Test and treat-impact of microbiological testing on antibiotic prescribing for Legionnaires' disease in Switzerland : results of the multicentre *SwissLEGIO* study

Bigler, Melina; Zacher, Florian; Dräger, Sarah; Albrich, Werner C; Mäusezahl, Daniel

Collaborators: Tognon, Mikael; Bernasconi, Enos; Schrenzel, Jacques

How to cite

BIGLER, Melina et al. Test and treat-impact of microbiological testing on antibiotic prescribing for Legionnaires" disease in Switzerland : results of the multicentre *SwissLEGIO* study. In: Pneumonia, 2025, vol. 17, n° 1, p. 17. doi: 10.1186/s41479-025-00171-1

This publication URL: https://archive-ouverte.unige.ch/unige:190136

Publication DOI: 10.1186/s41479-025-00171-1

Pneumonia

RESEARCH

Open Access

Test and treat—impact of microbiological testing on antibiotic prescribing for Legionnaires' disease in Switzerland: results of the multicentre *SwissLEGIO* study

Melina Bigler[1,2†], Florian Zacher[3†], Sarah Dräger[4,5], Werner C. Albrich[3†], Daniel Mäusezahl[1,2*†] and the SwissLEGIO Hospital Network

Abstract

Background Legionnaires' disease (LD) is a severe form of primarily community-acquired pneumonia (CAP). To confirm a Legionella infection, microbiological testing is required. The Swiss and European guidelines recommend LD testing for all hospitalised CAP patients. However, the low positivity rate of such routine testing (1.5–3%) raises concerns about its cost-effectiveness and clinical utility. In a setting where routine testing is recommended, this multicentre study evaluated the impact of LD testing on the clinical management of the infection and antimicrobial prescribing.

Methods Data from medical records of 195 community-acquired LD (CALD) patients from 20 Swiss hospitals (August 2022–March 2024) were analysed. We assessed the clinical management of CALD, focusing on the impact of microbiological testing on antibiotic prescribing. The appropriateness of antibiotic choice and duration of treatment was assessed using a standardised pathway analysis approach. Factors associated with unsupported antibiotic prescribing were assessed using mixed-effects logistic regression analysis.

Results Microbiological testing was initiated promptly, with results available within 24 h after presenting to the hospital for 85.1% and within 48 h for 92.3% of patients. Antibiotics with Legionella coverage were initiated in 88.2% of patients within 24 h of admission. A positive Legionella test influenced antibiotic prescribing: 97.9% of patients received antibiotics active against *Legionella* spp., and 79.6% were prescribed appropriate and targeted monotherapy within 24 h of receiving the test result. Overall, 35.4% of patients were treated with antibiotics for a median of 4 days (IQR 3–4 days) longer than guidelines recommend (defined as > 10 days for immunocompetent or > 21 days for immunocompromised patients). Prolonged treatment was associated with CALD severity and antibiotic use > 2 days

†Melina Bigler and Florian Zacher contributed equally to this work.

†Werner C. Albrich and Daniel Mäusezahl are joint senior authors.

*Correspondence:
Daniel Mäusezahl
daniel.maeusezahl@unibas.ch

Full list of author information is available at the end of the article

postdischarge (proxy for clinical stability reached). 38.5% of patients with impaired renal function received a suboptimal loading dose of levofloxacin.

Conclusion Routine aetiological testing for LD has improved the clinical management of CALD by facilitating rapid detection of CALD cases and timely initiation of appropriate and targeted antibiotic therapy. Future antimicrobial stewardship efforts should sensitise physicians that a shorter duration of antibiotic treatment for CALD of 5 to 7 days according to the latest Swiss CAP guidelines is sufficient and safe.

Keywords Legionnaires' disease, Legionella, Community-acquired pneumonia, Switzerland, Urinary antigen test, Multicentre study, Antibiotic prescriptions, Antimicrobial stewardship, Duration of treatment

Background

Legionnaires' disease (LD) is a severe pneumonia caused by Gram-negative *Legionella* spp. bacteria. In the past ten years, the number of reported LD cases has risen steadily [1, 2], and LD is estimated to account for approximately 4–7% of community-acquired pneumonia (CAP) cases in Europe [3, 4]. The clinical and radiological manifestations of LD closely resemble those of other CAP aetiologies, making microbiological testing essential for accurate diagnosis [5]. The urinary antigen test (UAT) is the first-line diagnostic test for LD due to its low cost, easy sample collection, and relatively simple analysis procedure [2, 6]. However, the UAT is limited to the detection of *L. pneumophila* and has the highest sensitivity for serogroup 1 (86% vs 74–79% for all serogroups 1 to 15) [6]. Polymerase chain reaction (PCR), in contrast, has the potential to detect all *Legionella* species and is increasingly being used in clinical practice. Compared to the UAT, PCR is more expensive, requires the collection of adequate samples from the lower respiratory tract, and represents a more complex technology with a longer turn-around time [2, 6]. PCR is therefore not (yet) recommended as an equivalent alternative to the UAT for routine diagnostics [4, 7]. Since *Legionella* spp. are intracellular pathogens, LD requires treatment with antibiotics that reach high intracellular concentrations in alveolar macrophages, the primary site of infection. Recommended antibiotics include quinolones, macrolides, and, alternatively, tetracyclines [5, 6].

In accordance with German/Austrian and European recommendations, the Swiss guidelines for the diagnosis and treatment of CAP advise that all hospitalised CAP patients undergo a Legionella UAT [4, 7, 8]. If a Legionella infection is confirmed, targeted monotherapy with quinolones, macrolides, or doxycycline and discontinuation of ineffective β-lactams are recommended. This test–and–treat approach aims to ensure early initiation of appropriate antibiotic treatment for community-acquired LD (CALD) and timely de-escalation of the empiric β-lactam therapy. Timely initiation of LD-appropriate antibiotic treatment reduces mortality and intensive care unit (ICU) admission rates [9–12]. De-escalated and targeted antibiotic therapy for LD may also reduce toxicity and other antibiotic-related adverse effects (including secondary infections such as *Clostridioides difficile*-associated colitis), reduce selection pressure for antibiotic resistance, and contribute to ongoing antimicrobial stewardship efforts [13–16].

However, routinely performed microbiological LD tests in hospitalised CAP patients have a relatively low positivity rate (approximately 1.5–3%) [17–19], and concerns about the cost-effectiveness and clinical utility of such routine testing have been raised [20, 21]. In contrast to the European guidelines, American CAP guidelines advise against routine testing in hospitalised patients. Instead, they recommend LD testing only for severe CAP or in patients presenting with epidemiological risk factors for LD [21]. Yet, risk factor-guided testing for CALD is challenging in clinical practice [9, 18], and the best approach for integrating microbiological testing for LD in the clinical management of hospitalised patients with CAP remains somewhat unclear [9, 22]. Studies evaluating the impact of a positive LD diagnostic test on the clinical management of CALD are hence important but remain scarce. The few existing studies are often constrained by small sample sizes and focused on clinical practices in selected tertiary care centres [23–25]. Using data from a Swiss prospective multicentre study [26], we examined the clinical management of CALD in a representative patient cohort recruited from 20 university and cantonal hospitals. In Switzerland, routine testing for CALD is recommended for all hospitalised CAP patients [8]. We assessed how promptly patients with CAP were tested for LD upon presentation to the hospital and evaluated the impact of a positive microbiological test on antibiotic prescribing for LD.

Methods

Data sources and study population

This study uses data from a national case–control and molecular source attribution study on Legionnaires' disease in Switzerland (*SwissLEGIO*). The study design of *SwissLEGIO* has been reported in detail elsewhere [26]. In brief, CALD patients were recruited from August 2022 to March 2024 from all greater regions of Switzerland (Supplementary file 1, SFig. 1). Recruitment occurred

through a hospital network of 15 cantonal and five university hospitals, which jointly reported approximately 45% of all notified CALD cases in Switzerland during the recruitment period [27, 28]. Electronic medical records for the CALD-associated hospital visit were reviewed, and information on age, sex, health-seeking prior to the hospital visit, comorbidities, reported symptoms, date of symptom onset, date of hospital admission/emergency department (ED) visit, date of CALD diagnosis, laboratory and radiological parameters, and timing, duration, dosage and route of administration of all antibiotic prescriptions were extracted using standardised electronic case report forms.

