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Antimicrobial use at the end of life: a retrospective cohort study

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Antibiotic resistance poses a global threat. Antibiotics are administered to 80–90% of terminally ill patients but evidence of their effectiveness in improving survival or symptom relief at the end of life (EOL) is scarce. To determine the proportion of deceased patients that continue antibiotic treatment after documented EOL discussion and the decision to prioritise symptom relief over active treatment. As secondary aims to compare the groups with and without antibiotics after EOL discussion in terms of differences in demographics, type of infection, mean survival time after EOL discussion and if fluid therapy followed the same trend as antibiotic use. This was a retrospective cohort study including 100 patients aged 18 years or older who died with continued or discontinued antibiotics after EOL discussion, at Blekinge Hospital from January 2022 to February 2024. Patients were excluded if they received curative intended treatment until death, did not receive antibiotics during hospitalisation, or the antibiotic treatment was ended before EOL discussion. Medical record data were compared, using chi-2- , Fisher's exact- and t-tests, between patients who continued antibiotics or not after EOL discussion, in terms of demographics, focus of infection and survival time after EOL discussion. Ethical approval was granted by the Swedish Ethical Review Authority on 2023–12-14 (Dnr: 2023–07647-01). A total 36% (36/100) patients continued antibiotic treatment after EOL discussion. The most prescribed antibiotics were piperacillin-tazobactam (37%) and cefotaxime (32%) and the most common site of infection was pneumonia (45%). There was no statistical significance in survival time after EOL discussion between patients with antibiotics after EOL discussion or not (mean 2.7 days (range 0–11); IQR 1–3 vs 1.9 days (range 0–10); IQR 0.75–3; 95% CI 0.46–1.05; p = 0.082). Patients who continued antibiotics were also significantly more likely to continue with intravenous fluids (11/36 (31%) vs 3/64 (5%); between-group difference of 26%; 95% CI 0.10–0.42; p = 0.001). After EOL discussion more than one-third of inpatients continued antibiotics despite a shift to symptom relief, reflecting ongoing challenges in antimicrobial stewardship in palliative care.

Abbreviations

EOL End of life.
UTI Urinary tract infection

Antibiotic resistance poses a major global threat and is one of the leading causes of death globally[1]. Appropriate use of antibiotics in hospitals is important to effectively treat patients with infections and reduce unnecessary prescribing and development of antibiotic resistance. As expected, in Sweden, elderly patients represent a large proportion of hospitalised patients[2], and advanced age is associated with multimorbidity and increasing mortality[3]. Approximately 40% of Swedes die in hospitals[4]. Infections are common among elderly and terminally ill patients[5,6] and are a common cause of both hospital admission and complications during hospitalisation due to factors such as increasing incidence of multiple medical conditions, polypharmacy, immunosuppression, malnutrition, wounds, catheters[7] and poor function[8]. The prevalence of infection at the time of death is up to 63%[9].

Exposure to antibiotics increases with age and is at its highest in the last two weeks of life[10]. More than half of patients at the end of life (EOL) receive antibiotics[9,11]. Broad-spectrum antibiotics such as quinolones and cephalosporins are most commonly prescribed for the indication urinary tract infection and pneumonia[10].

Knowledge is limited regarding whether this extensive use of antibiotics in terminally ill patients improves survival or provides symptom relief, or whether the use of broad-spectrum antibiotics in this population

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merely contributes to antimicrobial resistance without patient benefit. Survival appears unaffected by antibiotic treatment in terminally ill hospitalized patients with suspected infection[6,12], and antibiotics may not improve symptoms, except in cases of urinary tract infection[6,8]. Moreover, such treatment may prolong the suffering of patients nearing death[13]. The risks associated with antimicrobial use at the EOL include the development of multidrug-resistant organisms, lack of efficacy, increased symptomatic burden, and excess cost[14]. There is no conclusive evidence that antimicrobials provide any symptomatic benefit at the EOL, although existing studies lack control groups and display methodological heterogeneity[15]. Given these challenges, it is important to understand local prescribing patterns at EOL.

The primary aim of this study was to investigate what proportion of deceased patients at a regional Swedish hospital continued antibiotic treatment after documented EOL discussion and the decision to prioritise symptom relief over active treatment. Secondary aims were to compare patients who continued or discontinued antibiotics after EOL discussion in terms of their demographics, type of infection, mean survival time after EOL discussion, and trends in fluid therapy use.

Methods

Study design and population

This was a retrospective cohort study of patients aged eighteen years or older who died at Blekinge Hospital between January 2022 and February 2024. Blekinge Hospital is a regional, publicly funded hospital in Sweden serving a population of approximately 160 000. Patients were included if they had received antibiotics during hospitalisation and had a documented end-of-life (EOL) discussion, indicating a transition from life-prolonging treatment to symptom-oriented care, after which antibiotic therapy was either continued or discontinued. Symptom-oriented care was defined as treatment provided after EOL discussion when the goal of care had shifted from life-prolonging to comfort and relief of symptoms. Date of death was identified via the National Board of Health and Welfare's death register.

