Cellulitis in the Emergency Department: A prospective cohort study with patient-centred follow-up

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ORIGINAL RESEARCH

Cellulitis in the Emergency Department: A prospective cohort study with patient-centred follow-up

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Abstract

Objective: There is substantial practice variation in the management of cellulitis with limited prospective studies describing the course of cellulitis after diagnosis. We aimed to describe the demographics, clinical features (erythema, warmth, swelling and pain), patient-reported disease trajectory and medium-term follow-up for ED patients with cellulitis.

Methods: Prospective observational cohort study of adults diagnosed with cellulitis in two EDs in Southeast Queensland, Australia. Patients with (peri)orbital cellulitis and abscess were excluded. Data were obtained from a baseline questionnaire, electronic medical records and follow-up questionnaires at 3, 7 and 14 days. Clinician adjudication of day 14 cellulitis cure was compared to patient assessment. Descriptive analyses were conducted.

Results: Three-hundred patients (mean age 50 years, SD 19.9) with cellulitis were enrolled, predominantly affecting the lower limb (75%). Cellulitis features showed greatest improvement between enrolment and day 3. Clinical improvement continued gradually at days 7 and 14 with persistent skin erythema (41%) and swelling (37%) at day 14. Skin warmth was the feature most likely to be resolved at each time point. There was a discrepancy in clinician and patient assessment of cellulitis cure at day 14 (85.8% *vs.* 52.8% cured).

Conclusions: A clinical response of cellulitis features can be expected at day 3 with ongoing slower improvement over time. Over one third of patients had erythema or swelling at day 14. Patients are less likely than clinicians to deem their cellulitis cured at day 14. Future research should include parallel patient and clinician evaluation of cellulitis to help develop clearer definitions of treatment failure and cure.

Key findings

- The first study to report the treatment response of all four hallmark features of cellulitis (skin erythema, warmth, swelling and pain) at multiple time points over a 14-day period.
- Patient-centred outcomes with a focus on patient described symptom severity and impression of cellulitis resolution.
- The present study may help inform conversations between clinicians and patients about expected disease trajectory for cellulitis.

Key words: *cellulitis, ED, infection, patient-centred, skin and soft tissue infection (SSTI).*

Introduction

Cellulitis is a bacterial infection of the cutaneous and/or subcutaneous tissues characterised by four hallmark signs and symptoms: erythema, warmth, swelling and pain. Cellulitis is a common and costly ED.[1,2] Therefore, understanding its clinical course and providing optimal management is paramount.

The clinical course of ED diagnosed cellulitis is reported poorly, with few prospective studies describing clinical response after diagnosis,[3–6] and none

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describing the trajectory of all four hallmark features over multiple timepoints. This is supported by a recent systematic review which assessed time to clinical response in patients with cellulitis treated with antibiotics. It found that most included studies did not measure clinical response at more than one time point.[7] The review concluded that further prospective studies with follow-up at multiple time points were required to delineate clinical response over time more accurately.

Treatment failure or cellulitis resolution have been variably defined in the literature and a systematic review found treatment failure rates between 0% and 29.5% based on a range of definitions.[8] Several included studies used clinician assessment, which may deviate from the patient's experience or impression.[8,9] This evidence gap can be addressed by assessing the clinical course of cellulitis and correlating this with patient reported and patient-centred outcomes. The aim of the present study was to describe demographics, clinical characteristics and management of patients diagnosed with cellulitis in the ED, with a focus on the medium-term trajectory of patient-reported cellulitis features (over multiple time points) and both patient and clinician assessment of cellulitis cure.

