ORIGINAL REPORT

Reported Penicillin Allergy Affects the Length of Hospital Stay in Patients with Erysipelas

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Patients with a reported penicillin allergy are often treated with less effective antibiotics. This study examined the impact of anamnestic penicillin allergy on the length of hospital stay in patients with erysipelas, a condition for which penicillin is considered the first-line therapy and addresses the question: Does anamnestic penicillin allergy directly affect the length of hospital stay in patients with erysipelas? This retrospective analysis included patients who were admitted to the University Medical Center Regensburg for the treatment of erysipelas. The data analysed were sex, age at diagnosis, body temperature at admission, C-reactive protein, leucocyte count, procalcitonin, length of hospital stay, Charlson Comorbidity Index and antibiotic therapy. Patients were divided into 2 groups: with and without the label anamnestic penicillin allergy. Multiple regression analysis showed that patients with anamnestic penicillin allergy stayed 1.83 days longer in hospital than patients without anamnestic penicillin allergy (mean length of stay 12.17±7.01 days for patients with anamnestic penicillin allergy compared to 10.34±4.80 days for patients without anamnestic penicillin allergy, as determined by a *t*-test *p*=0.046). According to our data, anamnestic penicillin allergy is associated with prolonged hospital stay. Therefore, delabelling of penicillin allergy should be widely implemented.

Key words: erysipelas; penicillin; drug hypersensitivity; hospitalization.

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SIGNIFICANCE

Erysipelas is a common infectious disease of the skin and penicillin is considered the first-line antibiotic treatment. Of 10 patients, 1 patient reports being allergic to penicillin and therefore is treated with alternative antibiotics. This allergy label is often based on past reports and has not been thoroughly verified. We analysed patients treated for erysipelas and compared those with a reported penicillin allergy to those without such a label. Patients who reported a penicillin allergy stayed in hospital 2 days longer than patients without such a report. These findings suggest that carrying a penicillin allergy label may negatively affect treatment outcomes.

Erysipelas is a common dermatological diagnosis, with an incidence rate ranging from 113 to 249 cases per 100,000 people (1, 2). It is an acute onset, bacterial infection of the skin and superficial and deep lymphatics that is most commonly caused by beta-hemolytic streptococci group A (*Streptococcus pyogenes*). Erysipelas most commonly presents unilaterally on the lower extremities and is characterized by acute, well-demarcated erythema and systemic inflammatory symptoms such as fever and chills (3, 4). In Germany and Austria, most dermatological departments treat patients with erysipelas on an inpatient basis with intravenous antibiotics (5). According to the current guidelines, hospitalization is recommended for patients presenting with signs of systemic inflammation, suspicion of a deeper or necrotizing infection or infection involving a critical location (e.g. the hands or face). Hospitalization is also recommended in cases of severe immunosuppression or comorbidities, treatment failure under outpatient management or lack of adherence to the therapy (4, 5).

Current German guidelines recommend intravenous benzylpenicillin (penicillin G) as a first-line treatment for hospitalized patients (4). The duration of antibiotic therapy ranges from 5 to 10 days (4, 5). Sequential oral antibiotic treatment with penicillin V may also be considered (4). Patients with penicillin allergy should receive clindamycin or, if there is a contraindication, vancomycin or macrolides (4).

A systematic review and meta-analysis published in 2025 (6) found that the global prevalence of adult patients labelled with penicillin allergy was 9.4%, with an even higher prevalence among hospitalized and older patients in high-income countries (7). The data suggest that over 94% of patients with anamnestic penicillin allergy tolerate the administration of penicillin-based

antibiotics without an adverse reaction (8) and that only fewer than 5% show a clinically significant penicillin hypersensitivity mediated by immunoglobulin E (IgE) or T lymphocytes (7). A misrepresented but documented penicillin allergy can lead to the use of more expensive, broad-spectrum, non-ß-lactam antibiotics, which may result in an increased number of adverse events and antibiotic resistance, as well as increased healthcare costs (9, 10). A penicillin allergy label affects the length of hospital stay (11). It is recommended that patients with anamnestic penicillin allergy be evaluated to identify those at low risk for allergic reactions by performing provocation testing with penicillin (12–15).

This study examined whether anamnestic penicillin allergy affects the length of hospital stays for inpatients with erysipelas.