CALD patients were eligible for inclusion in the study if they were 18 years or older, had a laboratory-confirmed Legionella infection, and were diagnosed with pneumonia. In accordance with the definitions of the Swiss public health authorities, a Legionella infection was considered confirmed if *Legionella* spp. was isolated from respiratory samples (culture), *L. pneumophila* antigen was detected in the urine (UAT), *Legionella* spp. nucleic acid was detected in respiratory samples (PCR), or a serological test for *Legionella* spp. was positive [26, 29]. Pneumonia was defined (according to the Swiss CAP guidelines) as the presence of a new infiltrate (chest X-ray, ultrasound, or computerised tomography scan) plus clinical symptoms suggestive of pneumonia (fever, chills, cough, sputum, dyspnoea, tachypnea, thoracic pain) at admission [8]. CALD patients were excluded if they had hospital-acquired LD (defined as reporting an overnight stay at a hospital or rehabilitation facility during the 14 days prior to first symptoms), coinfections requiring additional antibiotics during the hospital stay, or were transferred to another hospital within 72 h of admission.

Indicators for the clinical management of Legionnaires' disease

To describe the clinical management of CALD across hospitals, we assessed healthcare consultations prior to the LD diagnosis, the time from symptom onset to ED visit and to diagnostic confirmation of CALD, the results of CALD-specific microbiological tests, and the time from the ED visit to the initiation of adequate antibiotics (i.e., initiation of quinolones, macrolides, or doxycycline).

Assessment of appropriate antimicrobial use

To estimate the appropriateness of antibiotic treatment, we used an analysis pathway approach proposed by Magill et al. [30]. For the analysis pathway, definitions of supported and unsupported antimicrobial use (as proxies for appropriate and inappropriate or unnecessary use) were established based on the Swiss national CAP guidelines (version June 2024) [7, 8, 31]. Supplementary file 1 provides the details of the analysis pathway used in this study (SFig. 2 and STables 1–3). The quality of antibiotic prescriptions was categorised into supported and unsupported treatment at two different time points: (i) on admission and prior to the diagnostic confirmation of CALD and (ii) 24 h after a Legionella infection was confirmed. Antibiotic prescriptions were considered supported if it was evident from the standardised data collection forms that (i) the antimicrobial selection (active pharmaceutical ingredient (API) and dosage) and (ii) the duration of treatment were consistent with recommendations in the Swiss national CAP guidelines. Duration of treatment was only assessed for antibiotics with activity against *Legionella* spp. The duration of antibiotic treatment was considered supported if CALD patients were treated for five to ≤ 10 calendar days (≤ 21 calendar days for immunocompromised patients) with either quinolones, macrolides, doxycycline or a combination of these antibiotics.

We considered patients immunocompromised if at least one of the following conditions were present: treatment with steroids (≥ 7.5 mg prednisolone-equivalent/day for more than four weeks), treatment with cytostatic or immunosuppressive drugs (including biologicals), HIV infection with CD4 < 200/µl, neutropenia (< 0.5 g/l), a history of solid organ transplantation, a history of haematological stem cell transplantation, asplenia, or primary immunodeficiency.

Statistical analysis

For descriptive statistics, we present data as medians (interquartile ranges, IQRs) for continuous variables and n (%) for categorical variables. Confidence intervals (CIs) for proportions of supported and unsupported antibiotic prescriptions were calculated using random effect logistic regression to account for potential clustering on hospital level. Clustering at the hospital level is expected by design (prescribing practices are likely to be more similar within hospitals than between hospitals, for example due to differences in antimicrobial stewardship activities or also differences in local protocols).

A random effect logistic regression analysis was performed to identify factors associated with antibiotic treatment durations exceeding guideline recommendations. The outcome variable was defined as an antibiotic treatment duration longer than that recommended by the guidelines. Explanatory variable for the univariable logistic regression model were selected based on clinical plausibility and/or previously reported associations in the literature [32–34]. A list of the explanatory variables that were considered is provided in Supplementary file 1 (STable 6). In the multivariable model, we included immunosuppression, C-reactive protein concentration, severity (based on ICU admission), and antibiotic prescriptions for more than 48 h after discharge (whereas discharge

also serves as a proxy for reaching clinical stability) as fixed effects [32, 34]. The selection of these variables was based on the strength of the association between the potential predictor and prolonged treatment duration in the univariable model and/or previously shown strong associations reported in the literature. We accounted for confounding by including age and the Charlson Comorbidity Index in the model. To account for clustering, we again added the hospitals as random effects (random intercepts).

The statistical analysis was done using the statistical software R Version 4.4.1 (R Core Team, Vienna, Austria). The R package lme4 was used for random effect logistic regression modelling.

Table 1 Patient characteristics and clinical management of community-acquired Legionnaires' disease (CALD)

Characteristic	CALD patients (*n* = 195)
Female (%)	60 (30.8)
Age (years) (median [IQR])	68 [56–78]
Current smoker (%)	84 (43.1)
Hospital level	
Admitted to a cantonal hospital (%)	164 (84.1)
Admitted to a university hospital (%)	24 (12.3)
Treated as an outpatient (%)	7 (3.6)
Comorbidities	
Heart disease (%)	74 (37.9)
Heart failure (%)	16 (8.2)
Diabetes mellitus (%)	42 (21.5)
Chronic obstructive pulmonary disease (COPD) (%)	21 (10.8)
Moderate or severe chronic kidney disease (%)	26 (13.3)
Cerebrovascular diseases (%)	14 (7.2)
Malignancies (%)	23 (11.8)
Immunosuppression (%)	37 (19.0)
Charlson comorbidity index (median [IQR])	1.0 [0–3]
Disease severity	
Length of stay (LOS, days) (median [IQR])	7 [5–11]
ICU admission (%)	35 (17.9)
Antibiotics prescribed prior to hospital visit	
None (%)	146 (74.9)
Penicillins (%)*	41 (21.0)
Cephalosporins (%)	3 (1.5)
Quinolones (%)	1 (0.5)
Combination therapies (%)†	4 (2.1)
Laboratory diagnostics	
Time from symptom onset to pos. diagnostic test (days, median [IQR])	4 [3–7]
Time from hospitalisation to pos. diagnostic test (days, median [IQR])	0.50 [0.0–1.0]
Positive urinary antigen test (UAT)/performed UAT (% positivity)	181/190 (95.3)
Positive PCR/performed PCR (% positivity)	39/52 (75.0)
Positive culture/performed culture (% positivity)	38/108 (35.2)
Positive serology/performed serology (% positivity)	1/2 (50.0)
Antibiotic coverage for *Legionella* spp.	
within 24 h of hospital admission/emergency department visit (%)	172 (88.2)
within 24 h of laboratory-confirmed CALD diagnosis (%)	191 (97.9)

*amoxicillin or amoxicillin/clavulanic acid

†e.g. cephalosporins plus macrolides

Results

Patient characteristics and clinical management of Legionnaires' disease

In this analysis, 195 out of the 204 patients enrolled in the *SwissLEGIO* parent study were included (Supplementary file 1, SFig. 1). Seven patients were excluded due to coinfections requiring antimicrobial treatment (including three with suspected respiratory bacterial superinfections), and two patients were excluded due to an early referral to another hospital. Patient characteristics are shown in Table 1. The median age was 68 years (IQR 56–78 years), and 60 patients (30.8%) were female. Most patients (84.1%) were treated in a cantonal hospital, and seven (3.6%) were treated as outpatients. In total, 35 (17.9%) patients were admitted to the ICU, and 37 (19.0%) were immunocompromised. An allergic reaction to antibiotics was reported in five patients during hospitalisation (data not shown).

