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An outbreak of multi-drug-resistant *Acinetobacter baumannii* on a burns ICU and its control with multi-faceted containment measures

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SUMMARY

Background: Patients in burns centres are at high risk of acquiring multi-drug-resistant organisms (MDROs) due to the reduced skin barrier and long hospital stay.
Methods: This study reports the investigation and control of an outbreak of MDR *Acinetobacter baumannii* in a burns centre. The 27 patients hospitalized in the centre during the outbreak were screened regularly, and a total of 132 environmental samples were analysed to identify a potential source. Fourier-transform infra-red (FT-IR) spectroscopy and multi-locus sequence typing were applied to characterize the outbreak strain.
Results: Between August and November 2022, the outbreak affected eight patients, with 11 infections and three potentially related fatal outcomes. An interdisciplinary and multi-professional outbreak team implemented a bundle strategy with repetitive admission stops, isolation precaution measures, patient screenings, enhanced cleaning and disinfection, and staff education. FT-IR spectroscopy suggested that the outbreak started from a patient who had been repatriated 1 month previously from a country with high prevalence of MDR *A. baumannii*. Environmental sampling did not identify a common source. Acquisition of the outbreak strain was associated with a higher percentage of body surface area with burn lesions ≥2a [per percent increase: odds ratio (OR) 1.05, 95% confidence interval (CI) 0.99–1.12; *P*=0.09], and inversely associated with a higher nurse-to-patient ratio (per 0.1 increase: OR 0.34, 95% CI 0.10–1.12; *P*=0.06).
Conclusions: Burn patients with a higher percentage of body surface area with burn lesions ≥2a are at high risk of colonization and infection due to MDROs, particularly during periods of high workload. A multi-faceted containment strategy can successfully control outbreaks due to MDR *A. baumannii* in a burns centre.

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Background

Critically ill burn patients are at high risk of healthcare-associated infections [1,2]. Long-term hospitalization in intensive care, invasive life support and skin wounds represent critical risks and ports of entry for pathogens [3]. During recovery, burn patients often require repetitive courses of antibiotic therapy that act as an important driver for selection of multi-drug-resistant organisms (MDROs). These characteristics increase the risk of patient colonization with subsequent difficult-to-treat infections due to non-fermenting bacteria such as multi-drug-resistant (MDR) *Acinetobacter baumannii* [4–6]. Repatriated patients from countries with a high prevalence of MDROs are often colonized with such pathogens [7,8]. Most healthcare institutions screen repatriated patients, and implement contact isolation precaution measures while the results are pending. However, breaches in the implementation of isolation precaution measures allow pathogens to be transferred to other patients. In accordance with the ORION recommendations for outbreak reporting [9], this paper describes an outbreak due to MDR *A. baumannii* in a burns centre, and analyses the risk factors for transmission.

Methods

Setting

The outbreak occurred at University Hospital Zurich (USZ), Switzerland, a 941-bed tertiary care hospital with approximately 40,000 admissions per year. The burns centre at USZ is one of two national centres. The centre includes an intensive care unit (ICU) with eight single patient rooms, and three operating theatres for hydrotherapy and surgical interventions.

Case definition

All patients with at least one isolate of the outbreak strain, either in a clinical or a screening sample, were considered as potential cases. The outbreak strain was phenotypically resistant to all routinely tested antibiotics, including piperacillin/tazobactam, ceftazidime, cefepime, imipenem, meropenem, gentamicin, tobramycin, ciprofloxacin and levofloxacin. All isolates were susceptible to colistin, eravacyclin (according to the European Committee on Antimicrobial Susceptibility Testing [10], *Escherichia coli* is considered the reference micro-organism for eravacyclin) and cefiderocol (according to the Clinical and Laboratory Standards Institute [11]). Clonality was examined by Fourier-transform infra-red (FT-IR) spectroscopy and multi-locus sequence typing (MLST).

Patient and nursing characteristics

Microbiological analyses were performed by two different laboratories: the Institute of Medical Microbiology of the University of Zurich; and the Laboratory of the Department of Hospital Epidemiology at USZ. Patient data included age, sex, degree and surface area of burn wounds, length of stay in the burns centre, in-hospital mortality, and information on colonization and infection by the outbreak strain. For individuals suffering from an infection, information on the site of infection was collected. Treatment data included number of upper endoscopies, bronchoscopies and operative procedures. Ward data included work schedules of nurses and bed occupancies of the burns centre in order to calculate weekly mean nurse-to-patient ratios.