MATERIALS AND METHODS

Ethical approval

An ethics approval for the study was obtained from the Ethics Committee of the University of Regensburg (Ethic approval by the University Regensburg 24-3779-104, 29 May 2024). Consent for publication of the presented photographs has been obtained from the patients.

Patient data collection

The data were obtained from the discharge letters in the hospital's database. The data were extracted from the i.s.h.med software (Cerner Corporation, North Kansas City, MO, USA, run via SAP 6.0 software, SAP SE, Walldorf, Germany), the hospital management software used in our hospital. Patients were identified by their ICD-10 diagnosis code (A46), and the diagnoses were verified by reviewing their discharge letter. To ensure the best possible comparability, only cases of erysipelas of the lower extremities were included in this study. For the analysis, we selected all inpatient clinical cases diagnosed with erysipelas from 2010 to 2024 that had a recorded history of anamnestic penicillin allergy (n=125). After screening, 44 cases had to be excluded due to duplication or a body location other than the lower extremities. Key patient characteristics (sex, date of birth and dates of admission and discharge) were systematically recorded and used to calculate the patient's age at the time of hospital treatment and the length of hospital stay. The laboratory data extracted included levels of c-reactive protein (CRP), procalcitonin (PCT), leucocytes, creatinine, bilirubin, alanine aminotransferase (ALT) and international normalized ratio (INR). Based on the diagnosis stated in the discharge letter, the Charlson Comorbiditiy Index (CCI), a score that measures the 10-year survival probability based on 17 diseases, was calculated and documented (16). Additionally, we extracted data on transfers to the intensive care unit (ICU) and the Department of Internal Medicine during the hospital stay. We recorded the type and duration of antibiotic treatment and the continuation of oral antibiotic treatment after discharge. The body temperature taken at hospital admission was obtained from the discharge letter. For each patient case, one photograph of erysipelas taken on the day of admission and during hospitalization was randomly selected and saved.

To investigate the impact of anamnestic penicillin allergy, data were extracted from 103 most recent inpatient clinical cases without anamnestic penicillin allergy.

Investigator score for erysipelas photos

Photos of erysipelas taken on the day of admission were scored by 3 experienced, board-certified dermatologists (K. D., S. K., and J. K.). Anonymized photos were sorted randomly, and the reviewers were blinded to the patient's characteristics. Since there is no standardized scoring system for assessing the severity of erysipelas, a clinical score was established as follows: 0=no erysipelas; 1=bright erythema, measuring no more than 20 cm², no significant edema; 2=obscure erythema, measuring more than 20 cm² or erythema with significant edema; 3=bullous and/or haemorrhagic erysipelas or erythema passing joint (**Fig. 1**). A total of n=50 photos were scored.

Statistical analysis

The sample size was estimated in consultation with the Center for Clinical Studies. Statistical analysis was performed using IBM SPSS version 25 (Armonk, NY, USA). A Student t-test was used to compare the length of hospital stay between patients with and without anamnestic penicillin allergy. Multiple regression analysis was performed to evaluate the impact of clinical variables (e.g. age at diagnosis, body temperature, erysipelas scoring by photos and levels of laboratory counts, including CRP and PCT) and the range of comorbid conditions using the 10-year mortality prediction score CCI. Results were considered statistically significant at $p<0.05$.

RESULTS

Group characteristics

Eighty-one patients diagnosed with erysipelas of the lower extremities and with anamnestic penicillin allergy between 2010 and 2024 were included in the study. These patients were compared with 103 patients who had been diagnosed with erysipelas of the lower extremities but who did not have anamnestic penicillin