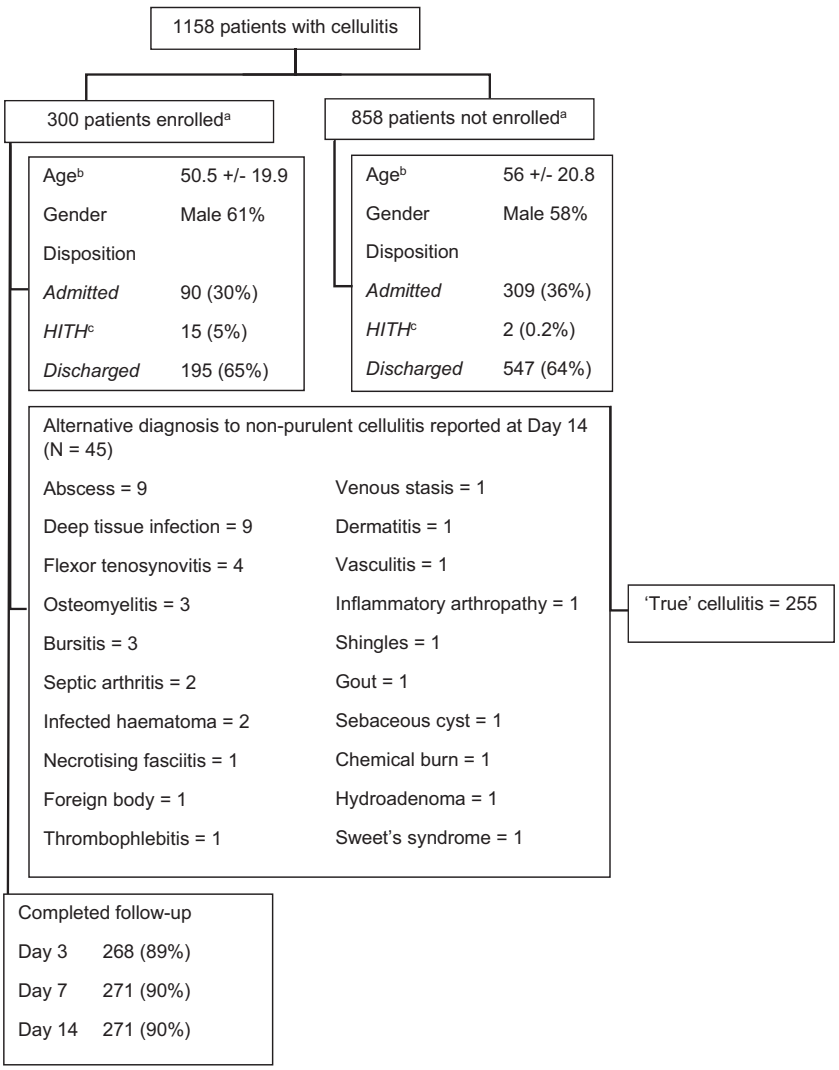

Figure 1. (a) Enrolled and not enrolled cohorts were similar in terms of sex and disposition. The enrolled cohort was younger (mean age difference 5.5 years, 95% CI: 2.8–8.2). (b) Years, mean ± standard deviation. (c) Hospital in the home (HITH, outpatient IV antibiotics).

Methods

Study design and setting

This was a prospective observational cohort study conducted between May 2021 and June 2022 in the EDs of two public hospitals within the same health service in Australia. One is a tertiary facility and the other is a general hospital with around 120 000 and 66 000 attendances in 2020, respectively. The study was approved by the Health District's Human Research and Ethics Committee (HREC/2020/QGC/63149). We adhered to the STROBE statement for reporting cohort studies (Supplement 1).[10]

Eligibility and recruitment

All adult (≥18 years) patients with a treating clinician ED diagnosis of cellulitis requiring antibiotics were eligible for enrolment. Patients were screened, recruited and written informed consent was obtained by the treating ED clinician or member of the research team. All facets of cellulitis treatment were at the discretion of the treating clinician. Participation was voluntary, and subjects were allowed to discontinue study participation at any time.

Exclusion criteria

Patients with periorbital cellulitis, orbital cellulitis or cellulitis with an abscess that required formal incision and drainage were excluded. We also excluded patients with return ED visits within 14 days with cellulitis affecting a body area that had already received an ED diagnosis of cellulitis.

Data collection

A standardised digital enrolment form was used to record patient demographics and co-morbidities. Cellulitis-specific data collected at the time of enrolment included symptom duration, any pre-hospital treatment, presence of fever, nausea or vomiting, size of erythema (mm measurement) and the degree of erythema, warmth

TABLE 1. *Patient, cellulitis and management and treatment characteristics (n = 300)*

Characteristic	*N*	%
Demographics		
Sex = male	183	61.0
Aboriginal or Torres Strait Islander	10	3.3
Age (mean and SD) years	50.5 (19.9)	
Occupational status		
Unemployed	31	10.3
Employed/student	150	50.0
Retired	74	24.7
Unknown	45	15.0
Patient medical history		
BMI (median and IQR) kg/m^2	28 (24–34)	
BMI ≥30 kg/m^2	114	38.0
Current smoker	68	22.7
Prior history of cellulitis	59	19.7
Peripheral vascular disease	41	13.7
>10 standard alcohol drinks weekly	31	10.3
Diabetes (insulin dependent)	16	5.3
Diabetes (not insulin dependent)	14	4.7
Renal failure	16	5.3
Cancer/chemotherapy/ immunomodulator use	10	3.3
Steroid use	10	3.3
Liver failure	3	1.0
Human immunodeficiency virus	2	0.7
None of above noted	97	32.2
Cellulitis characteristics		
Location of infection†		
Leg	170	56.7
Foot	54	18.0
Arm	37	12.3
Hand	34	11.3
Other	22	7.3
Face and/or neck	14	4.7
Days from onset to presentation (median, IQR)	3 (1.8–5)	
Antibiotics prior to presentation (yes)	135	45.0
Days on antibiotics (median, IQR)	3 (1–5)	
ED findings		
Size of area affected		
<10 cm^2	25	8.3
10–40 cm^2	52	17.3

(*Continues*)

and swelling (all 5-point Likert scales: 1 = absence of symptom, 2 = slight, 3 = moderate, 4 = very, 5 = extreme). Pain was recorded on a 11-point numerical rating scale (0 = no pain, 10 = worst pain) (Supplement 2).[11]

Follow-up was performed by completion at days 3, 7 and 14 from ED presentation *via* a standardised questionnaire *via* telephone or email. Patient-reported degree of skin erythema, warmth, swelling and pain were recorded. Patient determined cellulitis progress and cure were recorded on a 5-point Likert scale (1 = completely resolved, 2 = improved 3 = remained the same, 4 = worsened, 5 = significantly worsened). Adverse events, return visits to ED or other healthcare providers and treatment changes were collected at each follow-up. Day 14 follow-up included collection of patient-reported alternative diagnoses made and patient satisfaction regarding their overall care received (0 = not satisfied, 10 = entirely satisfied). (Supplement 2).