Risk factor analysis for acquisition of the outbreak strain

Risk factors for acquisition of the outbreak strain were calculated using univariable logistic regression, and clonal outbreak strains alone were analysed. Patient characteristics included gender, age, and the percentage of body surface area with burn lesions ≥2a [12]. Treatment exposures included the number of bronchoscopies, the number of upper gastrointestinal endoscopies, and the number of operative procedures prior to first detection of the outbreak strain or ward discharge in non-affected patients. Staff workload was tested by modelling nurse-to-patient ratios. As screenings were scheduled once weekly, the nurse-to-patient ratio of the week preceding the first detection of the outbreak strain in patients with acquisition of the outbreak strain were considered, whereas the nurse-to-patient ratio of the latest week prior to transfer from the burns ICU in patients without acquisition of the outbreak strain were considered.

Patient screening

From 12th August to 21st November 2022, ward screenings were scheduled weekly. Each screening included a respiratory specimen (tracheobronchial secretions), groin swabs, rectal swabs, urine cultures in patients with a urinary catheter, and wound swabs in patients with wounds. Patients hospitalized on general wards but who received hydrotherapy or surgical interventions in the burns centre were also screened as described.

Environmental sampling

Environmental samples included high-touch surfaces in the patient zone (e.g. respirators, monitors), shared areas (e.g. medication preparation area, storage), medical devices (e.g. endoscopes, ultrasound devices, blood gas analyser), and sinks in the burns centre as well as in the resuscitation room of the emergency department. For environmental samples collected from surfaces, swabs (eSwab, Copan, Brescia, Italy) were used and put into Amies medium after sampling. Air was collected in patient rooms and the operating theatres of the burns centre (MAS-100 NT, MBV, Staefa, Switzerland; running for 5 min at a rate of 100 L/min, Columbia agar with 5% sheep blood). Surfaces that were considered as potentially relevant for pathogen transmission were sampled repetitively to minimize falsenegative results. Environmental samples were analysed in the Laboratory of the Department of Hospital Epidemiology at USZ.

Molecular characterization

Typing of *A. baumannii* isolates was performed in two steps by FT-IR spectroscopy and MLST. Samples for FT–IR analysis were prepared as reported previously [13]. Spectra in the wavenumber range for carbohydrates (1300–800/cm) were acquired, visualized and processed by IR-Biotyper Version 4.0.3.7334 (Bruker Daltonics GmbH & Co. KG, Bremen, Germany) and OPUS Version 8.2.28 (Bruker Optik GmbH, Leipzig, Germany) using Euclidean distance, unweighted pair group method with arithmetic mean and the dimension reduction method PCA 0.95/20. MLST was performed in isolates that were considered identical by FT-IR spectroscopy, as reported previously [13]. Average nucleotide identity (ANI) values were calculated with the Kostas Lab (Atlanta, GA, USA) ANI calculator [14]. This publication made use of the PubMLST website (https://pubmlst.org/) developed by Jolley and sited at the University of Oxford [15].

Outbreak control measures

Table I summarizes the outbreak management measures. An interdisciplinary and multi-professional outbreak team was established with staff from infection prevention and control, the burns centre and anaesthesiology. Patients colonized and/or infected with the outbreak strain received contact isolation precaution measures and 'dedicated nursing'. Colonized and non-colonized patients were separated spatially in the burns centre and treated in different hydrotherapy rooms. A stop on admissions was issued for non-burn patients. Weekly screening of non-colonized/infected patients was scheduled for patients on the burns centre. Contact isolation precautions were maintained after transfer to other wards, and until there had been three repetitive negative screening tests for the outbreak strain. The infection prevention and control team performed observations of daily routine, and regular meetings were scheduled with the staff. Consumption of alcohol-based hand rub was monitored. High-touch surfaces in the patient zone were disinfected three times per day, and patient room floors were disinfected twice per day. After discharge, patient rooms were manually disinfected twice, followed by an enhanced environmental disinfection method, either ultraviolet-C (UV–C) radiation or hydrogen peroxide vaporization. Shared spaces were manually disinfected twice daily, and subjected to enhanced environmental disinfection twice during the outbreak period. In Calendar Week 47, after all patients had been transferred to other wards, enhanced environmental disinfection of the entire burns centre was performed using vaporized hydrogen peroxide.