Prior to hospital presentation, 49 patients (25.1%) were prescribed antibiotics in the outpatient setting. Outpatient prescriptions for CAP were consistent with guideline recommendations in 43 of 49 patients (87.8%) and most patients received oral amoxicillin or amoxicillin/clavulanic acid. All patients were diagnosed with CALD after hospital admission: 166 patients (85.1%) had diagnostic results available within 24 h, and 180 patients (92.3%) had results available within 48 h. The UAT was performed in 190 patients (97.4%), culture was performed in 108 patients (55.4%), and PCR was performed in 52 patients (26.7%). Cultures and UATs were performed by all 20 hospitals, with UATs always done in-house (Supplementary file 1, STable 4). Cultures were either performed in-house or respiratory samples were sent to the National Reference Centre for Legionella after confirmation of LD by UAT or PCR [35]. PCR testing was performed by 14 of the 20 hospitals—11 used primers targeting *L. pneumophila*, and three hospitals used multiplex PCR to detect both *L. pneumophila* and *Legionella* spp.. In 10 hospitals, Legionella PCR was part of a multiplex respiratory panel (Supplementary file 1, STables 4–5). Of the tests performed in CALD patients, the positivity rate was 95.3% for the UAT, 75.0% for PCR, and 35.2% for cultures. Nine patients were diagnosed solely by PCR, one patient exclusively by seroconversion (Supplementary file 1, STable 4), and one patient exclusively by culture (detection of *L. pneumophila* serogroup 1).

Overall, 172 patients (88.2%) received antibiotics with activity against *Legionella* spp. within 24 h of presentation

to the hospital, and 191 patients (97.9%) received antibiotics with activity against *Legionella* spp. within 24 h of the diagnostic confirmation of the infection. Three patients received inadequate treatment beyond 24 h after diagnosis (two patients received β-lactam- and one patient a cephalosporin monotherapy). One patient received no antibiotics within 24 h post-diagnosis. Patients who did not receive antibiotics with activity against *Legionella* spp. within 24 h after presenting to the hospital were more likely to have a negative UAT (27.3% vs. 1.8%, $p < 0.001$), and the median time from hospitalisation to laboratory-confirmed CALD diagnosis was significantly longer (median 2 days vs 0 days, $p < 0.001$).

Assessment of appropriate antimicrobial use

Appropriateness of antibiotic prescriptions was assessed at two different time points: (i) on admission and prior to the diagnostic confirmation of CALD (appropriateness of empiric CAP treatment) and (ii) 24 h after the Legionella infection was confirmed (appropriateness of LD-targeted antibiotic treatment).

Empiric CAP therapy prior to a confirmed Legionella infection

At the hospital, empiric antibiotic therapy for CAP was initiated in 137 patients (70.3%) prior to the diagnosis of CALD. Combination therapy with β-lactams (ceftriaxone or amoxicillin/clavulanic acid) and macrolides was prescribed in 69 of the 137 CALD patients (50.4%). Twenty patients received a monotherapy with either amoxicillin/clavulanic acid or ceftriaxone (14.6%), and 19 CALD patients (13.9%) received either piperacillin/tazobactam or cefepime (Table 2). Patients receiving piperacillin/tazobactam or cefepime were frequently immunocompromised or required ICU treatment.

According to the Swiss CAP guidelines, first-line empiric treatment for mild pneumonia is amoxicillin/clavulanic acid. For moderate pneumonia, a macrolide may be added optionally to the β-lactam therapy. Therefore, empiric treatment for mild to moderate CAP according to the Swiss CAP guidelines does not necessarily cover *Legionella* spp.. The antibiotics prescribed empirically for CAP provided coverage for *Legionella* spp. in 107 out of the 137 CALD patients (78.1%). The CRB-65 score was similar between patients who were treated with β-lactam monotherapy and patients who received β-lactam–macrolide combination therapy. Overall, empiric treatment was consistent with CAP guideline recommendations in 81 out of 137 patients (59.1%, 95% CI: 48.4–71.0). Most patients with unsupported CAP therapy were either prescribed antibiotics with too broad of a spectrum (22 of 54, 40.7%) or the prescribed antibiotic dosage was suboptimal (26 of 54, 48.1%) (Table 2).

Table 2 Estimating the appropriateness of empiric antibiotic prescriptions for community-acquired pneumonia (CAP) in patients subsequently diagnosed with Legionnaires' disease (CALD)

	Total
Empiric CAP therapy prior to confirmed CALD-diagnosis	***n*= 195**
Empiric CAP treatment prescribed (%)	137 (70.3)
No empiric CAP treatment prescribed (%)	58 (29.7)
Empiric CAP treatment prescribed (%)[†]	*n = 137*
Any empiric CAP treatment with *Legionella* spp. coverage[*]	107 (78.1)
Monotherapy with amoxicillin/clavulanic acid	15 (10.9)
Monotherapy with ceftriaxone	5 (3.6)
Monotherapy with quinolone	12 (8.8)
Monotherapy with macrolide	6 (4.4)
Monotherapy with doxycycline	0 (0.0)
Combination therapy with ceftriaxone plus macrolides	21 (15.3)
Combination therapy with amoxicillin/clavulanic acid plus macrolides	48 (35.0)
Treatment with cefepime or piperacillin/tazobactam	19 (13.9)
Prescribed empiric CAP treatment supported by guidelines (%)	*n = 137*
Supported	81 (59.1)
Dose too low	26 (19.0)
Spectrum too broad	22 (16.1)
Spectrum too narrow	6 (4.4)
Insufficient data to estimate appropriateness	2 (1.5)

[†]percentages do not add up to 100%, as sometimes two categories apply

[*]includes all mono and combination therapies with macrolides, quinolones and doxycycline

Targeted antibiotic treatment for community-acquired Legionnaires' disease

Patients diagnosed with CALD were primarily treated with quinolones. Levofloxacin was prescribed to 137 (70.3%) and moxifloxacin to six patients (3.1%). Combination therapy with quinolones and macrolides was prescribed to nine patients (4.6%). In 72 patients (36.9%), we observed a switch from a macrolide to a quinolone during treatment (Table 3). Switching from a macrolide to a quinolone often coincided with the discontinuation of β-lactams.

Figure 1 summarises the results of the pathway analysis to estimate appropriate antibiotic prescribing 24 h after diagnostic confirmation of CALD (cf. Supplementary file 1, SFig. 2). For 191 patients, data allowed for the assessment of both the supported choice and duration of the antibiotic prescriptions: in 152 of 191 patients (79.6%, 95% CI: 72.0–85.3), the antibiotic choices (API and dosage) were consistent with guideline recommendations within 24 h of the diagnostic confirmation of a Legionella infection. Accounting for the duration of treatment being supported, 98 out of 191 patients (51.3%, 95% CI: 42.3–59.6) were prescribed antibiotics consistent with national CAP guidelines.