Data on clinical variables including vital signs, antibiotic treatment, disposition, hospital length of stay and return ED visit details were collected from the hospital electronical medical records (EMR) for all patients during their 14-day follow-up.

Two emergency medicine clinicians independently reviewed the data available and determined cellulitis cure at day 14. The clinicians defined cure as the disappearance of warmth and pain with improvement in erythema and swelling, consistent with previous cellulitis studies.[5,12] Clinicians also determined patients to be cured if the patients reported cure with only mild persisting symptoms or when there was an EMR note documenting cure. Discordance of cure assessment occurred in 5% of cases which were resolved *via* consensus.

Data categorisation

The 11-item numerical pain rating score was categorised into no pain (0), mild (1–3), moderate (4–6) and severe pain (7–10).[11] Secondary outcomes (e.g. ED or general practitioner [GP] visits, symptoms post-ED discharge, days off normal activities)

TABLE 1. *Continued*

Characteristic	*N*	%
>40 cm^2	223	74.3
Nausea and/or vomiting (yes)	74	24.7
C-reactive protein (median, IQR) ($n = 169$)	28 (7.8–91.3)	
White cell count (mean, SD) ($n = 271$)	10.6 (4.0)	
Vital signs (worst)		
Fever ≥38.0°C	48	16.0
Tachypnoea (>20 breaths/min)	37	12.3
Tachycardia (>100 beats/min)	70	23.3
Hypotension (<90 mmHg systolic blood pressure)	3	1.0
Any of: fever, tachypnoea, tachycardia, hypotension	104	34.7
Antibiotic treatment in ED		
Route and dose frequency whilst in ED		
Oral only	77	25.7
IV single dose and discharged on orals	35	11.7
IV multiple doses and discharged on orals/none	85	28.3
IV in ED and discharged to hospital in the home (HITH)	14	4.7
IV in ED and admitted	89	29.7
Type of IV antibiotic administered in ED ($n = 247$)		
Flucloxacillin	172	69.6
Penicillin not flucloxacillin	61	24.7
Lincomycin/clindamycin	11	4.7
Other‡	3	1.2
Discharge antibiotic (for ED and short stay unit to home, $n = 195$)		
Flucloxacillin or dicloxacillin	130	66.7
Cephalosporin	30	15.4
Clindamycin	14	7.2
Amoxicillin–clavulanic acid	8	4.1
Trimethoprim–sulfamethoxazole	5	2.6
Other§	8	4.1
Discharge disposition		
Home	115	38.3
Short Stay Unit (SSU)	123	41.0
SSU then home	*80*	*26.7*
SSU then HITH	*11*	*3.7*
SSU then hospital ward	*32*	*10.6*
Hospital in the home (HITH)	3	1.0

were tallied for each time point and cumulatively across time points.

Data analysis

SPSS v26.0 (IBM Corp, Armonk, NY) and Python 3.10.8 (Python Software Foundation) were used to conduct descriptive statistics, inferential statistics for categorical data (i.e. chi-square, Mann–Whitney *U* test and Fisher's exact as appropriate) and logistic regression modelling. Means and standard deviations (SD) or medians and interquartile ranges (IQR) were reported as appropriate. Separate descriptive analyses were conducted for all patients enrolled, for all patients enrolled without an alternative diagnosis during follow-up and for patients with cellulitis who were not enrolled. Univariate and multivariable logistic regression analyses were performed to identify predictors of cellulitis cure at day 14 (Supplement 3).

Results

During the study period, 300 patients were enrolled and 90% completed follow-up at day 14 with 95% completing at least one follow-up questionnaire (day 3, 7 or 14). Recruitment and relevant characteristics are reported in Figure 1. Enrolled patients had a mean age of 50 years (SD 19.9), and 38% had a body mass index (BMI) ≥30 kg/m^2, 14% had peripheral vascular disease and 10% had diabetes. The median duration of cellulitis prior to presentation was 3 days (IQR 1.8–5.0) and almost half of patients had been prescribed antibiotics prior to ED presentation ($n = 135$, 45%), typically for 3 days (IQR 1–5). The most affected area was the leg ($n = 170$, 57%) followed by the foot ($n = 54$, 18%) and arm ($n = 37$, 12%). Patients had more than one area affected in 10% ($n = 30$) of cases. The area of skin involvement was typically large (>40 cm^2 in $n = 223$, 74% of cases). Patient demographics and their cellulitis characteristics are described in Table 1.