Ethical approval

Zurich Cantonal Ethics Commission (Req-2022-01351) waived the need for a formal ethical evaluation based on the Swiss law on research on humans.

Results

Course of outbreak

At the beginning of August 2022 (Calendar Week 31), an *A. baumannii* with the same antibiotic resistance pattern as the isolates of two patients who had recently been repatriated from Kosovo and Northern Macedonia was isolated from a patient who had been hospitalized for more than 2 weeks in the burns centre (Figure 1). Prior to August 2022, MDR *A. baumannii* had not been detected in patient samples on the burns ICU for years. Admissions for non-burn patients were stopped, and containment measures and weekly screening of negative patients were established immediately. From Calendar Week 32–35, MDR *A. baumannii* isolates were detected in five additional patients. The stop on admissions was lifted after 3 weeks without any new cases. All other measures, including room treatment with UV-C or vaporized hydrogen peroxide after discharge, remained in place. In Calendar Week 40, the outbreak strain was detected again in one patient, prompting reinforcement of all containment measures including the stop on admissions, which again was lifted 3 weeks later. In Calendar Week 44, the outbreak strain was isolated from two additional patients, and the stop on admissions was re-established. No new cases occurred afterwards, and in Calendar Week 47, all patients with the outbreak strain had been transferred to general wards. The remaining patients of the burns centre were temporarily transferred to other ICUs in the hospital to allow intensified cleaning and enhanced disinfection with

Table I
Containment measures

Assembling an interdisciplinary and multi-professional outbreak team
Stop on admissions for non-burn patients[a]
Contact isolation of colonized and/or infected patients
Spatial separation of colonized and non-colonized patients
Dedicated nursing
Weekly screening of non-colonized patients on the intensive care unit
Observation and review of daily routine by infection control staff
Training and staff education
Encouraging 'speak-up'
Enhanced disinfection (increased frequency, ultraviolet-C, vaporized hydrogen peroxide)
Emptying the burns centre for terminal cleaning
Support from infection prevention and control to regular wards hosting case patients after transfer
Contact isolation and repetitive screening of patients in regular wards receiving treatment in the operating theatre of the burns centre

[a] University Hospital Zurich is one of two national burns centres in Switzerland with a commitment to accept burn patients.

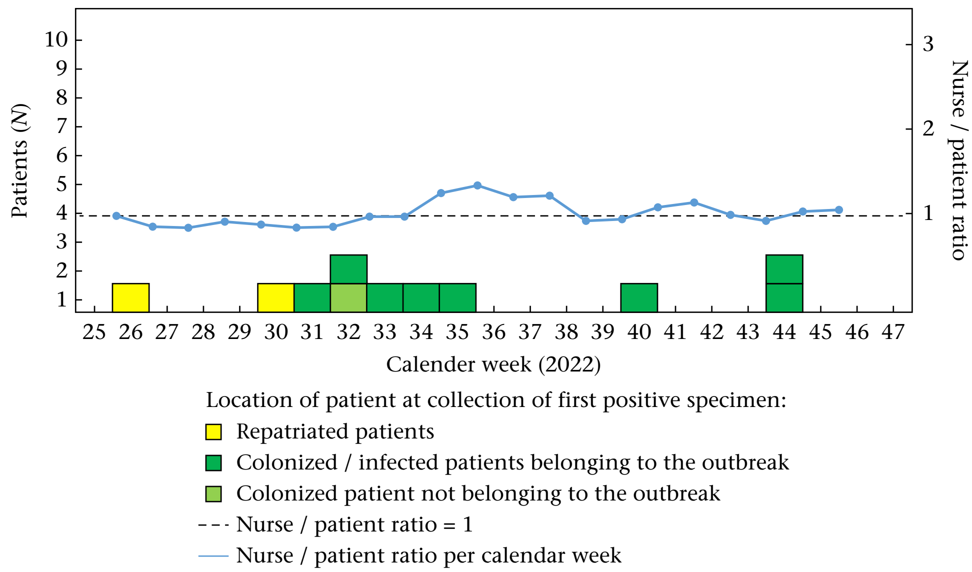

Figure 1. Epicurve of the *Acinetobacter baumannii* outbreak and weekly average nurse-to-patient ratio.