The two most common reasons for unsupported antibiotic treatment were the continuation of β-lactams after

Table 3 Estimating the appropriateness of antibiotic prescriptions for the targeted therapy of community-acquired Legionnaires' disease (CALD)

	Total
Antibiotic treatment for Legionnaires' disease	***n*** **= 195**
Prescribed antibiotics for CALD (%)	
Monotherapy with quinolones	71 (36.4)
Monotherapy with macrolides	39 (20.0)
Monotherapy with tetracyclines	1 (0.5)
Switch from macrolides to quinolones	72 (36.9)
Combination therapy of quinolones and macrolides	9 (4.6)
Others*	3 (1.5)
Prescribed antibiotic choices supported by guideline recommendations for the treatment of CALD (%)◊	
Supported	152 (79.6)
β-lactams continued > 24 h after CALD diagnosis	21 (11.0)
Dose too low	11 (5.8)
Dose too high	1 (0.5)
Antibiotics did not cover *Legionella* spp.	4 (2.1)
Spectrum too broad (other reasons than continuation of β-lactams)†	2 (1.0)
Insufficient data to estimate appropriateness	4 (2.1)
Duration of treatment	***n*** **= 195**
Duration of treatment supported by guideline recommendations for the treatment of CALD (%)◊	
Supported	124 (64.6)
Unsupported	68 (35.4)
Insufficient data to estimate appropriate duration	3 (1.5)
Duration of antibiotic treatment for CALD (median [IQR])	11 [10–15]
Excess days of treatment (median [IQR])‡	4 [3–4]
Continuation of antibiotics > 48 h after discharge (%)	120 (62.5)
Days of antibiotic prescriptions after discharge (median [IQR])	6 [4–9]
Total excess days of antibiotic treatment after discharge/ total excess days of antibiotics prescribed (%)	182/275 (66.2)

*including switch from quinolones to macrolides, and from macrolides/quinolones to tetracyclines

◊observations with insufficient data to estimate appropriateness/duration of antibiotic prescriptions are treated as missing

†for example: continued treatment with combination of macrolides and quinolones without continued β-lactams

‡beyond the recommended 11 days of treatment (22 days for immunocompromised patients)

the confirmation of CALD and suboptimal antibiotic dosing (Table 3). In 21 patients (11.0%), β-lactams were continued for more than 24 h after confirmation of CALD and in the absence of any documented coinfection. In 11 patients (5.8%), the prescribed antibiotic dose was lower than recommended per clinical guidelines. Notably, a significant proportion of patients with renal impairment (10 out of 26, or 38.5%) were affected by suboptimal dosing. In four patients (2.1%), the prescribed antibiotic regimen did not cover *Legionella* spp. 24 h after the diagnostic confirmation of LD.

Antibiotic treatment duration for community-acquired Legionnaires' disease

Prolonged antibiotic treatment duration was a relevant factor in unsupported treatment for CALD. Overall, in 68 patients (35.4%), the duration of *Legionella* spp. treatment exceeded the recommended duration. The median duration of excess treatment was four days (IQR 3–4 days). Notably, 66.2% of these excess antibiotic treatment days were prescribed as part of continued outpatient therapy after hospital discharge.

We assessed factors associated with prolonged treatment in univariable (STable 6 in Supplementary file 1) and multivariable analyses (Fig. 2). ICU admission and antibiotic prescriptions for more than 48 h after discharge (and therefore likely often after clinical stability was reached) were independently associated with a longer than recommended treatment duration with quinolones, macrolides or doxycycline. In contrast, immunocompromised patients were more likely to receive antibiotics for an appropriate duration, as treatment regimens of up to 21 days were permitted in this group. The observed switch from macrolides to quinolones during treatment was not associated with excessive treatment duration (STable 6 in Supplementary file 1).

Discussion

The optimal approach to integrating microbiological testing for *Legionella* spp. into the clinical management of hospitalised CAP patients remains a subject of debate [9, 22]. Concerns have been raised regarding both the cost-effectiveness and clinical utility of such routine testing [20, 21]. To date, the impact of aetiological testing for *Legionella* spp. on the clinical management of the infection has only been evaluated in studies with small sample sizes and were conducted in selected tertiary care hospitals [20, 23–25]. These studies could therefore only provide limited evidence on the broader impact of a guideline-recommended test-and-treat approach for managing CALD. In this multicentre study, conducted in a setting where routine testing for LD is recommended for all hospitalised CAP patients [8], we assessed the impact of aetiological testing for *Legionella* spp. on the clinical management of CAP and antimicrobial prescribing in a representative Swiss CALD cohort from 20 study sites.

Overall, we found that routine aetiological testing for LD has improved the clinical management of CALD. Consistent with Swiss guideline recommendations, testing for *Legionella* spp. was promptly initiated, with most patients having diagnostic results available within 24 h of presenting to the hospital. Diagnostic testing for CALD also facilitated a timely initiation of appropriate and targeted therapy for LD: 88.2% of patients received

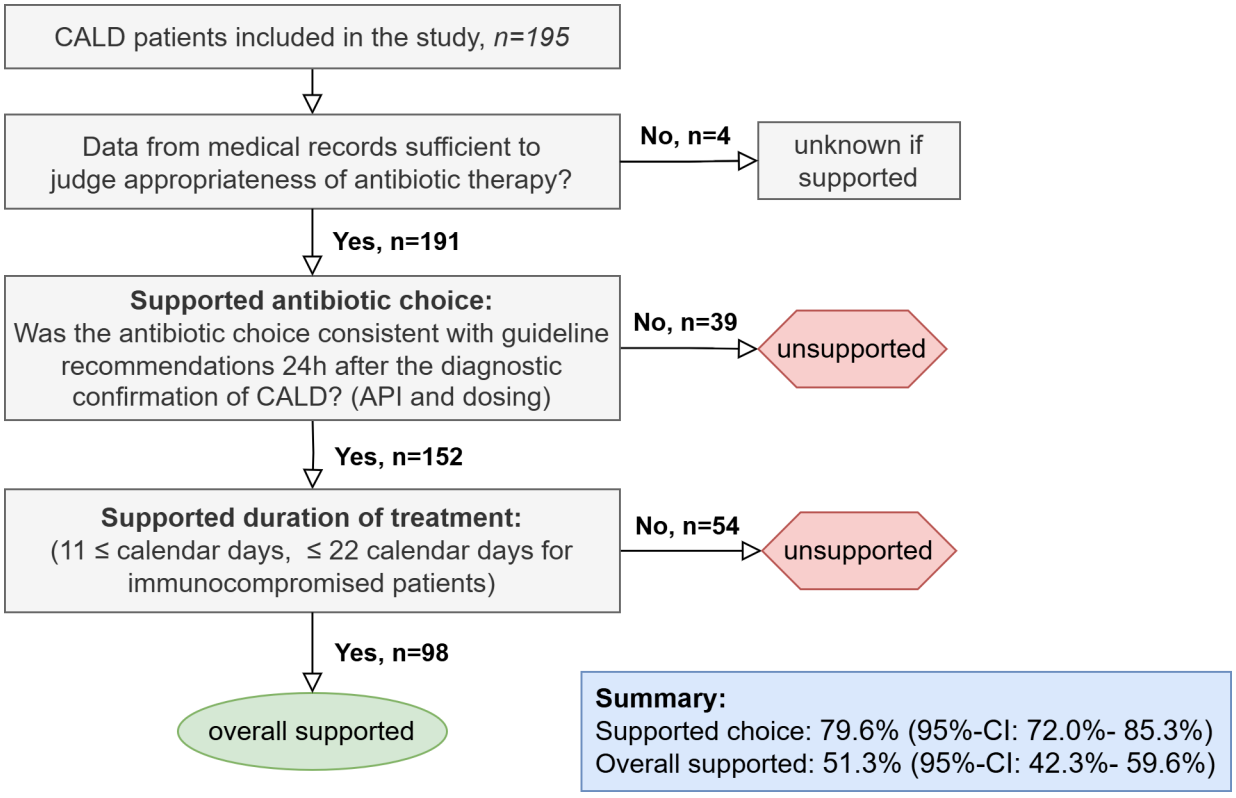

Fig. 1 Summary of the pathway analysis results. API: active pharmaceutical ingredient. CALD: Community-acquired Legionnaires' disease

