84–5.08, p = 0.113). There was no difference in adverse outcomes such as rehospitalisation (adjusted OR 0.52, 95% CI 0.23–1.2, p = 0.127), or CAP-associated complications (2.7% vs 4.56%; adjusted OR 0.64, 95% CI 0.21–1.93, p = 0.428). Detailed results are shown in table 2.

As shown in table 3, the second analysis (B) with regard to type of hospital did not reveal a significant difference between LOS in university hospitals and non-university hospitals (mean LOS 9.9 vs 7.8 days; MD –1.22 days, 95% CI –0.06 to 2.51, p = 0.061). On the other hand, total duration of antibiotics (11.0 vs 8.3 days; MD 2.59 days, 95% CI 1.69–3.49, p <0.001), and intravenous antibiotic treatment (6.6 vs 4.9 days; MD 1.35 days, 95% CI 0.46–2.23, p = 0.003) were significantly longer in university hospitals. These significant findings were confirmed in adjusted regression analyses. Because time to clinical stability was significantly different in university hospitals compared with non-university hospitals (4.42 vs 2.5 days), we performed a sensitivity analysis adjusted for time to clinical stability. After full adjustment there was no longer any significant difference in the duration of intravenous antibiotic treatment, but the significance in total duration of antibiotics remained robust (appendix, supplementary table S1). CAP-associated complications were lower in non-university hospitals (5.79% vs 1.55%; adjusted OR 3.66, 95% CI 1.06–12.71, p = 0.041). There was no difference in adverse advents such as rehospitalisation (adjusted OR 1.27, 95% CI 0.63–2.56, p = 0.501), or death within 30 days (adjusted OR 5.54, 95% CI 0.7–43.9, p = 0.105).

Table 4 shows results of the third analysis (C) comparing outcomes in regard to DRG implementation. There was no significant difference in LOS (mean LOS 9.7 vs 8.8 days; adjusted MD 0.69 days, 95% CI 1.92 to –0.54, p = 0.271) before and after DRG implementation. Also, there was no significant difference in time to clinical stability or use of antibiotics between the two groups. Death from any cause within 30 days or rehospitalisation were similar before and after the implementation of DRGs. CAP-associated complications tended to be lower after the implementation of the DRG reimbursement system (6.1% vs 3.03%; adjusted OR 0.34, 95% CI 0.13–0.91, p = 0.032).

Sensitivity analysis

We also performed sensitivity analyses, adjusting the models for additional parameters. Adjusting the models for ARDS and ICU admission did not affect the analysis, particularly for LOS. Also, inclusion of mortality into the model did not change the outcomes estimates. Models also remained mostly robust when adding time to clinical stability and bacteraemia with the exception of the duration of intravenous antibiotic treatment in analysis B as mentioned above, and of CAP-associated complications in analysis B that were no longer significantly differing when adjusting

as well for time to clinical stability and bacteraemia (supplementary table S1).

Discussion

In this secondary analysis of a previous randomised controlled trial, we assessed LOS and adverse patient outcomes across different Swiss hospitals in regard to use of a PCT-based antibiotic stewardship protocol, type of hospital, and time period before and after DRG implementation. Because of possible differences in patient populations across these institutions, multivariable adjustment was made. The study revealed three key findings. First, the centre using a PCT-based antibiotic stewardship protocol had a significantly reduced LOS of 3.9 days and a shorter duration of antibiotic treatment of about 2 days with otherwise similar patient outcomes. Second, patients in university-type hospitals had longer antibiotic courses and more CAP-related complications, but the type of the institution did not influence LOS. Third, in our cohort of CAP patients DRG implementation did not affect any measures of outcome in the observed time period.

Implementation of biomarker-based treatment protocols – if well-conceived and implemented – facilitates daily work and is effective in improving LOS and clinical outcomes [19–21]. Efficacy, practicability and safety of a PCT-guided antibiotic stewardship protocol have been investigated in several randomised controlled trials although LOS was not reduced in these studies [25, 43–46]. Also, real-life studies found favourable outcomes when the PCT algorithm was used outside of trial conditions [47, 48]. Our results are in line with these findings and show a lower use of resources in regard to antibiotic treatment and LOS with similar patient outcomes in the centre enforcing a PCT-

Table 1: Baseline characteristics of patients according to: (A) use of antibiotic stewardship protocol including procalcitonin; (B) type of institution (university vs non-university); (C) historical time period in relation to the introduction of DRG reimbursement.