vaporized hydrogen peroxide. The outbreak was declared over in Calendar Week 48. In Calendar Week 52, one additional burn patient on a general ward tested positive for *A. baumannii* with a similar phenotypic antibiotic resistance pattern but without genotypic confirmation. The patient had been hospitalized in the burns centre after Calendar Week 48, where he had three negative screening tests (Calendar Weeks 48–51). At the same time, one case patient was still hospitalized on a general ward, but at a different location. Transmission could not be fully disclosed, but most likely occurred outside the burns centre. No further cases were detected thereafter.

Patient characteristics

Apart from the two repatriated patients, a total of 27 patients were treated in the burns centre during the outbreak period (Table II). The median age was 39.0 years [interquartile range (IQR) 32.5–58.5], eight patients (29.6%) were female, and 21 (77.8%) were burn patients. Nine (42.8%) patients had MDR *A. baumannii*, with four cases of ventilator-associated pneumonia, four wound infections and three bloodstream infections. Two patients had a fatal outcome that was considered to be related to the outbreak strain. All positive patients were burn patients.

Risk factor analysis for acquisition of the A. baumannii *outbreak strain*

In the univariable logistic regression, a higher percentage of body surface area with burn lesions ≥2a tended to be associated with acquisition of the outbreak strain [per percent increase: odds ratio (OR) 1.05, 95% confidence interval (CI)

Table II
Patient characteristics

Variable	Total patients (*N*=27)	Patients colonized/ infected with outbreak strain (*N*=8)[a]	Patients not colonized/ infected with outbreak strain (*N*=18)
Age in years, median (IQR)	39.0 (32.5–58.5)	34.5 (22.5–65.0)	40.0 (35.0–56.0)
Female sex	8 (29.6%)	3 (37.5%)	5 (27.8%)
Burn patient	21 (77.8%)	8 (100%)	12 (66.7%)
Percentage of body surface area with burn lesions ≥2a, median (IQR)	25.5% (17.0–33.5)	29.8% (23.5–37.3)	22.3% (0.0–32.5)
Admission via resuscitation room	21 (77.8%)	8 (100%)	12 (66.7%)
Operations until event or end of ICU stay, median (IQR)	2 (1–4)	2 (2–4)	2 (0–2)

IQR, interquartile range; ICU, intensive care unit.
[a] One patient with multi-drug-resistant *Acinetobacter baumannii* featuring different typing results by Fourier-transform infra-red spectroscopy and multi-locus sequence typing was excluded.

Table III
Risk factor analysis for acquisition of the outbreak-related multidrug-resistant *Acinetobacter baumannii*

Variable	OR (95% CI)	*P*-value
Age (per year increase)	0.99 (0.94–1.04)	0.64
Gender		0.62
Male	Reference	
Female	1.56 (0.24–9.99)	
Percentage of body surface area with burn lesions ≥2a (per percent increase)	1.05 (0.99–1.12)	0.09
Nurse-to-patient ratio (per 0.1 increase)	0.34 (0.10–1.12)	0.06
Number of bronchoscopies[a]	2.31 (0.97–7.94)	0.10
Number of upper gastrointestinal endoscopies[a]	1.18 (0.63–2.22)	0.59
Number of operative procedures[a]	1.19 (0.75–1.90)	0.43

OR, odds ratio; CI, confidence interval.
[a] Prior to first detection of the outbreak strain for patients colonized/infected with the outbreak strain or until discharge from the burns centre.

0.99–1.12; *P*=0.09] (Table III). A higher nurse-to-patient ratio tended to be protective against acquisition of the outbreak strain (per 0.1 increase: OR 0.34, 95% CI 0.10–1.12; *P*=0.06). No significant association was found between *A. baumannii* acquisition and age, gender, number of bronchoscopies, number of upper gastrointestinal endoscopies and number of operative procedures.