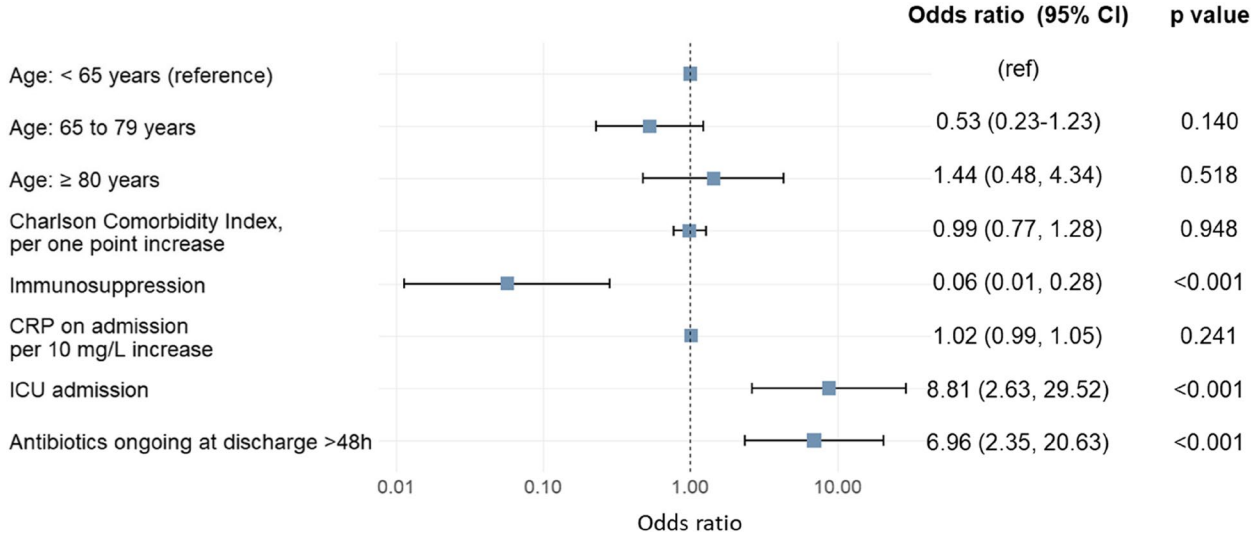

Fig. 2 Parameters associated with excessive treatment duration in the multivariable mixed effect logistic regression model, accounting for clustering at the hospital level

antibiotics with Legionella coverage within 24 h of admission. Additionally, and in line with findings from another Swiss study [36], testing improved adherence to CAP treatment guidelines for the LD-specific treatment compared to the initial empiric CAP treatment, where the dose and antibiotic spectrum chosen were often suboptimal. However, for 35.4% of CALD patients, the duration of antibiotic treatment exceeded guideline recommendations. Additionally, patients with impaired renal function often received a suboptimal loading dose for levofloxacin.

Swiss guidelines align with the German, Austrian and European CAP guidelines and recommend performing a Legionella UAT for all hospitalised CAP patients; they generally advocate for restrained macrolide use

for the empiric treatment of CAP [4, 7, 8]. According to the guidelines, adding macrolides to empiric β-lactam therapy is optional for moderate pneumonia. For severe pneumonia, β-lactam–macrolide combination therapy is strongly recommended. The guidelines also advise that macrolides should be discontinued after one to three days of empirical coverage if suspicion of an atypical pathogen cannot be further substantiated [7, 8]. Consequently, not all hospitalised CAP patients treated according to guidelines are prescribed macrolides and thus, receive adequate empirical antibiotics for LD. In our study, 78.1% of CALD patients received empiric antibiotics covering *Legionella* spp. Timely microbiological testing increased the proportion of CALD patients receiving antibiotics covering *Legionella* spp. to 88.2% within 24 h of presenting at the ED. Delayed testing increased the likelihood of inadequate coverage for LD 24 h post-admission. Overall, these findings suggest that routine testing for *Legionella* spp. promotes timely and appropriate antibiotic therapy for LD, which is critical to reducing mortality and ICU admission risk [9–12].

In our study, 88.2% of CALD patients received adequate antibiotics for LD within 24 h of hospital presentation, a higher proportion than previously reported [9, 11, 37]. Notably, a large cohort study from the U.S. recently found that only 77% of CALD patients received antibiotics with adequate coverage for LD within the first two days of hospitalisation, despite American guidelines generally recommending β-lactam–macrolide combination therapy for all hospitalised CAP patients [9, 21]. A key difference between our study and the U.S. study was the timing of diagnostic testing. In our study, 85.1% of patients were tested for LD within 24 h of hospital presentation, whereas in the U.S., testing often occurred two or more days after admission. This delay in testing may be due to American guidelines recommending the UAT only for severe pneumonia or when LD risk factors are present [21]. However, the benefits of such risk factor- and severity-guided testing remain unclear [9, 18, 22]. For instance, Bellew et al. systematically screened hospitalised CAP patients for LD using UAT and found no association between Legionella pneumonia and CAP severity [18]. Additionally, studies indicate that identifying CALD patients based on a predefined list of general clinical characteristics and epidemiological risk factors alone is challenging in clinical practice [9, 18]. Epidemiological risk factors, in particular, may vary by region and may be specific to certain settings [26]. Consistent with these observations, a recently published study from Sweden found that Legionella infections were rarely considered as a cause for CAP in cases later confirmed as LD [37].

We also assessed the impact of LD testing on CAP guideline adherence. Before LD was diagnostically confirmed, 59.1% (95% CI: 48.4–71.0) of CALD patients received empiric antibiotics aligned with the recommendations in the Swiss CAP guidelines (API and dose). The prevalence of unsupported empiric CAP treatment was similar to that reported in previous studies [30, 38]. Aetiological testing for LD improved guideline adherence for CALD-specific treatment: within 24 h of a confirmed LD diagnosis, 79.6% (95% CI: 72.0–85.3) of patients received targeted monotherapy with quinolones, macrolides or doxycycline, whereas only 11.0% continued receiving β-lactams. The results revealed a high level of awareness of LD among physicians and good adherence to the test-and-treat recommendations [7, 8]. These findings also suggest that most physicians consider targeted LD treatment to be safe. Indeed, we observed a low rate of bacterial respiratory coinfections in the *SwissLEGIO* parent study (three out of the 204 (1.5%) enrolled LD patients), which is consistent with previous findings [9]. This alleviates concerns about an increased risk of relapse with targeted therapy [20, 21].

Despite the strong adherence to the test-and-treat recommendations for the management of CALD, our findings also highlight opportunities to further optimise antibiotic prescribing. We observed that 35.4% of patients received macrolides or quinolones for longer than the guideline-recommended 10 days (or >21 days in immunocompromised patients). Such prolonged treatment is a common cause of unsupported therapy as defined by CAP guidelines [30, 32, 34]. A recent Swiss study, for example, reported that 32% of CAP patients had prolonged treatment [32]. Our regression analysis revealed that neither the severity of CALD nor increased inflammation markers alone fully explain decisions to choose longer treatment regimens. The median excess duration of four days (IQR 3–4 days), further indicated that many patients were treated for 14 instead of 10 days. Historically, the treatment duration for CALD in immunocompetent patients was indeed 14 days due to the lower efficacy of erythromycin, the former first-line antibiotic [5, 39, 40]. However, studies on new-generation macrolides and quinolones demonstrate that prolonged treatment for CALD provides no clinical benefit and may even increase the risk of adverse events [7, 33]. In recent years, the recommended treatment duration for LD has, therefore, been aligned with that of other common CAP pathogens [6, 7]. The latest version of the Swiss CAP guidelines even recommends treating CALD for 5–7 days instead of the previously recommended 10 days [8]. A recent study has further suggested that a single high dose of intravenous azithromycin of 1.5 g is sufficient to treat selected cases of LD [41]. Considering our findings and the latest evidence from the literature, we argue that shorter treatment courses would have likely been safe

for many CALD patients with unsupported treatment durations in our cohort. Notably, 66.2% of excess days of antibiotics were prescribed in the outpatient care setting. Unnecessary postdischarge antibiotic prescriptions may therefore be an important target for future antimicrobial stewardship programmes, as has also been suggested by other studies [32–34, 42]. A second common reason for unsupported antibiotic use in CALD patients was suboptimal levofloxacin dosing in patients with renal impairment. As a concentration-dependent antibiotic, levofloxacin requires an initial loading dose before dose adjustment for renal insufficiency. Alternatively, moxifloxacin or azithromycin, which do not require renal dose adjustments, may be more suitable for this specific patient population [8].