TABLE 1. *Continued*

Characteristic	*N*	%
Hospital ward	59	19.7
Median length of stay (hours) and (IQR) by discharge type		
All patients ($n = 300$)	7.9 (4.7–19.3)	
Patients discharged home or to HITH ($n = 118$)	4.7 (3.0–7.0)	
Patients discharged to short stay then home ($n = 80$)	19.7 (14.6–24.0)	
Patients discharged to short stay then admitted, or directly admitted ($n = 91$)	72.0 (25.5–96.0)	

BMI, body mass index; IQR, interquartile range; IV, intravenous; SD, standard deviation. †Twenty-nine patients had multiple areas involved. ‡Other antibiotics: azithromycin ($n = 1$), ciprofloxacin ($n = 1$), gentamicin ($n = 1$). §Other antibiotics: phenoxymethylpenicillin ($n = 3$), erythromycin ($n = 2$), ciprofloxacin ($n = 1$), doxycycline ($n = 1$), none ($n = 1$).

Cellulitis management

Three quarters ($n = 223$, 74%) of patients were treated with IV antibiotics. Over one-third (36%, 80/223) of these patients had fever and/or tachycardia and 1% had hypotension. Approximately one-quarter ($n = 63$, 28%) of patients prescribed IV antibiotics had been on oral antibiotics for ≥72 h. Flucloxacillin followed by a cephalosporin were the most common antibiotic agents prescribed (Table 1). Two-thirds of patients (65%) were discharged home from the ED either directly or *via* an ED short stay admission unit. Those admitted to short stay and then home had a total length of stay (LOS) of less than 1 day (median 19.7 h, IQR 14.6–24.0). Thirty percent of patients ($n = 91$) were admitted to hospital with a median LOS of 3 days (72.0 h, IQR 25.5–96.0).

Cellulitis features

At enrolment, most patients had all four hallmark features of cellulitis (skin erythema 99%, warmth 97%, swelling 96% and pain 91%). These four features were reported as moderate in severity with a mean Likert score between 3.1 and 3.4 for skin erythema, warmth and swelling and a mean pain score of 4.6. The severity of these features reduced at each follow-up time point (3, 7 and 14 days). At day 3, warmth was the feature most frequently resolved (88/268; 33%) and swelling the least likely to be resolved (48/268; 18%). At day 7, on average, all four features of cellulitis were graded as either not present or mild severity. Further reduction in cellulitis feature severity was noted at day 14, although more gradual compared to the days 3 and 7 time points (see Fig. 2a). Over one-third of patients still reported (i.e. more than 'none at all') skin erythema and swelling at day 14 (Fig. 2b).

Response to treatment and cure

Over three-quarters of patients ($n = 211$) saw an improvement in cellulitis at day 3 (78.7%; 95 CI 73.4–83.2); and 10 patients reported cellulitis cure. By day 7, a quarter of patients ($n = 69$) reported that their cellulitis was cured (25.5%; 95% CI 20.6–31.0), and by day 14 this was 52.8% (95% CI 46.8–58.6). The number and proportion of patients deemed to be cured based on clinician adjudication at day 14 was 236 of 275, or 85.8% (95% CI 81.2–89.5%) (Table 2).

Persistent cellulitis features (erythema, swelling, warmth or pain) were present in 31% (44/143) of the patients who self-reported cellulitis cure at day 14. In the clinician adjudicated cellulitis cure group, 51% (118/232) had persistent skin changes. The features most likely to still be present at day 14 when cellulitis was deemed cured by both patients and clinicians were erythema and/or swelling (patients 38/143 = 27%, clinicians 109/232 = 47%). These features were twice as prevalent when clinicians determined cure compared to when patients self-reported cure (erythema 33% *vs.* 15%, swelling 30% *vs.* 17%). Warmth was infrequently present in both patient and clinician determined cure cohorts (3/143 = 2% *vs.* 20/232 = 9%) (Fig. 2b,c).

An alternative diagnosis was reported by 45 patients (15%) at day 14 (Fig. 1). There were no statistically significant differences in the trajectory of hallmark cellulitis features or cure rates between the overall cohort and if the cohort had patients with alternative diagnoses removed (Supplements 4 and 5).

Adverse events, follow-up and satisfaction (Table 3)

Community GP review occurred for 87 patients (30.5%), and 52 patients (18.2%) had a return ED visit during the 14-day follow-up. Over two-thirds ($n = 187$, 69%) of patients remained on antibiotics on day 7 and 73 (26.9%) were still taking antibiotics on day 14 (Table 3). Adverse events during the 14-day follow-up were commonly reported (55%) but mostly mild (Table 3). The median total days off activities was 2 (IQR 4–7).

Predictors of cure

Logistic regression did not identify any independent predictors for cellulitis cure (Supplement 6).