		A			B			C		
Characteristic	**All patients (n = 784)**	**PCT-enforced centre (n = 148)**	**Non-PCT-enforced centres (n = 636)**	**p-value**	**University hospitals (n = 432)**	**Non-university hospitals (n = 341) ***	**p-value**	**Before Implementation of DRG (n = 295)†**	**After Implementation of DRG (n = 330)†**	**p-value**
Demographics										
Age (years)	69.8 (17.1)	70.2 (18.2)	69.6 (16.8)	0.7	70.7 (16.6)	67.2 (16.8)	0.0017	69.15 (17.8)	70.1 (15.8)	0.45
Female Sex	298 (38.0%)	58 (39.2%)	239 (37.6%)	0.72	151 (35.0%)	83 (43.0%)	0.055	112 (38.0%)	122 (37.0%)	0.8
Previous history										
Current smoker	201 (25.6%)	45 (30.4%)	156 (24.5%)	0.14	104 (24.1%)	48 (24.9%)	0.83	60 (20.3%)	92 (27.9%)	0.028
Body mass index (kg/m^2)	26.6 (6.3)	27.0 (5.4)	26.5 (6.5)	0.4	26.6 (6.9)	26.4 (5.6)	0.68	26.7 (5.7)	26.4 (7.2)	0.54
Coexisting Illnesses										
Diabetes	155 (19.8%)	28 (18.9%)	127 (20.0%)	0.77	94 (21.8%)	32 (16.6%)	0.13	61 (20.7%)	65 (19.8%)	0.77
Heart failure	142 (18.1%)	28 (18.9%)	114 (18.0%)	0.78	90 (20.9%)	23 (11.9%)	0.007	55 (18.6%)	58 (17.6%)	0.74
COPD	136 (17.3%)	26 (17.6%)	110 (17.3%)	0.94	81 (18.8%)	26 (13.5%)	0.11	50 (16.9%)	57 (17.3%)	0.91
Cerebrovascular disease	69 (8.8%)	15 (10.1%)	54 (8.5%)	0.53	41 (9.5%)	11 (5.7%)	0.11	23 (7.8%)	29 (8.8%)	0.65
Renal failure	251 (32.0%)	52 (35.1%)	199 (31.3%)	0.37	149 (34.6%)	44 (22.8%)	0.003	104 (35.3%)	89 (27.1%)	0.027
Neoplastic disease	54 (6.9%)	16 (10.8%)	38 (6.0%)	0.037	28 (6.5%)	10 (5.2%)	0.53	21 (7.1%)	17 (5.2%)	0.31
Clinical history and findings										
History of chills	319 (40.6%)	42 (28.4%)	277 (43.6%)	<0.001	207 (47.9%)	68 (35.2%)	0.003	141 (47.8%)	134 (40.6%)	0.071
History of cough	662 (84.3%)	129 (87.2%)	532 (83.6%)	0.29	363 (84.0%)	160 (82.9%)	0.72	239 (81.0%)	284 (86.1%)	0.089
Confusion	51 (6.5%)	9 (6.1%)	42 (6.6%)	0.82	33 (7.6%)	8 (4.1%)	0.10	21 (7.1%)	20 (6.1%)	0.59
Body temperature (°C)	37.6 (1.0)	37.4 (0.8)	37.7 (1.0)	0.003	37.9 (0.9)	37.1 (0.9)	<0.001	37.6 (0.94)	37.7 (1.02)	0.48
Laboratory values										
CRP (mg/l)	173.7 (115.7)	163.3 (112.4)	176.2 (116.4)	0.22	164.9 (111.0)	201.2 (122.2)	<0.001	183.7 (121.5)	169.1 (109.9)	0.12
Creatinine (µmol/l)	103.6 (61.3)	114.3 (62.8)	101.0 (60.7)	0.018	103.5 (65.4)	95.7 (49.1)	0.14	106.8 (67.4)	96.1 (54.2)	0.029
Albumin (mg/dl)	31.6 (5.9)	32.3 (5.0)	31.4 (6.1)	0.13	29.9 (5.7)	36.5 (4.8)	<0.001	31.5 (5.6)	31.3 (6.7)	0.75
Severity of disease										
Total PSI (points)	91.1 (36.7)	92.5 (38.4)	90.8 (36.3)	0.61	94.9 (36.2)	81.4 (34.2)	<0.001	91.2 (37.4)	90.3 (35.0)	0.75
PSI class I	92 (11.72%)	18 (12.16%)	74 (11.64%)	0.86	39 (9.03%)	33 (17.1%)	<0.001	39 (13.22%)	33 (10%)	0.42
PSI class II	141 (17.96%)	23 (15.54%)	118 (18.55%)		70 (16.2%)	47 (24.35%)		47 (15.93%)	70 (21.21%)	
PSI class III	166 (21.15%)	29 (19.59%)	136 (21.38%)		94 (21.76%)	39 (20.21%)		65 (22.03%)	68 (20.61%)	
PSI class IV	280 (35.67%)	56 (37.84%)	224 (35.22%)		162 (37.5%)	59 (30.57%)		105 (35.59%)	116 (35.15%)	
PSI class	106 (13.5%)	22 (14.86%)	84 (13.21%)		67 (15.51%)	15 (7.77%)		39 (13.22%)	43 (13.03%)	
Initial randomisation										
Intervention group (steroids)	392 (50.0%)	76 (51.4%)	316 (49.7%)	0.72	214 (49.5%)	172 (50.4%)	0.80	147 (49.8%)	163 (49.4%)	0.91

COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; DRG = diagnosis-related group; PCT = procalcitonin; PSI = Pneumonia Severity Index
Data are mean (standard deviation) or n (%) unless otherwise stated.
* Two hospitals were excluded: one was characterised as a basic hospital, the other was the PCT-enforced centre from analysis A.
† Two of the involved hospitals were excluded (as they had an AP-DRG reimbursement system in place before Swiss DRG was implemented on 1 January 2012).

based antibiotic stewardship protocol. This was also true when the analysis was adjusted for important confounders. In the non-PCT-enforced centres, the PCT algorithm was known as well, but even if its use was encouraged, its implementation was not emphasised in the same manner. As adherence to the PCT algorithm was not an endpoint in the underlying trial, we cannot investigate adherence rates to the PCT algorithm in individual patients. However, we know from a previous study, that overall algorithm compliance outside of study conditions was about 90% in the PCT-enforced centre [48]. Importantly, due to the lack of patient-level data about the use of PCT in this study, we can only find an association of PCT-based antibiotic protocol use and LOS, which does not prove causality. Previous randomised trials did not find reduced LOS associated with PCT use. Other clinical pathways, such as discharge management programmes, that influence LOS may also be different across centres. As hospitals' or physicians' process of care were not an endpoint in the underlying trial, and as there was no censoring of transfers to nurse-led care wards, to rural (step-down) or to rehabilitation clinics, direct exploration of these factors is not possible, and we lack the possibility to further analyse their influence. Also, we found a significant difference in time to clinical stability in the PCT-enforced centre compared with other centres, suggesting a possible unmeasured bias or differences in recording of clinical stability. Still, when this factor was included in the regression analysis, results remained robust,

Table 2: Patient outcomes according to use of antibiotic stewardship protocol including procalcitonin.

Outcomes	PCT-enforced (n = 148)	Non-PCT-enforced (n = 636)	Regression analysis unadjusted HR or OR or mean difference (95% CI)	Regression analysis adjusted * HR or OR or mean difference (95% CI)
Clinical based measures				
Time to clinical stability – days†	3.0 (2–3.42)	4.0 (3.5–4.25)	HR 1.43 (1.19–1.73), p <0.001	HR 1.41 (1.16–1.70), p <0.001
Total duration of antibiotics – days	8.4 (4.6)	10.2 (5.4)	Mean difference 1.80 days (2.76–0.84), p <0.001	Mean difference 1.85 days (2.77–0.92), p <0.001
Intravenous antibiotic treatment – days	4.0 (3.1)	6.1 (5.2)	Mean difference 2.10 days (3.0–1.2), p <0.001	Mean difference 2.10 days (2.96–1.25), p <0.001
Process of care measures (clinical effectiveness)				
Death from any cause within 30 days – n (%)	10 (6.76%)	19 (2.99%)	OR 2.35 (1.07–5.17), p = 0.033	OR 2.07 (0.84–5.08), p = 0.113
Rehospitalisation – n (%)	7 (4.7%)	53 (8.3%)	OR 0.55 (0.24–1.23), p = 0.143	OR 0.52 (0.23–1.20), p = 0.127
CAP-associated complication until day 30 – n (%)	4 (2.7%)	29 (4.56%)	OR 0.58 (0.2–1.68), p = 0.316	OR 0.64 (0.21–1.93), p = 0.428
Process of care measures (economic effectiveness)				
Length of stay – days	5.3 (4.0)	9.2 (8.0)	Mean difference 3.92 days (5.24–2.6), p <0.001	Mean difference 3.92 days (5.16–2.68), p <0.001

CI = confidence interval; HR = hazard ratio; OR = odds ratio; PCT = procalcitonin
Data are mean (standard deviation) or n (%) unless otherwise stated.
* Adjustment for the following possible confounders: Pneumonia Severity Index; maximal level of C-reactive protein, age, initial randomisation, current smoking status, presence of chronic obstructive pulmonary disease, diabetes mellitus, cerebrovascular disease, congestive heart failure, malignancy and renal insufficiency.
† Median (interquartile range).