Unnecessary antibiotic exposure (through excessive treatment duration) and suboptimal dosing can contribute to antimicrobial resistance [43]. Although several mechanisms of resistance to quinolones and macrolides have been described in in vitro studies [44, 45], antibiotic resistance in *Legionella* spp. has historically not been considered a major problem in clinical practice. To date, fluoroquinolone-resistant *L. pneumophila* strains have been isolated from an LD patient in the Netherlands and two patients in France [45, 46]. However, it is also noteworthy that comprehensive data on the susceptibility of *Legionella* spp. to antibiotics and its correlation with clinical efficacy remain limited, as systematic resistance monitoring and standardised testing methods are still under development [47, 48] Given the limited options for antibiotics effective against *Legionella* spp., optimising LD treatment is essential to mitigate the potential risk of resistance.

Our study has some limitations. We did not include a comparison group of non-LD CAP patients and, therefore, did not assess the impact of routine testing for CALD on the clinical management of non-LD CAP patients. We also state but did not directly assess the cost-effectiveness of routine testing. Although such economic analyses remain scarce, they are important to inform ongoing discussions about routine Legionella testing [18, 20, 22]. Future research should therefore prioritise comprehensive economic evaluations that include assessments of diagnostic yield, antibiotic use, clinical outcomes, and total hospital costs. To assess appropriate antibiotic prescribing, we used a predefined pathway analysis approach [30] and systematically extracted data from electronic medical records using standardised case report forms. This allowed us to objectively and systematically assess antibiotic prescriptions across all 20 study sites [30, 49]. However, it likely overestimated the proportion of CALD patients receiving unsupported antibiotic treatment. Unlike expert reviews of individual patient records, our approach could not fully capture clinical or laboratory changes during hospitalisation or subtle shifts in the immune status of patients who might have justified prolonged or broader treatment. Additionally, we could not evaluate the de-escalation of antibiotics from intravenous to oral administration. Finally, we did not assess the impact of the involvement of disease specialists in the management of CALD (although we do not expect this to affect the generalizability of our results). Despite these limitations, our study provides valuable insights into the impact of aetiological testing for *Legionella* spp. on the management of CALD in a representative Swiss cohort. Moreover, our pathway analysis approach allows for replication in other settings, offering comparability that is harder to achieve with expert-opinion-based assessments [49].

Conclusion

The decision to recommend routine aetiological testing in CAP guidelines depends on several factors, including the impact of the test on the clinical management of CAP, patient outcomes, antimicrobial stewardship efforts, public health activities, and economic costs [21, 22]. In this study, we focused on assessing the impact of aetiological testing on the management of CALD and adherence to antibiotic treatment guidelines. We found that aetiological testing for *Legionella* spp. had a direct (and positive) impact on the clinical management of CALD. First, timely LD testing ensured that appropriate antibiotics for LD were reliably prescribed at hospital admission. Such timely initiation of appropriate treatment for LD has been previously shown to reduce mortality and ICU admission risk. Second, a confirmed LD diagnosis led to targeted and de-escalated antibiotic prescriptions for LD, thus contributing to ongoing antimicrobial stewardship efforts to reduce unnecessary antibiotic use. However, about a third of CALD patients received antibiotics active against Legionella for longer than recommended by Swiss guidelines. Sensitising physicians about the safety of shortened antibiotic treatment courses for LD and advocating for cautious antibiotic prescribing after hospital discharge should be goals of future antimicrobial stewardship efforts.

Abbreviations

API	Active pharmaceutical ingredient
CALD	Community-acquired Legionnaires' disease
CAP	Community-acquired pneumonia
CI	Confidence interval
ED	Emergency department
ICU	Intensive care unit
IQR	Interquartile range
LD	Legionnaires' disease
PCR	Polymerase chain reaction
UAT	Urinary antigen test

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s41479-025-00171-1.

Supplementary Material 1.

Acknowledgements

We warmly thank Fabienne B. Fischer and Manuel Wiederkehr for their scientific input and support in coordinating the study and data collection and Jan Hattendorf for the statistical support. We are grateful for the unfailing support of the entire ***SwissLEGIO*** study team during data collection: Gabriel Escher, Natascha Roser, Dominik Schnyder, Chiara Strozzi, Malina Vaucher, Mariasole Villa, Paula Savary, Elise Blandenier, Estelle Prêtre and Lucie Prêtre. At the Federal Office of Public Health, we thank Marianne Jost, Mirjam Mäusezahl-Feuz, and Sabine Basler for inputs and discussions surrounding the ***SwissLEGIO*** case–control study. Finally, we would like to thank all the additional hospital staff from the ***SwissLEGIO*** hospital network for their support during the CALD patient recruitment and data collection: Dr. Andréa Künzli, Dr. Olivier Clerc and Camille Schilt from the cantonal hospital Neuchâtel; Maira Biggiogero from the Clinica Moncucco; Jane Frangi and Luisa Vicari from the Ente Ospedaliero Cantonale; Vanessa Deggim-Messmer from the cantonal hospital Fribourg; Dr. Mikaël de Lorenzi-Tognon from the university hospital Geneva; Daniela Hirter and Pia Scherler from the Insel university hospital Bern; Dr. Peter M. Keller from the university hospital Basel; Kristin Abig, Andrea Kloetzer, Dr. Susanne Graf, and Dr. Carmen Volken from the cantonal hospital Baselland; and Dr. Emily West from the university hospital Zurich.

The SwissLEGIO hospital network:

Isabel Akers (Departement Innere Medizin, Spital Limmattal, Schlieren, Switzerland), Michele Arena (Clinical Research Unit, Clinica Moncucco, Lugano, Switzerland), Diane Bandeira (Laboratoire de microbiologie, Hôpital cantonal de Fribourg, Fribourg, Switzerland), Livia Berlinger (Medical Microbiology, Cantonal Hospital Lucerne, Luzern, Switzerland), Enos Bernasconi (Infectious Diseases Service, Ente Ospedaliero Cantonale, Lugano, Switzerland; University of Geneva, Genève, Switzerland; University of Southern Switzerland, Lugano, Switzerland), Delphine Berthod (Central Institute, Valais Hospitals, Sion, Switzerland), Maria Boesing (University Center for Internal Medicine, Kantonsspital Baselland, Liestal, Switzerland; University of Basel, Basel, Switzerland), Romana C. Calligaris-Maibach (Zentrallabor Mikrobiologie, Kantonsspital Baden, Baden, Switzerland), Riccarda Capaul (Zentrallabor, Kantonsspital Graubünden, Chur, Switzerland), Christian Chuard (Service d'infectiologie, Hôpital cantonal de Fribourg, Fribourg, Switzerland), Antony Croxatto (ADMED Microbiology, La Chaux-de-Fonds, Switzerland), Sara Droz (Institute for Infectious Diseases, University of Bern, Bern, Switzerland), Alexis Dumoulin (Central Institute, Valais Hospitals, Sion, Switzerland), Veronique Erard (Service d'infectiologie, Hôpital cantonal de Fribourg, Fribourg, Switzerland), Alessandra Franzetti Pellanda (Clinical Research Unit, Clinica Moncucco, Lugano, Switzerland), Andrée Friedl (Klinik für Infektiologie & Infektionsprävention, Kantonsspital Baden, Baden, Switzerland), Urs Führer (Infektiologie, Spitalzentrum Biel, Biel, Switzerland), Valeria Gaia (Reference Center for Legionella, Department of Laboratory Medicine, Ente Ospedaliero Cantonale, Bellinzona, Switzerland), Christian Garzoni (Clinic of Internal Medicine and Infectious Diseases, Clinica Moncucco, Lugano, Switzerland), Gilbert Greub (Lausanne University Hospital, Lausanne, Switzerland; Institute of Microbiology, University of Lausanne, Lausanne, Switzerland), Christine Gutmann (Infectious Diseases Service, Kantonsspital Winterthur, Winterthur, Switzerland), Eva Hitz (Institut für Labormedizin, Kantonsspital Aarau AG, Aarau, Switzerland), Philipp Kaiser (Infectious Diseases Service, Cantonal Hospital Lucerne, Luzern, Switzerland), Jörg Leuppi (University Center for Internal Medicine, Kantonsspital Baselland, Liestal, Switzerland; University of Basel, Basel, Switzerland), Irena Mitrović (Medical Microbiology, Cantonal Hospital Lucerne, Luzern, Switzerland), Fabienne Nieland (Department of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, Zürich, Switzerland; University of Zurich, Zürich, Switzerland), Matthaios Papadimitriou-Olivgeris (Infectious Diseases Service, Lausanne University Hospital, Lausanne, Switzerland; Central Institute, Valais Hospitals, Sion, Switzerland), Roberta Petrino (Emergency Medicine Unit, Department of Critical Care, Ente Ospedaliero Cantonale, Lugano, Switzerland), Benjamin Preiswerk (Infektiologie, Stadtspital Zürich, Zürich, Switzerland), Martin Risch (Zentrallabor, Kantonsspital Graubünden, Chur, Switzerland), Jacques Schrenzel (Division of Laboratory Medicine, Geneva University Hospitals, Genève, Switzerland), Philip E. Tarr (University Center for Internal Medicine, Kantonsspital Baselland, University of Basel, Basel, Switzerland), Maria C. Thurnheer (Department of Infectious Diseases, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland), Miriam Vazquez (Department of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, Zürich, Switzerland; University of Zurich, Zürich, Switzerland), Alexander Wepf (Institute for Laboratory Medicine, Kantonsspital Winterthur, Winterthur, Switzerland).