Discussion

This is a novel, prospective cohort study focusing on patient self-report

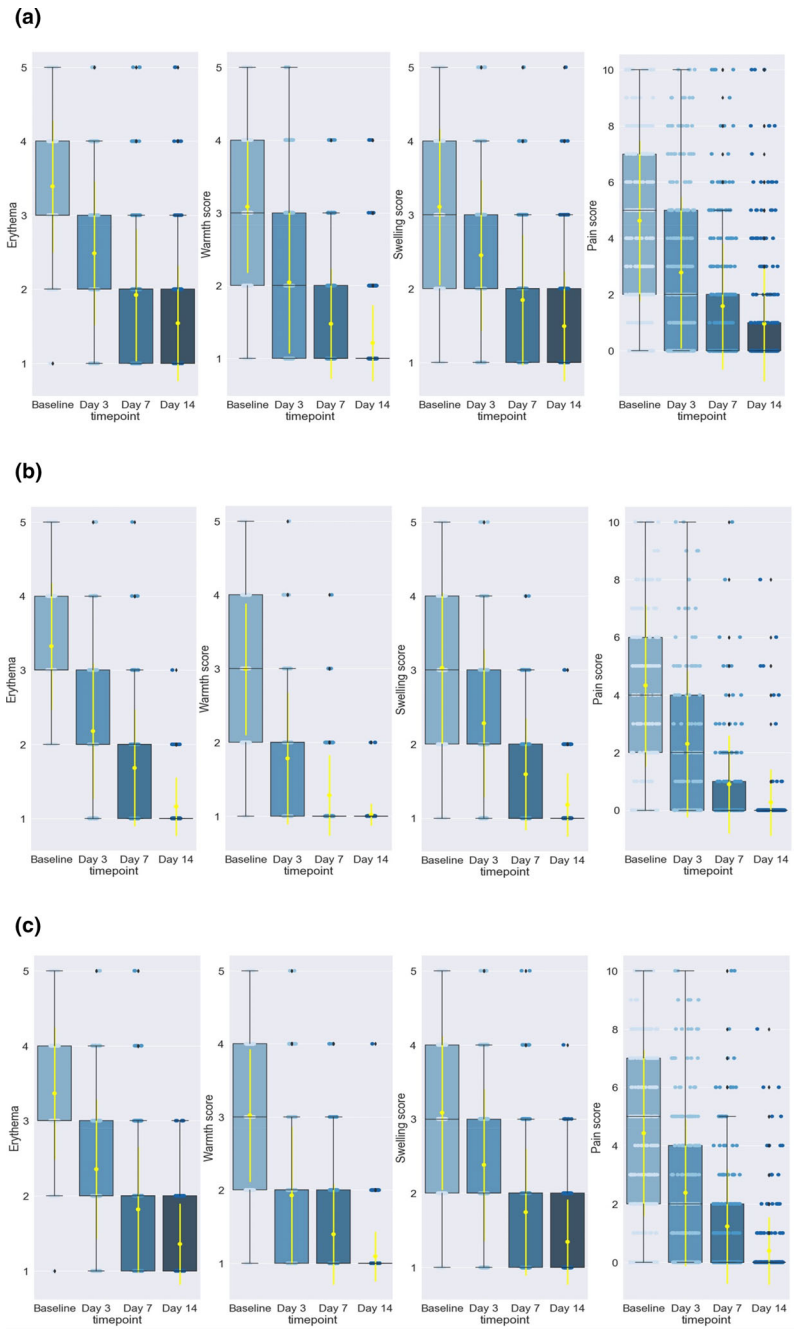

Figure 2. Symptom response during 14-day follow-up. (a) Whole cohort (n = 300). (b) Patients who reported cellulitis resolution at day 14 (n = 143). (c) Patients with clinician adjudicated cellulitis resolution at day 14 (n = 236). Likert scores: 1 = none, 2 = slight, 3 = moderate, 4 = very, 5 = extreme.

of cellulitis features over time and cellulitis cure. It is the first ED study to report the treatment response of all four hallmark features of cellulitis (skin erythema, warmth, swelling and pain) at multiple time points over a 14-day period.[3,5,7,9,12,13]

Our study demonstrated improvement of all hallmark features of cellulitis by day 3 of treatment, supporting the recommendation from a recent systematic review that the optimal time for clinical reassessment is between 48 and 96 h.[8] Despite this early improvement, many patients had persistent mild symptoms after completing a (guideline recommended) 5-day course of antibiotics[14,15] and one-third of patients had persistent erythema and swelling at day 14. In the absence of fever, pain, warmth, or erythema extension these findings are suggestive of a residual inflammatory response rather than persistent infection, which should not require ongoing antibiotics. This is consistent with prior literature which reported persistent inflammation (e.g. erythema) in almost 30% of patients 2 weeks post-treatment.[13] These findings can provide reassurance to patients and clinicians that isolated persistent mild erythema and swelling reflects residual inflammation rather than infection.[16]

Skin erythema is the most reported cellulitis clinical feature and is often used as a surrogate marker for treatment response.[9,17] In contrast, skin warmth is the least reported clinical feature in the cellulitis literature.[7,9] Our study identified warmth as the feature which responds to treatment the earliest and is the most likely to be resolved at each time point, whereas erythema is more likely to persist at day 14. Clinically differentiating between infection and residual skin inflammation can be difficult.[13] The high rate of persistent erythema in patients with cellulitis cure in the present study suggests that using erythema as the main or sole indicator of treatment response or cure may result in an overestimation of treatment failure. Alternatively, warmth may be an underappreciated indicator of treatment response or cure.