Table 3: Patient outcomes according to type of hospital.

Outcomes	University hospitals* (n = 432)	Non-university hospitals* (n = 193)	Regression analysis unadjusted HR or OR or mean difference (95% CI)	Regression analysis adjusted † HR or OR or mean difference (95% CI)
Clinical based measures				
Time to clinical stability – days§	4.42 (4.0–5.0)	2.5 (2.19–3.0)	HR 0.57 (0.48–0.68), p <0.001	HR 0.59 (0.5–0.71), p <0.001
Total duration of antibiotics – days	11.0 (5.6)	8.3 (4.0)	Mean difference 2.76 days (1.83–3.69), p <0.001	Mean difference 2.59 days (1.69–3.49), p <0.001
Intravenous antibiotic treatment – days	6.6 (5.8)	4.9 (3.1)	Mean difference 1.69 days (0.78–2.6), p <0.001	Mean difference 1.35 days (0.46–2.23), p = 0.003
Process of care measures (clinical effectiveness)				
Death from any cause within 30 days – n (%)	16 (3.7%)	1 (0.52%)	OR 7.39 (0.97–56.08), p = 0.053	OR 5.54 (0.7–43.9), p = 0.105
Rehospitalisation – n (%)	41 (9.49%)	12 (6.22%)	OR 1.58 (0.81–3.08), p = 0.178	OR 1.27 (0.63–2.56), p = 0.501
CAP-associated complication until day 30 – n (%)	25 (5.79%)	3 (1.55%)	OR 3.89 (1.16–13.04), p = 0.028	OR 3.66 (1.06–12.71), p = 0.041
Process of care measures (economic effectiveness)				
Length of stay – days	9.9 (8.9)	7.8 (5.1)	Mean difference 2.12 days (0.78–3.46), p = 0.002	Mean difference 1.22 days (–0.06–2.51), p = 0.061

CI = confidence interval; HR = hazard ratio; OR = odds ratio
Data are mean (standard deviation) or n (%) unless otherwise stated.
* Two hospitals were excluded: one was characterised as a basic hospital; the other was the PCT-enforced centre from analysis A.
† Adjustment for the following possible confounders: Pneumonia Severity Index, maximum level of C-reactive protein, age, initial randomisation, current smoking status, presence of chronic obstructive pulmonary disease, diabetes mellitus, cerebrovascular disease, congestive heart failure, malignancy and renal insufficiency.
§ Median (interquartile range).

arguing against such effects being solely responsible for the observed differences in LOS.

Of note, although in univariate analysis mortality was higher in the centre using a PCT-based antibiotic stewardship protocol, results were no longer statistically significant after multivariable adjustment, arguing for confounding effects. In addition, although antibiotic duration in this study was higher than in previous randomised controlled trials performed at the same institution (mean 8.4 vs 5.7 in ProHOSP [25]), the effect was still significant compared with the other institutions.

We also found some differences in CAP patients treated in university hospitals compared with non-university hospitals. There was a significant difference in total duration of antibiotic and intravenous antibiotic treatment. These differences were robust after adjustment for severity of illness using the PSI and comorbidities. When adjusted also for time to clinical stability – as this, too, differed significantly between university hospitals and non-university hospitals – the duration of intravenous antibiotic treatment was no longer significantly different, but the significance in total duration of antibiotics remained stable. In our study the type of the institution did not influence LOS.

These findings are largely consistent with the literature, where variation in quality of care among different types of hospitals was found as well [2, 16]. As a result of differences in healthcare systems in different countries and a lack of standardised classification for hospital types, such comparisons may be limited. Most common is the classification into major teaching, minor teaching, and nonteaching hospitals [16, 49–51], or the distinction into regional, rural, and urban/metropolitan hospitals [13, 19, 52]. There is no consensus regarding quality of care in teaching versus nonteaching hospitals. No difference in patient outcomes was found in two reviews from the US comparing teaching with nonteaching hospitals, and patients from general internal medicine with mixed (medical and surgical) patients [50, 51]. An older study from Keeler et al. found that the quality of care was better in teaching hospitals than in nonteaching hospitals. However, quality of care was measured by rating physicians' performance and more objective criteria such as mortality or LOS were not used [52].