Authors' contributions

Conceptualisation of the study: M.B., W.C.A., S.D. and D.M. Data collection: F.Z., M.B. and the members of the ***SwissLEGIO*** hospital network. Statistical analysis: M.B. Data interpretation: M.B., F.Z., S.D., W.C.A. and D.M. Writing of the original draft of the manuscript: M.B. with F.Z. Critically revised the manuscript for important intellectual context and edited W.C.A., D.M., S.D. and the ***SwissLEGIO*** hospital network members. All the authors reviewed and approved the final version of the manuscript.

Funding

Open access funding provided by University of Basel

The ***SwissLEGIO*** parent study is funded by the Swiss Federal Office of Public Health (grant no. 142004673). No additional funding was received for the analysis presented herein.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Commission of Northwestern and Central Switzerland (EKNZ, 2022–00880). The study was conducted in accordance with the principles of Good Epidemiological Practice [50] and the Declaration of Helsinki. All study participants provided written informed consent prior to study enrolment. All study data are stored in accordance with Swiss data protection laws.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Swiss Tropical and Public Health Institute, Basel, Switzerland
[2]University of Basel, Basel, Switzerland
[3]Division of Infectious Diseases, Infection Prevention and Travel Medicine, HOCH Health Ostschweiz, Cantonal Hospital, St. Gallen, Switzerland
[4]Division of Internal Medicine, University Hospital Basel, Basel, Switzerland
[5]Department of Clinical Research, University of Basel, Basel, Switzerland

Received: 13 February 2025 / Accepted: 10 May 2025
Published online: 25 July 2025

References

1. Samuelsson J, Payne Hallstrom L, Marrone G, Gomes DJ. Legionnaires' disease in the EU/EEA*: increasing trend from 2017 to 2019. Euro Surveill. 2023;28(11):2200114.
2. Fischer FB, Mäusezahl D, Wymann MN. Temporal trends in legionellosis national notification data and the effect of COVID-19, Switzerland, 2000–2020. Int J Hyg Environ Health. 2023;247:113970.
3. Graham FF, Finn N, White P, Hales S, Baker MG. Global perspective of Legionella infection in community-acquired pneumonia: a systematic review and meta-analysis of observational studies. Int J Environ Res Public Health. 2022;19(3):1907.