We found a discrepancy between patient and clinician adjudicated cellulitis cure, with one-third fewer patients reporting their cellulitis to be cured after 14 days compared to clinician determination of cure (53% *vs.* 86%). The clinician adjudicated cure rate is consistent with existing literature (80–98%).[4,7,12,13,18] Clinicians deemed more cases to be cured despite residual skin changes (50% *vs.* 31%), suggesting interpreting this as non-infectious inflammatory skin changes. This is an opportunity to inform conversations between patients and clinicians about

TABLE 2. *Resolution during follow-up*

	Patient impression of resolution						Clinician impression of resolution	
	Day 3 ($n = 268$)		Day 7 ($n = 271$)		Day 14 ($n = 271$)		Day 14 ($n = 275$)[a]	
	n	% (95% CI)	*n*	% (95% CI)	*n*	% (95% CI)	*N*	% (95% CI)
Resolved	10	3.7 (2.0–6.7)	69	25.5 (20.6–31.0)	143	52.8 (46.8–58.6)	236	85.8 (81.2–89.5)
Improved	211	78.7 (73.4–83.2)	189	69.7 (64.0–74.9)	118	43.5 (37.8–49.5)		
Unchanged	31	11.6 (8.3–16.0)	9	3.3 (1.8–6.2)	3	1.1 (0.4–3.2)		
Worse	10	3.7 (2.0–6.7)	3	1.1 (0.4–3.2)	7	2.6 (1.3–5.2)		
Significantly worse	6	2.2 (1.0–4.8)	1	0.4 (0.1–2.1)	0	0.0 (0.0–1.4)		

[a]Clinician impression of resolution was based on patient follow-up/description of symptoms and review of follow-up notes on the electronic medical record. There were four cases where an assessment of resolution could be made based on medical records in the absence of the patient completing day 14 follow-up.

the expected course of cellulitis and improve antibiotic stewardship. This would require knowledge translation strategies including an integrated clinician-patient interaction supported by education, common shared decision-making tools and patient involvement in cellulitis research. This is supported by prior research where patients diagnosed with cellulitis felt misinformed about the condition, including the duration of symptoms.[16,19]

Semi-synthetic penicillins (e.g. flucloxacillin/dicloxacillin) were the most frequently prescribed antibiotics, in keeping with local guidelines.[14,15] There is no consensus on the ideal duration of antibiotics in cellulitis; however, studies and guidelines indicate that 5 days is appropriate.[12,14,15] We observed a high rate of antibiotic use at day 7 (69%) and day 14 (27%), suggesting that patients are being prescribed longer courses or receiving repeat prescriptions. This may be because of the absence of universal definition of cure as well as clinicians and patients interpreting persistent (mild) symptoms as infection, resulting in further antibiotic prescription.[20]

Recommendations

Future research should compare the simultaneous patient description of symptoms and in-person clinician assessment. This would improve the understanding of the gap(s) between clinicians and patients. Better understanding of the patient's perspective will allow for the development of definitions of treatment failure that better align with the patient experience. It will also inform clinicians on how to best educate patients on the expected clinical course of cellulitis. Future studies should establish clear definitions of treatment failure that distinguish between infection and residual inflammatory changes. To achieve this the clinical course of cellulitis should be followed over a longer timeframe and focus on warmth as a key marker of treatment response.

Limitations

The study aimed for consecutive recruitment, recruiting 26% of eligible patients. The reasons for missed recruitments included: limited research staff available to support clinicians and, high rates of staff turnover which was further compounded by the COVID-19 pandemic and associated restrictions. The demographics non-enrolled patients were similar to enrolled patients and the demographics of the enrolled cohort are similar to those reported in previous studies,[13,21–24] suggesting that the cohort is representative. Further, cellulitis misdiagnosis relied on patients reporting an alternative diagnosis being made prior to day 14 follow-up. Our rate of alternative diagnoses (15%) is on the lower end of the range reported in a recent systematic review[25] which raises the possibility that some patients with a cellulitis mimic were included, potentially leading to an underestimation of cure rates and account for some patients continuing to take antibiotics at days 7 and 14. Furthermore, although the clinician adjudication of cellulitis cure at day 14 used definitions consistent with prior literature, it was based upon clinical interpretation of the data provided by the patient and medical record, making misclassification bias possible. Finally, we do not know the antibiotic sensitivities or causative organism (including methicillin-resistant *Staphylococcus aureus*) for those enrolled. We are unable to comment to what extent the described trajectory and cure assessments may have been influenced by inadequate antibiotic choice. However, this reflects real-world practice with sensitivities not often being available to ED clinicians at time of diagnosis.