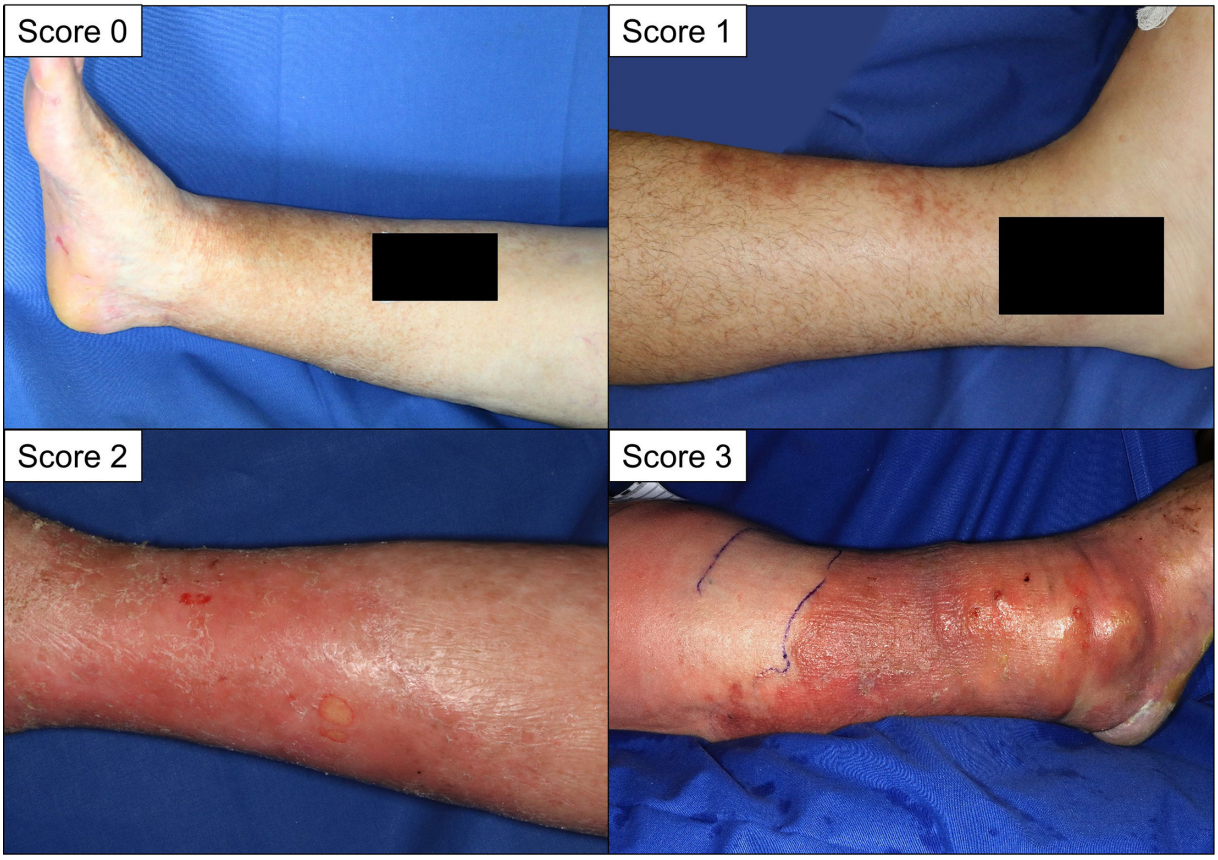

Fig. 1. Example pictures of erysipelas. Scoring was done by following criteria: 0=no erysipelas; 1=bright erythema, measuring no more than 20 cm², no significant edema; 2=obscure erythema, measuring more than 20 cm² or erythema with significant edema; 3=bullous and/or haemorrhagic erysipelas or erythema passing joint.

allergy. The clinical variables of the 2 study cohorts are presented in **Table I**.

The anamnestic penicillin allergy group had a higher proportion of female patients (53.1%) than the no-penicillin allergy group (44.7%), which had a higher proportion of male patients. The age at diagnosis differed between patients with and without anamnestic penicillin allergy by around 7 years. Leucocyte counts at hospital admission differed marginally (12.51±5.43 /nL vs 12.70±5.49 /nL) as well as PCT counts, see Table I; there was no statistically significant difference between the 2 groups (p=0.810 for leucocyte counts and p=0.815 for PCT).

CRP levels were significantly higher in the no-penicillin allergy group (124.51±99.78 mg/L vs 83.45±83.51 mg/L, p=0.003). CCI scores were higher in the group without anamnestic penicillin allergy (3.5±2.60 vs 2.72±2.39, p=0.038). Temperature at admission did not significantly differ between the 2 groups, with an overall mean temperature of 37.45°C.