4. Woodhead M, Blasi F, Ewig S, Garau J, Huchon G, Ieven M, et al. Guidelines for the management of adult lower respiratory tract infections–full version. Clin Microbiol Infect. 2011;17(Suppl 6):E1-59.
5. Cunha BA, Burillo A, Bouza E. Legionnaires' disease. Lancet. 2016;387(10016):376–85.
6. Viasus D, Gaia V, Manzur-Barbur C, Carratalà J. Legionnaires' disease: update on diagnosis and treatment. Infect Dis Ther. 2022;11(3):973–86.
7. Ewig S, Kolditz M, Pletz M, Altiner A, Albrich W, Dromann D, et al. Management of Adult Community-Acquired Pneumonia and Prevention - Update 2021 - Guideline of the German Respiratory Society (DGP), the Paul-Ehrlich-Society for Chemotherapy (PEG), the German Society for Infectious Diseases (DGI), the German Society of Medical Intensive Care and Emergency Medicine (DGIIN), the German Viological Society (DGV), the Competence Network CAPNETZ, the German College of General Practitioneers and Family Physicians (DEGAM), the German Society for Geriatric Medicine (DGG), the German Palliative Society (DGP), the Austrian Society of Pneumology Society (OGP), the Austrian Society for Infectious and Tropical Diseases (OGIT), the Swiss Respiratory Society (SGP) and the Swiss Society for Infectious Diseases Society (SSI). Pneumologie. 2021;75(9):665–729.
8. Schweizerische Gesellschaft für Infektiologie. Ambulant-erworbene Pneumonie: https://ssi.guidelines.ch/guideline/3007/de. Accessed 23 Aug 2024.
9. Allgaier J, Lagu T, Haessler S, Imrey PB, Deshpande A, Guo N, Rothberg MB. Risk factors, management, and outcomes of Legionella pneumonia in a large. Nationally Representative Sample Chest. 2021;159(5):1782–92.
10. Lettinga KD, Verbon A, Weverling GJ, Schellekens JF, Den Boer JW, Yzerman EP, et al. Legionnaires' disease at a Dutch flower show: prognostic factors and impact of therapy. Emerg Infect Dis. 2002;8(12):1448–54.
11. Falcone M, Russo A, Tiseo G, Cesaretti M, Guarracino F, Menichetti F. Predictors of intensive care unit admission in patients with Legionella pneumonia: role of the time to appropriate antibiotic therapy. Infection. 2021;49(2):321–5.
12. Viasus D, Di Yacovo S, Garcia-Vidal C, Verdaguer R, Manresa F, Dorca J, et al. Community-acquired Legionella pneumophila pneumonia: a single-center experience with 214 hospitalized sporadic cases over 15 years. Medicine (Baltimore). 2013;92(1):51–60.
13. Dyar OJ, Huttner B, Schouten J, Pulcini C, Antimicrobi EESG. What is antimicrobial stewardship? Clin Microbiol Infec. 2017;23(11):793–8.
14. Viasus D, Vecino-Moreno M, De La Hoz JM, Carratalà J. Antibiotic stewardship in community-acquired pneumonia. Expert Rev Anti Infect Ther. 2017;15(4):351–9.
15. Tamma PD, Avdic E, Li DX, Dzintars K, Cosgrove SE. Association of adverse events with antibiotic use in hospitalized patients. Jama Intern Med. 2017;177(9):1308–15.
16. Schimmel JJ, Haessler S, Imrey P, Lindenauer PK, Richter SS, Yu PC, Rothberg MB. Pneumococcal urinary antigen testing in united states hospitals: a missed opportunity for antimicrobial stewardship. Clin Infect Dis. 2020;71(6):1427–34.
17. Fischer FB, Schmutz C, Gaia V, Mäusezahl D. Legionnaires' disease on the rise in Switzerland: a denominator-based analysis of national diagnostic data, 2007–2016. Int J Environ Res Public Health. 2020;17(19):7343.
18. Bellew S, Grijalva CG, Williams DJ, Anderson EJ, Wunderink RG, Zhu Y, et al. Pneumococcal and Legionella urinary antigen tests in community-acquired pneumonia: prospective evaluation of indications for testing. Clin Infect Dis. 2019;68(12):2026–33.
19. Lüthi-Corridori G, Roth AI, Boesing M, Jaun F, Tarr PE, Leuppi-Taegtmeyer AB, Leuppi JD. Diagnosis and therapy of community-acquired pneumonia in the emergency department: a retrospective observational study and medical audit. J Clin Med. 2024;13(2):574.
20. Falguera M, Ruiz-González A, Schoenenberger JA, Touzón C, Gázquez I, Galindo C, Porcel JM. Prospective, randomised study to compare empirical treatment versus targeted treatment on the basis of the urine antigen results in hospitalised patients with community-acquired pneumonia. Thorax. 2010;65(2):101–6.
21. Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, et al. Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med. 2019;200(7):e45–67.
22. Murdoch DR. Indications for microbiological testing in pneumonia: which patients should be tested? Clin Infect Dis. 2019;68(12):2034–5.
23. Garbino J, Bornand JE, Uckay I, Fonseca S, Sax H. Impact of positive legionella urinary antigen test on patient management and improvement of antibiotic use. J Clin Pathol. 2004;57(12):1302–5.
24. Engel MF, van Manen L, Hoepelman AIM, Thijsen S, Oosterheert JJ. Diagnostic, therapeutic and economic consequences of a positive urinary antigen test for Legionella spp. in patients admitted with community-acquired pneumonia: a 7-year retrospective evaluation. J Clin Pathol. 2013;66(9):797–802.
25. Dionne M, Hatchette T, Forward K. Clinical utility of a Legionella pneumophila urinary antigen test in a large university teaching hospital. Can J Infect Dis. 2003;14(2):85–8.
26. Fischer FB, Bigler M, Mäusezahl D, Hattendorf J, Egli A, Julian TR, et al. Legionnaires' disease in Switzerland: rationale and study protocol of a prospective national case-control and molecular source attribution study (SwissLEGIO). Infection. 2023;51(5):1467–79.
27. Federal Office of Public Health. Legionärskrankheit in der Schweiz und im Fürstentum Liechtenstein im Jahr 2023. BAG-Bulletin 34/2024. 2024. https://www.bag.admin.ch/bag/de/home/das-bag/publikationen/periodika/bag-bulletin.html. Accessed 25 Oct 2024.
28. Federal Office of Public Health. BAG-Bulletin 14/2024 2024. https://www.bag.admin.ch/bag/de/home/das-bag/publikationen/periodika/bag-bulletin.html. Accessed 25 Oct 2024.
29. Fischer FB. The epidemiology of legionnaires' disease in Switzerland: a re-emerging disease. Basel: University of Basel; 2024.
30. Magill SS, O'Leary E, Ray SM, Kainer MA, Evans C, Bamberg WM, et al. Assessment of the appropriateness of antimicrobial use in US hospitals. Jama Netw Open. 2021;4(3):e212007.
31. University Hospital Basel. Stanfordguide/infektioStandards 2024. https://webedition.sanfordguide.com/en/weissbuch. Accessed 15 Sept 2024.
32. Schaub C, Barnsteiner S, Schonenberg L, Bloch N, Drager S, Albrich WC, et al. Antibiotic treatment durations for common infectious diseases in Switzerland: comparison between real-life and local and international guideline recommendations. Glob Antimicrob Resist. 2023;32:11–7.
33. Vaughn VM, Flanders SA, Snyder A, Conlon A, Rogers MAM, Malani AN, et al. Excess antibiotic treatment duration and adverse events in patients hospitalized with pneumonia a multihospital cohort study. Ann Intern Med. 2019;171(3):153–63.
34. Yi SH, Hatfield KM, Baggs J, Hicks LA, Srinivasan A, Reddy S, Jernigan JA. Duration of antibiotic use among adults with uncomplicated community-acquired pneumonia requiring hospitalization in the United States. Clin Infect Dis. 2018;66(9):1333–41.
35. Ente Ospedaliero Cantonale. Reference Center for Legionella 2025. https://www.eoc.ch/ospedali-e-istituti/istituto-di-medicina-di-laboratorio/servizi-per-i-professionisti/centro-legionella.htm. Accessed 29 Apr 2025.
36. Cusini A, Rampini SK, Bansal V, Ledergerber B, Kuster SP, Ruef C, Weber R. Different patterns of inappropriate antimicrobial use in surgical and medical units at a tertiary care hospital in Switzerland: a prevalence survey. PLoS ONE. 2010;5(11):e14011.
37. Wikén C, Eliasson J, Alanko Blome M, Falt R, Resman F, Ljungquist O, et al. Clinical and epidemiological characteristics of Legionnaires' disease in Southern Sweden, a population-based study. Infect Dis (Lond). 2025;7:1–12.
38. Gürtler N, Erba A, Giehl C, Tschudin-Sutter S, Bassetti S, Osthoff M. Appropriateness of antimicrobial prescribing in a Swiss tertiary care hospital: a repeated point prevalence survey. Swiss Med Wkly. 2019;149:w20135.
39. Stout JE, Sens K, Mietzner S, Obman A, Yu VL. Comparative activity of quinolones, macrolides and ketolides against Legionella species using in vitro broth dilution and intracellular susceptibility testing. Int J Antimicrob Agents. 2005;25(4):302–7.
40. Stout JE, Yu VL. Legionellosis. N Engl J Med. 1997;337(10):682–7.
41. Karer M, Haider T, Kussmann M, Obermüller M, Tiehen C, Burgmann H, et al. Treatment of legionellosis including a single intravenous dose of 1.5 g azithromycin: 18-year experience at a tertiary care hospital. Int J Antimicrob Agents. 2022;59(1):106481.
42. Scarpato SJ, Timko DR, Cluzet VC, Dougherty JP, Nunez JJ, Fishman NO, et al. An evaluation of antibiotic prescribing practices upon hospital discharge. Infect Cont Hosp Ep. 2017;38(3):353–5.
43. Holmes AH, Moore LS, Sundsfjord A, Steinbakk M, Regmi S, Karkey A, et al. Understanding the mechanisms and drivers of antimicrobial resistance. Lancet. 2016;387(10014):176–87.
44. Massip C, Descours G, Ginevra C, Doublet P, Jarraud S, Gilbert C. Macrolide resistance in Legionella pneumophila: the role of LpeAB efflux pump. J Antimicrob Chemother. 2017;72(5):1327–33.
45. Shadoud L, Almahmoud I, Jarraud S, Etienne J, Larrat S, Schwebel C, et al. Hidden selection of bacterial resistance to fluoroquinolones in vivo: the case of Legionella pneumophila and humans. EBioMedicine. 2015;2(9):1179–85.

46. Bruin JP, Koshkolda T, IJzerman EPF, Lück C, Diederen BMW, Den Boer JW, Mouton JW. Isolation of ciprofloxacin-resistant in a patient with severe pneumonia. J Antimicrob Chemother. 2014;69(10):2869–71.
47. Portal E, Descours G, Ginevra C, Mentasti M, Afshar B, Chand M, et al. Legionella antibiotic susceptibility testing: is it time for international standardization and evidence-based guidance? J Antimicrob Chemother. 2021;76(5):1113–6.
48. Sewell M, Farley C, Portal EA, Lindsay DSJ, Ricci ML, Jarraud S, et al. Broth microdilution protocol for determining antimicrobial susceptibility of Legionella pneumophila to clinically relevant antibiotics. Microbiol Methods. 2025;228:107071.
49. Spivak ES, Cosgrove SE, Srinivasan A. Measuring appropriate antimicrobial use: attempts at opening the black box. J Microbiol Methods. 2025;228:107071.
50. Altpeter E, Burnand B, Capkun G, Carrel R, Cerutti B, Mäusezahl-Feuz M, et al. Essentials of good epidemiological practice. Soz Praventivmed. 2005;50(1):12–27.

Publisher's Note