Conclusion

This prospective cohort study shows that adults with cellulitis have clinical response to antibiotics by day 3. Over one-quarter of patients describe a degree of persistent

TABLE 3. *Secondary outcomes and other characteristics by time point during follow-up*

	Day 3 ($n = 268$)		Day 7 ($n = 271$)		Day 14 ($n = 271$)	
At each time point	*n*	%	*n*	%	*n*	%
Still taking antibiotic (yes)	259	96.6	187	69.0	73	26.9
Requiring further medical review since last follow-up						
Yes, in ED	26	9.7	16	5.9	10	3.7
Yes, with GP/OPD	21	7.8	49	18.1	56	20.7
No	221	82.5	206	76.0	205	75.6
New symptoms since last follow-up time point†						
No	173	64.6	185	68.3	210	77.5
Yes, minor/insignificant	39	14.6	43	15.9	36	13.3
Yes, moderate severity	29	10.8	25	9.2	17	6.3
Yes, major/severe	27	10.1	18	6.6	8	3.0
Symptom details ↑						
Nausea/vomiting	27	10.1	20	7.4	12	4.4
Diarrhoea	14	5.2	21	7.7	14	5.2
Constipation	17	6.3	10	3.7	8	3.0
Abdominal pain	13	4.9	16	5.9	10	3.7
Abscess formation	16	6.0	10	3.7	6	2.2
Rash (not including cellulitis)	3	1.1	8	3.0	4	1.5
Superficial thrombophlebitis	1	0.4	2	0.7	2	0.7
Deep vein thrombosis	2	0.7	0	0.0	1	0.4
Anaphylaxis	0	0.0	1	0.4	0	0.0
Other, not including above	10	3.7	7	2.6	9	3.3
Cumulative count to each time point	*n* $n = 268$	%	*n* $n = 279$	%	*n* $n = 285$	%
Symptoms reported (cumulative)‡						
Any	95	35.5	138	49.5	156	54.7
None	173	64.5	141	50.5	129	45.3
Worst severity reported						
Minor/insignificant	39	41.1	55	39.9	65	41.7
Moderate	29	30.5	45	32.6	49	31.4
Major/severe	27	28.4	38	27.5	42	26.9
Readmission and/or representation to ED						
Yes	29	10.8	43	15.4	52	18.2
No	239	89.2	236	84.6	233	81.8
GP or outpatient review						
Yes, GP	20	7.5	56	20.1	87	30.5
Yes, OPD	0	0.0	4	1.4	14	4.9
No	248	92.5	219	78.5	184	64.6
Patient satisfaction						
Patient satisfaction (numerical rating and IQR)						
All patients ($n = 271$)					10 (8–10)	

GP, general practitioner; OPD, outpatient department. †Does not include symptoms directly related to the area of cellulitis (erythema, warmth, swelling and pain). ‡Some patients reported multiple symptoms.

erythema or swelling at day 14 despite reporting cellulitis cure, which likely represents a residual inflammatory response. Skin warmth is the symptom that responds to treatment the earliest and is most often absent in patients reporting resolution. This suggests that warmth could be a more appropriate indicator of treatment response. Patients are less likely than clinicians to deem their cellulitis resolved at day 14, which highlights an important opportunity to inform conversations between patients and clinicians about the expected trajectory of cellulitis. Future studies should both address the discrepancy between clinician and patient understanding.

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Author contributions

NE and GK conceived the study. RN, NE and GK were involved in the study design. RN, GK, AS, RP and PS obtained research funding. RN and WD undertook recruitment of patients. RN and GS completed follow-up of the patients. AS provided statistical advice and analysed the data. RN drafted the article. GK, KY, RP and PS substantially contributed to revisions. RN takes overall responsibility for the paper.

All authors attest to meeting the four ICMJE.org authorship criteria: (1) substantial contributions to the conception or design of the work; or the acquisition, analysis or interpretation of data for the work; (2) drafting the work or revising it critically for important intellectual content; (3) final approval of the version to be published; and (4) agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Competing interests

RN, NE, AS, GS, WD, RP, PS, KY, report no conflict of interest. GK is a section editor for Emergency Medicine Australasia. He was not involved in any decision during the peer review process.