Consumption of alcohol-based hand rub

During the outbreak, a significant increase in alcohol-based hand rub consumption was observed (R package 'rateratio.test', *P*<0.001). Mean hand rub consumption was 1355.1 mL/patient-day (95% CI 1352.1–1358.1) during the outbreak period, compared with mean 273.7 mL/patient-day (95% CI 272.8–274.5) during the non-outbreak period in 2022.

Environmental testing

In total, 132 environmental samples were analysed for the outbreak strain (Table S1, see online supplementary material). With the exception of one air sample obtained during a dressing change of a colonized patient, all samples were negative.

Strain typing

Three clusters were identified by FT-IR spectroscopy (Figure 2). The largest cluster included isolates from a patient who had been repatriated in July 2022 and isolates from eight case patients, making this repatriated patient the index case. Notably, one patient (Patient 2) with suspected transmission based on the epidemiological link did not match the outbreak cluster. MLST confirmed the results of FT-IR spectroscopy with the cluster belonging to sequence type 2 (10 cluster-related isolates of sequence type 2, one isolate of sequence type 164). Interestingly, the isolate of the repatriated patient 1 in June 2022 was also sequence type 2. Assessing the average nucleotide identity (ANI) showed ANI values ≤98.04% for the isolate of Patient 2, and in the range of 98.01–99.96% for the isolate of Repatriated Patient 1 compared with the other isolates. Pairwise comparison of ANI values of all other outbreak-related isolates resulted in ANI values ≥99.98%. The differences in ANI values supported the findings from FT-IR spectroscopy that did not support clonality of isolates from Repatriated Patient 1 and outbreak-related isolates.

Discussion

This outbreak of MDR *A. baumannii* in a burns centre was driven by an unfavourable nurse-to-patient ratio. A higher percentage of body surface area with burn lesions ≥2a added to the risk of acquisition.

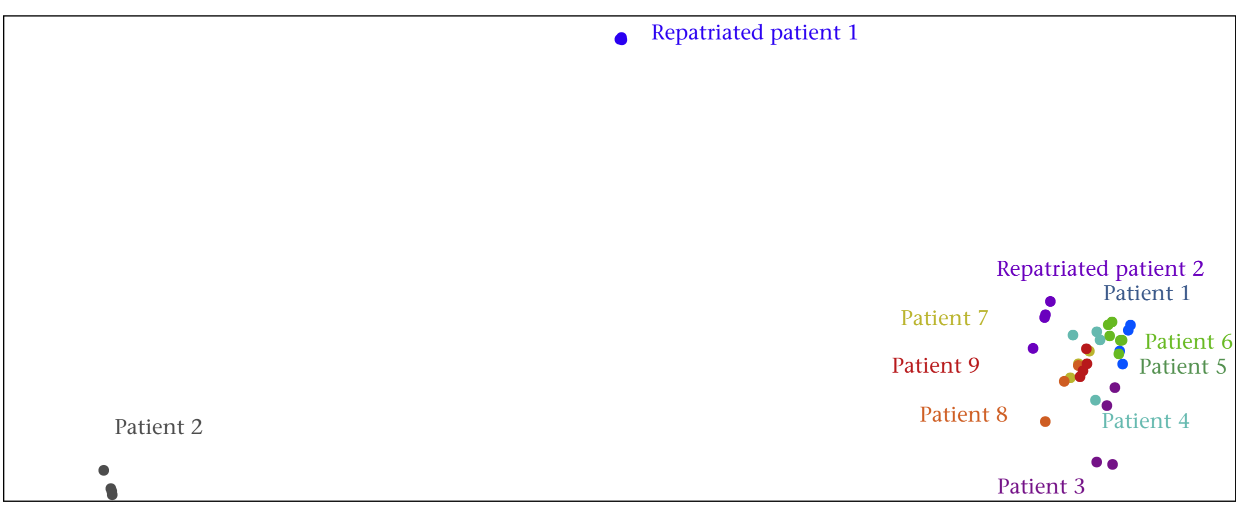

Figure 2. Clusters of *Acinetobacter baumannii* isolates, identified by Fourier-transform infra-red (FT-IR) spectroscopy. Dots of different colours correspond to different patients; dots of the same colour correspond to repetitive measurements with every patient's sample. Repatriated Patient 1 was transferred to University Hospital Zurich on 27th June 2022. Repatriated Patient 2 was transferred to University Hospital Zurich on 28th July 2022.