Table I. Clinical characteristics of all included patients. Leucocyte count, procalcitonin and C-reactive protein were measured on the day of hospital admission

	Penicillin allergy	No penicillin allergy
Sex	female=43, male=38	female=46, male=57
Age at diagnosis [y]	57.8 (±14,3)	65.3 (±16,4)
Leucocyte count [/nl]	12.70 (±5.49)	12.51 (±5.43)
PCT [ng/mL]	1.44 (±4.18)	1.61 (±3.79)
CRP [mg/L]	83.45 (±83.51)	124.51 (±99.78)
Charlson comorbidity index	2.72 (±2.39)	3.50 (±2.60)
Temperature at admission [°C]	37.47 (±0.97)	37.44 (±0.87)

Antibiotic treatment and transfers

All antibiotic treatments were given intravenously. In the group without anamnestic penicillin allergy, benzylpenicillin was administered as monotherapy in 49.5% of patients, 10.7% were treated with clindamycin and 35.9% were treated with a combination of benzylpenicillin and clindamycin. Only 4 patients (3.9%) received other antibiotics. In 24.3% of patients, the antibiotic treatment was changed during the hospital stay. In 27.2% of patients, further oral antibiotic treatment after discharge was recommended.

In the group of patients with anamnestic penicillin allergy, 69.1% received clindamycin, whereas 29.6% of patients were treated with antibiotic drugs other than penicillin or penicillin derivatives, primarily ceftriaxone (9.9%) and meropenem (4.9%). A treatment with moxifloxacin, clarithromycin or vancomycin was administered to 2 patients (2.5%) each. Only one patient received a combination of antibiotics (clindamycin and meropenem). In 23.5% of patients, the antibiotic

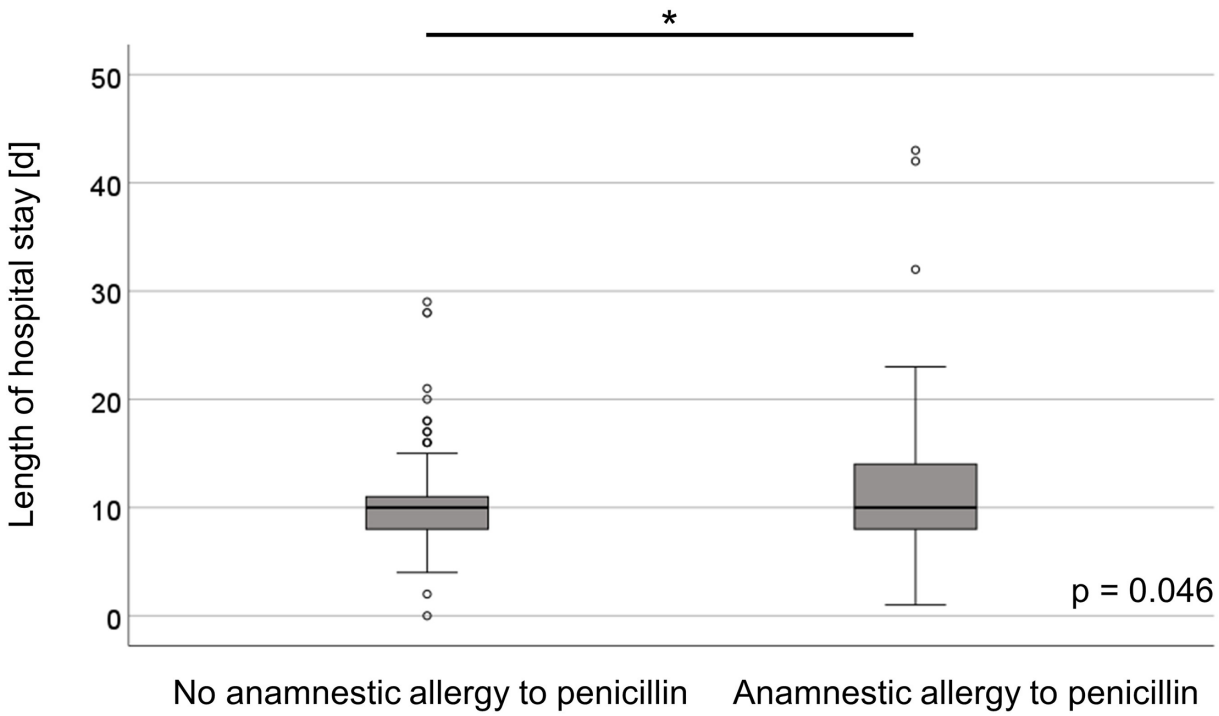

Fig. 2. Boxplot diagram showing the differences in the length of hospital stay in correlation with the presence of an anamnestic penicillin allergy.

regimen was changed during the hospital stay. Oral antibiotic treatment after discharge was recommended for 37.0% of patients. Four patients (4.9%) were transferred to an internal medicine ward, while 2 patients (2.5%) were admitted to the intensive care unit.