References

1. Raff AB, Kroshinsky D. Cellulitis: a review. *JAMA* 2016; **316**: 325–37. https://doi.org/10.1001/jama.2016.8825
2. Humphreys I, Akbari A, Griffiths R *et al*. Evaluating the cost of managing patients with cellulitis in Wales, UK: a 20-year population-scale study. *Int. Wound J*. 2023; **20**: 1–12. https://doi.org/10.1111/iwj.14088
3. Bernard P, Chosidow O, Vaillant L. Oral pristinamycin versus standard penicillin regimen to treat erysipelas in adults: randomised, non-inferiority, open trial. *BMJ* 2002; **325**: 864.
4. Clarke MC, Cheng AC, Pollard JG *et al*. Lessons learned from a randomized controlled trial of short-course intravenous antibiotic therapy for erysipelas and cellulitis of the lower limb (switch trial). *Infect. Dis*. 2019; **6**: ofz335. https://doi.org/10.1093/ofid/ofz335
5. Cranendonk DR, Opmeer BC, van Agtmael MA *et al*. Antibiotic treatment for 6 days versus 12 days in patients with severe cellulitis: a multicentre randomized, double-blind, placebo-controlled, non-inferiority trial. *Clin. Microbiol. Infect*. 2020; **26**: 606–12. https://doi.org/10.1016/j.cmi.2019.09.019
6. Moran GJ, Krishnadasan A, Mower WR *et al*. Effect of cephalexin plus trimethoprim-sulfamethoxazole vs cephalexin alone on clinical cure of uncomplicated cellulitis: a randomized clinical trial. *JAMA* 2017; **317**: 2088–96. https://doi.org/10.1001/jama.2017.5653
7. Yadav K, Krzyzaniak N, Alexander C *et al*. The impact of antibiotics on clinical response over time in uncomplicated cellulitis: a systematic review and meta-analysis. *Infection* 2022; **50**: 859–71. https://doi.org/10.1007/s15010-022-01842-7
8. Yadav K, Nath A, Suh KN, Sikora L, Eagles D. Treatment failure definitions for non-purulent skin and soft tissue infections: a systematic review. *Infection* 2020; **48**: 75–83. https://doi.org/10.1007/s15010-019-01347-w
9. Smith E, Patel M, Thomas KS. Which outcomes are reported in cellulitis trials? Results of a review of outcomes included in cellulitis trials and a patient priority setting survey. *Br. J. Dermatol*. 2018; **178**: 1028–34. https://doi.org/10.1111/bjd.16235
10. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. STROBE initiative. The strengthening the reporting of observational studies in epidemiology (STROBE)statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008; **61**: 344–9.
11. The British Pain Society. *Outcome Measures*. [Cited January 2019.] Available from URL: https://www.britishpainsociety.org/static/uploads/resources/files/Outcome_Measures_January_2019.pdf
12. Hepburn MJ, Dooley DP, Skidmore PJ, Ellis MW, Starnes WF, Hasewinkle WC. Comparison of short-course (5 days) and standard (10 days) treatment for uncomplicated cellulitis. *Arch. Intern. Med*. 2004; **164**: 1669–74. https://doi.org/10.1001/archinte.164.15.1669
13. Bruun T, Oppegaard O, Hufthammer KO, Langeland N, Skrede S. Early response in cellulitis: a prospective study of dynamics and predictors. *Clin Infect Dis* 2016; **63**: 1034–41. https://doi.org/10.1093/cid/ciw463
14. Sukumaran V, Senanayake S. Bacterial skin and soft tissue infections. *Aust Prescr* 2016; **39**: 159–63. https://doi.org/10.18773/austprescr.2016.058
15. Therapeutic Guidelines Limited. *Cellulitis and Erysipelas*. [Cited 2019.]. Available from URL: https://tgldcdp.tg.org.au/viewTopic?etgAccess=true&guidelinePage=Antibiotic&topicfile=cellulitis-erysipelas
16. Carter K, Kilburn S, Featherstone P. Cellulitis and

treatment: a qualitative study of experiences. *Br. J. Nurs.* 2007; **16**: S22–4, S26-8. https://doi.org/10.12968/bjon.2007.16.Sup1.27089
17. U.S. Department of Health and Human Services, Food and Drug Administration, Centre for Drug Evaluation and Research (CDER). *Guidance for Industry. Acute Bacterial Skin and Skin Structure Infections: Developing Drugs for Treatment*. [Cited October 2013.] Available from URL: https://www.fda.gov/media/71052/download
18. Kilburn SA, Featherstone P, Higgins B *et al.* Interventions for cellulitis and erysipelas. *Cochrane Database Syst. Rev.* 2010; **6**: CD004299.
19. Hamill LM, Thi Y-CE, Keijzers G. Picking the low-hanging fruit: why not choose oral antibiotics for skin and soft-tissue infections in the emergency department. *Emerg. Med. Australas.* 2019; **31**: 1119–22. https://doi.org/10.1111/1742-6723.13383
20. Zetts RM, Garcia AM, Doctor JN, Gerber JS, Linder JA, Hyun DY. Primary care physicians' attitudes and perceptions towards antibiotic resistance and antibiotic stewardship: a national survey. *Open Forum Infectious Diseases* 2020; **7**: ofaa244. https://doi.org/10.1093/ofid/ofaa244
21. Dong SL, Kelly KD, Oland RC, Holroyd BR, Rowe BH. ED management of cellulitis: a review of five urban centers. *Am. J. Emerg. Med.* 2001; **19**: 535–40. https://doi.org/10.1053/ajem.2001.28330
22. Quirke M, Saunders J, O'Sullivan R, Wakai A. The management of cellulitis in emergency departments: antibiotic-prescribing practices and adherence to practice guidelines in Ireland. *Eur. J. Emerg. Med.* 2016; **23**: 173–8. https://doi.org/10.1097/MEJ.0000000000000245
23. Donald M, Marlow N, Swinburn E, Wu M. Emergency department management of home intravenous antibiotic therapy for cellulitis. *Emerg. Med. J.* 2005; **22**: 715–7. https://doi.org/10.1136/emj.2004.018143
24. Murray H, Stiell I, Wells G. Treatment failure in emergency department patients with cellulitis. *CJEM* 2005; **7**: 228–34. https://doi.org/10.1017/s1481803500014342
25. Cutler TS, Jannat-Khah DP, Kam B, Mages KC, Evans AT. Prevalence of misdiagnosis of cellulitis: a systematic review and meta-analysis. *J. Hosp. Med.* 2022; **18**: 1–8. https://doi.org/10.1002/jhm.12977

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