Patients with burn wounds are more likely to be colonized with MDROs, particularly with MDR *Pseudomonas aeruginosa* and *A. baumannii* [16–18]. Repetitive courses of antibiotic therapy drive selection of MDROs in burn patients. The extensive environmental sampling did not identify a common source of the outbreak strain. Thus, transmission was most likely propagated, driven by direct transmission (e.g. via hands) and indirect transmission from temporarily contaminated surfaces (e.g. on shared medical devices). The outbreak started during a period with a high workload. Unfavourable nurse-to-patient ratios result in shortcuts and errors. Inverse correlations between hand hygiene compliance and workload have been described in several studies [19–23]. This was confirmed by the present study, where the average weekly nurse-to-patient ratio was inversely associated with transmission of the outbreak strain. Of note, in the first meetings at the burns centre, the staff mentioned work overload in the preceding weeks in addition to the need for support by float nurses. A significant association between nurse staffing level and healthcare-associated infections has been reported previously [24], as well as an association between staffing level and mortality in intensive care [25].

This outbreak was controlled with a bundle of measures. With respect to limited ICU capacity and economic considerations, the stop on admissions was lifted twice, each time after 3 weeks without detection of new cases. Each time the stop on admissions was lifted, transmission of the outbreak strain reappeared until final outbreak control was achieved. An important milestone of outbreak control may have been the transfer of the last colonized patient to a regular ward in Calendar Week 47. All remaining patients were then removed from the burns centre, and intensified cleaning and disinfection was performed.

One particular challenge was sustaining compliance with infection control measures. Initially, the staff of the burns centre were convinced of a common source of the outbreak. However, regular meetings, negative results of environmental sampling, and staff training and education helped to raise awareness about the importance of infection prevention and control to control the outbreak. The outbreak ended after 3 months. Another study reported an *A. baumannii* outbreak in a Swedish burns centre that lasted for 6 months [18]. The authors also described a bundle approach, including elements of education, hand hygiene, dress code, surface disinfection, and environmental and patient screening. In line with the present study, no common source was identified [18].

The degree of burn wounds was associated with acquisition of the outbreak strain in this outbreak. Burn wounds are at risk of colonization and infection due to MDROs [16–18]. In a recent systematic review and meta-analysis on Gram-negative wound infections in burn patients, *A. baumannii* was the most common causative pathogen [26].

FT-IR spectroscopy and MLST aided understanding of the dynamics of the outbreak. The findings suggested that one patient with MDR *A. baumannii*, in whom transmission of the outbreak strain was suspected, did not belong to the cluster. In addition, the strain from the first repatriated patient 1 belonged to the identical sequence type as the outbreak strain, and would have been linked to the outbreak if MLST alone had been used. Thus, FT-IR spectroscopy had higher discriminatory power than MLST. Also, FT-IR spectroscopy had a short turnaround time.

The study has several strengths. Ward screenings were performed early and over a prolonged period of time to identify ongoing transmission events. Environmental sampling was performed to potentially identify a common source. Two strain-typing methods were used simultaneously. Together, these activities and methods allowed understanding of the dynamics of the outbreak, and helped in decision-making regarding prevention measures.

The study also has limitations. First, as there was simultaneous implementation of containment measures, it was not possible to quantify the role of individual measures. However, the bundled strategy controlled the outbreak successfully within a comparably short time. Second, weekly screenings resulted in inaccuracy for the exact date of acquisition of the outbreak strain. This affected the analysis of nurse-to-patient ratio, which had to be performed on a weekly basis although daily numbers were available. Third, the dataset did not include information on the nurse-to-patient ratio prior to the outbreak. Thus, an analysis on changes in nurse-to-patient ratio over time was not possible.

Burn patients with a higher percentage of body surface area with burn lesions $\geq$2a are at high risk of colonization and infection due to MDROs, particularly during periods of high workload. A multi-faceted containment strategy can successfully control outbreaks due to MDR *A. baumannii* in a burns centre.

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Conflict of interest statement
PWS received travel grants from Pfizer and Gilead, speaker's honoraria from Pfizer, and fees for advisory board activity from Pfizer and Gilead outside of the submitted work.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2024.01.002.

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