One patient in each of the compared groups died during the hospital stay for reasons other than erysipelas or its complications (one with RSV pneumonia, one with acute-on-chronic kidney failure).

Length of hospital stay

The mean length of hospital stay was 11.15 days and differed significantly between the anamnestic penicillin allergy group (12.17±7.01 days) and the no-anamnestic penicillin group (10.34±4.80 days) (*t*-test: p=0.046; **Fig. 2**). These differences in the length of hospital stays remained statistically significant in the multiple linear regression analysis when potential confounders such as first-line antibiotic treatment, CRP, CCI, age at diagnosis and sex were included (p=0.016, regression coefficient 2.224; **Table II**). However, no significant effect on the length of hospital stay was seen for the parameters first-line antibiotic treatment, CRP, CCI, age at diagnosis or sex. Interestingly, no statistically significant difference in the length of hospital stay was observed between 51 patients treated with benzylpenicillin (9.38±4.6 days) and 67 patients treated with clindamycin (11.27±7.2 days; p=0.102). Also, 37 patients treated with a combination of benzylpenicillin and clindamycin (12.37±5.2 days) showed no significant difference in the length of hospital stay compared to patients receiving clindamycin or benzylpenicillin alone.

Investigator score for erysipelas photos

Fourteen photos of erysipelas from patients with anamnestic penicillin allergy and 36 photos of patients without anamnestic penicillin allergy were included. Interrater Reliability Fleiss Kappa was 0.399, fair. There was no statistically significant difference in the median severity score of erysipelas at admission between the 2 groups (p=0.838). There was no grade 0 (no visible erysipelas) in either group: 5.6% of patients without penicillin allergy vs 7.1% of patients with anamnestic penicillin allergy had grade 1 erysipelas, 50.0% vs 42.9% had grade 2 erysipelas, and 44.4% vs 50.0% had grade 3 erysipelas. There was no significant difference in the length of hospital stays between grade 1 and grade 2 erysipelas, or between grade 2 and

Table II. Multiple regression analysis showed a correlation between the length of hospital stay and anamnestic penicillin allergy

Category	Unstandardized coefficients		
	B	Std. error	*p*
Anamnestic penicillin allergy	2.224	0.915	0.016
Age at diagnosis	−0.016	0.039	0.686
First-line antibiotic treatment	0.791	0.404	0.052
Charlson Comorbidity Index	0.427	0.234	0.070
Sex	0.359	0.900	0.691
CRP at diagnosis	0.006	0.005	0.182

grade 3 erysipelas, as determined by a *t*-test (p=0.188, p=0.086). However, there was a statistically significant difference in the length of hospital stays between grade 1 and grade 3 erysipelas, as determined by a *t*-test (p=0.043). No significant associations were observed when comparing the median grading of erysipelas with body temperature or CRP at admission (data not shown). Due to the limited number of follow-up photographs available, the investigator score could not be used to evaluate the clinical course.

DISCUSSION

The main objective of this study was to examine potential correlations between the length of hospital stays and anamnestic penicillin allergy in patients with erysipelas of the lower extremities who had been treated as inpatients at the Department of Dermatology of the University Medical Center Regensburg in Germany. Our dataset showed a significantly longer hospital stay for patients with anamnestic penicillin allergy (mean difference of 1.83 days), which can have an impact on clinical risks and treatment costs (17). This effect persisted after adjustment for age, sex, CRP levels, first-line antibiotic treatment and comorbidities using the CCI. There was no difference between the groups in the investigator score for erysipelas photos, indicating that the clinical presentation was unlikely to represent a source of bias. In comparison, large cohort studies and matched cohort studies have shown an increased length of hospital stay of 5–10% (18, 19) in patients with a penicillin allergy label compared to patients without such a label, whereas the increase observed in our cohort was 17.7%. As patients were enrolled over a 14-year period many different clinicians were involved in their treatment, we do not believe that clinician-related bias had a significant influence. The increased length of stay may be attributable to treatment with a significantly higher number of antibiotics, as well as antibiotics with a broader spectrum. These antibiotics are associated with a lower effectiveness in treating certain infections, as well as adverse events, Clostridium difficile infection and drug-resistant organisms (7, 19). Nevertheless, we did not find a statistically significant impact of the antibiotic regimens used on the length of hospital stays. However, a trend toward longer hospital stays could be observed in patients not treated with penicillin (p=0.052). A larger sample may be needed to clarify this issue.