We found significant differences only in the duration of the antibiotic courses and a trend in regard to LOS. Thus, our analysis did not reveal big differences in quality of care between university and non-university hospitals. The fact that there was no significant difference in the duration of intravenous antibiotic treatment after also adjusting for time to clinical stability and bacteraemia emphasises that patient-based criteria to determine the duration of an intravenous treatment are more important than the type of institution. The longer duration of antibiotic treatment in university hospitals found in our analysis possibly reflects the medical education and research activity found at bigger teaching hospitals, which lead to less effective clinical pathways and management processes. But as LOS was not directly influenced, this finding cannot be numbered among the crucial factors of process of care to increase efficiency of hospitals.

Summing up the two analyses, we speculate that implementation of clinical and management pathways in an institution could help standardise physicians' practice preferences, increase efficiency of pathways, and thereby improve quality of care. But again, prioritised core areas (like a focus on research or highly specialised medicine) cannot, indeed, be obliterated with practice guidelines and optimising patient processes.

Thirdly, no significant difference in LOS and outcomes was found in regard to introduction of the DRG system. It was generally assumed that LOS would be reduced with the introduction of a DRG-based reimbursement system. Several studies in various countries have investigated the effect of a prospective payment system (PPS) such as the DRG-based reimbursement system on quality of care, but

Table 4: Patient outcomes according to time of implementation of reimbursement based on drug-related groups.

Outcomes	Before implementation of DRG* (n = 295)	After implementation of DRG* (n = 330)	Regression analysis unadjusted HR or OR or mean difference (95% CI)	Regression analysis adjusted† HR or OR or mean difference (95% CI)
Clinical based measures				
Time to clinical stability – days§	3.64 (3.0–4.36)	4 (3.42–4.42)	HR 1.07 (0.92–1.26), p = 0.381	HR 1.02 (0.85–1.21), p = 0.871
Total duration of antibiotics – days	10.4 (5.8)	10.0 (4.8)	Mean difference 0.40 days (1.26–(–)0.47), p = 0.37	Mean difference 0.14 days (0.98–(–)0.71), p = 0.756
Intravenous antibiotic treatment – days	6.2 (5.9)	6.0 (4.5)	Mean difference 0.22 days (1.06–(–)0.62), p = 414	Mean difference –0.08 days (0.92–(–)0.76), p = 0.857
Process of care measures (clinical effectiveness)				
Death from any cause within 30 days – n (%)	9 (3.1%)	8 (2.4%)	OR 0.79 (0.30–2.07), p = 0.631	OR 1.14 (0.39–3.36), p = 0.815
Rehospitalisation – n (%)	23 (7.8%)	30 (9.1%)	OR 1.18 (0.67–2.09), p = 0.562	OR 1.13 (0.60–2.12), p = 0.701
CAP-associated complication until day 30 – n (%)	18 (6.1%)	10 (3.03%)	OR 0.48 (0.22–1.06), p = 0.069	OR 0.34 (0.13–0.91), p = 0.032
Process of care measures (economic costs)				
Length of stay – days	9.7 (8.9)	8.8 (7.0)	Mean difference 0.93 days (2.18–(–)0.33), p = 0.146	Mean difference 0.69 days (1.92–(–)0.54), p = 0.271

CI = confidence interval; DRG = diagnosis-related group; HR = hazard ratio; OR = odds ratio

Data are mean (standard deviation) or n (%) unless otherwise stated.

* Two of the involved hospitals were excluded as they had an All Patient-DRG reimbursement system in place before SwissDRG was implemented on 1 January 2012.

† Adjustment for the following possible confounders: Pneumonia Severity Index, maximum level of C-reactive protein, age, initial randomisation, current smoking status, presence of chronic obstructive pulmonary disease, diabetes mellitus, cerebrovascular disease, congestive heart failure, malignancy and renal insufficiency, and for the treating centre.