Approximately 10% of patients are reported to have anamnestic penicillin allergy; however, a true allergy is present in fewer than 10% of patients labeled as such (7, 20). It is challenging to delabel anamnestic penicillin allergy, as IgE antibodies against penicillin are lost in about 80% of patients within 10 years (20). Patients with a label are denied the benefits of penicillin or even ß-lactam therapy and are treated with more expensive or less effective drugs that may lead to adverse consequences (20). Thus, patients with anamnestic penicillin allergy should undergo careful clinical evaluation to identify individuals at low risk for true allergy who may be eligible for penicillin treatment. Using the PEN-FAST score among others, which helps to establish a real penicillin allergy, may aid decision-making for risk evaluation (14). In our cohort, all patients with erysipelas and anamnestic penicillin allergy received antibiotic treatment other than penicillin or penicillin derivatives. The occurrence of adverse events such as death or transfer to the intensive care unit was not statistically significant. Our study lacks data on other complications associated with different antibiotic drug regimens, a topic that could be addressed in future studies. There might be an impact on the comparability of data, though data are lacking for penicillin allergy labels for specific infection types. To our knowledge, this is the first study with an erysipelas cohort. A meta-analysis of erysipelas showed a similar efficacy and incidence of adverse effects for treatment with macrolides or lincosamides compared with ß-lactam antibiotics (21). Our study showed no significant effect on the length of hospital stays in association with antibiotic treatment. Among other factors, clinical skin findings are an important aspect in deciding on the duration of antibiotic therapy for erysipelas. In our study, we addressed the clinical development of the skin findings to evaluate their impact on the length of hospital stays. Due to the retrospective design of the study, we unfortunately lacked photographs of the clinical development for most of our patients. However, we observed comparable clinical development in both groups in the few cases that could be evaluated.

Studies on delabeling patients with anamnestic penicillin allergy have shown a reduction in excess bed days and costs, emphasizing the importance of allergy assessment in hospitals (18, 22). Further investigations and prospective studies are needed to clarify whether a longer hospital stay is associated with anamnestic allergy in all types of infectious diseases. As penicillin is a well-tolerated, economical and very effective antibiotic drug, it should be used as the first-line treatment when indicated. In our study, 85.4% of patients without anamnestic penicillin allergy were treated with penicillin. Although not significant, we observed a trend of shorter hospital stays for patients treated with penicillin. Physicians should not switch to another antibiotic drug without further evaluating the presence of a real anamnestic penicillin allergy.

Penicillin allergy labels are common, but there is a lack of data on specific types of infection. To our knowledge, this is the first study to show a statistically significant correlation between anamnestic penicillin

allergy and the length of hospital stays among patients with erysipelas of the lower extremities. Delabeling is relevant for the clinical course, healthcare system costs and the prevention of multidrug resistance.

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Data availability statement: The dataset used for this study is not public but available from the corresponding author upon reasonable request.

Ethics declarations: An ethics approval for the study was obtained from the Ethics Committee of the University of Regensburg (Ethic approval by the University Regensburg 24-3779-104, 29 May 2024). Consent for publication of the presented photographs has been obtained from the patients.

Disclosure: Conceptualization: A.S., N.S., F.H., S.K., K.D.; Data curation: A.S. J.K., S.K., K.D.; Formal analysis: A.S., K.D.; Funding acquisition: K.D.; Investigagion: A.S., J.K., S.K., K.D.; Methodology: A.S., J.K., F.H., S.K., K.D.; Project administration: K.D.; Resources: A.S., K.D.; Software: K.D.; Supervision: S.K., K.D.; Validation: A.S., K.D.; Visualization: A.S., K.D.; Wirting – orginal draft: A.S., N.S.; Writing – review & editing: J.K., F.H., S.K., K.D.

The authors have no conflicts of interest to declare.

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