§ Median (interquartile range).

results are controversial. Some studies documented a reduction of LOS after implementation of a PPS in the US in Medicare patients or in patients with hip fractures in a tertiary care setting [53–55]. They revealed that the PPS increased the likelihood that a patient will be discharged in an unstable condition [54], but no significant long-term effect on outcomes was documented [55]. In Switzerland a *post-hoc* analysis of CAP patients found a significantly shorter LOS of about 20% in hospitals that used DRG reimbursement systems compared with hospitals using a fee-for-service system, without apparent harmful effect on outcomes [56]. This is also confirmed by a Japanese study focusing on women with breast cancer, which disclosed a shorter LOS as well while maintaining the quality of care after implementing DRGs in 2003 [57]. On the other hand, several studies performed in Germany or in Switzerland observed no significant change of LOS due to the introduction of G-DRG or SwissDRG [58, 59], or revealed that the reduction of LOS was not inevitably connected to the introduction of DRGs [32, 34]. The lack of effect in the present study may be explained by the short time period since the implementation of DRGs, as changes in practice need time. In addition, although the sample size was rather large, it may have been underpowered to find significant differences.

Our study has important limitations. First, as shown, LOS is strongly influenced by location-specific and hospital-specific factors, which makes it difficult to compare with other regions and healthcare systems. Therefore, our study, which was embedded in the northern part of Switzerland, may not be applicable to other regions or countries. Second, we only included patients with CAP, so that generalisation to other diagnoses is not possible, and further studies are required to validate the findings for other medical problems. Third, as with any observational study, there is potential residual confounding despite our attempt to adjust for multiple factors. The study thus shows associations but does not proof causal effects.

In conclusion, we found differences in LOS associated with use of an antibiotic stewardship protocol including PCT, which remained robust after multivariable adjustment, while the type of hospital and the model of reimbursement did not influence LOS in our CAP cohort. These data support the implementation of practice guidelines for in-hospital treatment of CAP patients. More health service research studies are needed to better understand factors associated with low quality of care and to establish causal effects.

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Appendix: Sensitivity analysis

Table S1: Fully adjusted regression analysis including time to stability and bacteraemia for all of the patient outcomes measured.

Outcomes	A) PCT-enforced vs non-PCT-enforced Regression analysis fully adjusted HR or OR or MD (95% CI)*	B) University vs non-university hospitals† Regression analysis fully adjusted OR or MD (95% CI)*	C) Before vs after implementation of DRG§ Regression analysis fully adjusted OR or MD (95% CI)*
Clinical based measures			
Total duration of antibiotics – days	MD 0.97 days (1.75–(–)0.18), p = 0.016	MD 1.47 days (0.69–2.25), p <0.001	MD 0.02 days (0.74–(–)0.70), p = 0.957
Intravenous antibiotic treatment – days	MD 1.23 days (1.94–(–)0.52), p = 0.001	MD 0.21 days ((–)0.54–0.95), p = 0.589	MD 0.10 days ((–)0.60–0.80), p = 0.779
Process of care measures (clinical effectiveness)			
Death from any cause within 30 days – n (%)	OR 2.38 (0.93–6.06), p = 0.07	OR 5.02 (0.62–40.6), p = 0.130	OR 1.27 (0.42–3.89), p = 0.673
Rehospitalisation – n (%)	OR 0.65 (0.28–1.52), p = 0.323	OR 0.99 (0.48–2.06), p = 0.995	OR 1.30 (0.68–2.49), p = 0.424
CAP-associated complication until day 30 – n (%)	OR 1.67 (0.50–5.66), p = 0.407	OR 2.78 (0.64–12.06), p = 0.173	OR 0.46 (0.15–1.41), p = 0.174
Process of care measures (economic costs)			
Length of stay – days	MD 2.63 days (3.68–(–)1.57), p <0.001	MD 0.35 days (1.46–(–)0.76), p = 0.536	MD 0.39 days (1.44–(–)0.66), p = 0.463

CI = confidence interval; DRG = Diagnosis-Related Group; MD = mean difference; OR = odds ratio; PCT = procalcitonin

Data are mean (standard deviation) or n (%) unless otherwise stated;

* Adjustment for the following possible confounders: Pneumonia Severity Index, maximum level of C-reactive protein, age, initial randomisation, current smoking status, presence of chronic obstructive pulmonary disease, diabetes mellitus, cerebrovascular disease, congestive heart failure, malignancy and renal insufficiency, as well as bactaeremia and time to stability.

† Two hospitals were excluded: the first was characterised as a basic hospital, the second was the PCT-enforced hospital from analysis A.

§ Two of the involved hospitals were excluded as they had an All Patient-DRG reimbursement system in place before SwissDRG was implemented on 1 January 2012.