All deceased inpatients during the study period were identified. Patients were then randomly sampled and included one by one until the target sample size was reached. To estimate the proportion of patients continuing with antibiotics after EOL discussion, the required sample size was calculated using a standard formula for proportions, assuming an expected prevalence of 30% with a margin of error of 10% and a 95% confidence interval. This resulted in a minimum required sample size of 81 patients.

Patients were excluded if they received curative antibiotic treatment until death, if their antibiotics had been discontinued prior to EOL discussion, or if they never received antibiotics during hospitalisation. Curative antibiotic treatment was defined as antibiotic therapy administered with the aim of curing an infection as part of ongoing life-prolonging care. ICU patients were also excluded, as intensive treatments (e.g. vasopressors, mechanical ventilation) may influence survival trajectories and treatment decisions. Furthermore, ICU patients may be potential organ donors, which could affect continuation of antibiotics after EOL discussions. Excluding patients dying in the ICU allowed the study to focus on typical inpatient care and EOL management outside of the ICU setting.

Data collection and categorizations

Medical records were retrospectively reviewed and the proportion of deceased with ongoing antibiotic treatment after EOL discussion was calculated and presented using descriptive statistics. Data were also collected regarding demographic data (age, sex, specialty unit, days admitted, relevant comorbidities), documented EOL discussion, data regarding the type of infection and antibiotics and the number of days between EOL discussion and death. EOL discussion was defined as a physician note in the medical journal indicating a transition from life-prolonging treatment to a primary focus on symptom relief or comfort care, an ICD diagnosis code palliative care or both. The discussion typically involved the patient when possible and/or family members when the patient lacked decision-making capacity. Information regarding existing advance care directives was recorded (Appendix 1).

The patient's social security number was replaced with a study ID. The code key that links the social security number to the study ID was stored in a locked drawer separately from the list of patient information. Only the researcher reviewing the records had access to the code key and to the list.

Statistical analyses

Primary outcome was the proportions of patients continuing with antibiotic treatment after EOL discussion. As secondary outcome a comparison between the two groups, including statistical analysis using descriptive statistics, chi-2 test, Fisher's exact test and t-test, was made in terms of demographic differences, difference in the type of infection, mean survival time after EOL discussion and if fluid therapy followed the same trend as antibiotic use. The statistical analyses were conducted using PSPP version 2.0.0-pre 3.

Ethical considerations

Ethical approval was granted by the Swedish Ethical Review Authority on 2023-12-14 (Dnr: 2023-07,647-01), and all methods were performed in accordance with relevant national regulations, institutional guidelines and with the amended Declarations of Helsinki. Since all included patients are deceased, consent could not be obtained. To secure the integrity of the deceased and their next of kin the data collected was de-identified and only the researcher with the code key had access to patients' identity.

Results

Population and characteristics

After reviewing 290 medical records, a total 100 patients were included (Fig. 1). The median age was 81 (IQR 75–88.25; range 34 –98) years and 59% were male (Table 1). The median time from admission to death was 7.5 days (IQR 3.75–12.25; range 0–58 days). Overall, 90/100 (90%) participants had at least one comorbidity, the most frequent underlying conditions were malignancy (19 vs 27 patients; 46%) and chronic kidney disease (14 vs 29 patients; 43%). Only 40% (12 vs 28 patients) of all patients had a confirmed infection (defined as (1) positive blood-, urine-, or NPH-culture together with symptoms; and/or (2) positive radiology together with symptoms).

A total of 36 patients (36%) continued antibiotic treatment after EOL discussion.

There were no statistically significant differences between the group with or without antibiotics after EOL discussion in terms of demographics, relevant comorbidities, the proportion with documentation of EOL discussion and the proportion with a care limitation plan. The infectious disease speciality unit was more prone to end antibiotics after EOL discussion (2/17 (11.8%); 95% CI 0.02–0.36; RR 0.29) and the cardiology patients appeared more likely to continue antibiotic treatment compared to the rest of the population (5/6 (83,3%); 95% CI 0.36–1.0; RR 2.53). However, this finding should be interpreted cautiously given the very small sample size and should be considered exploratory.

Infection characteristics

The most prescribed antibiotic was piperacillin-tazobactam (37%) closely followed by cefotaxime (32%). The most common site of infection was pulmonary (45%) followed by UTI (19%). 10 patients (10%) received more than one antibiotic. There was a trend toward higher continuation of antibiotics after EOL discussion among patients with *Clostridioides difficile* (4/5 (80%) vs 1/5 (20%); 95% CI 0.28–0.99;), and continuation of quinolones was proportionally higher than discontinuation (4/5 (80%) vs 1/5(20%); 95% CI 0.28–0.99). However, these findings should be interpreted cautiously given the small sample size. Infection characteristics are summarised in Table 2.

Mortality

Median time from EOL discussion to death was 2.3 days (IQR 1–3; range 0–11 days). There was a trend towards 0.8 day longer survival after EOL discussion in the group that continued antibiotic treatment, however no significant difference was shown (Mean 2.7 days (range 0–11); IQR 1.3 vs 1.9 days (range 0–10); IQR 0.75–3; 95% CI 0.46–1.05; $p = 0.082$). Twenty-one patients (21%) died within one day of the documented EOL discussion. In the group receiving antibiotics the mean number of days with continued antibiotics was 1.75 days (IQR 1–2.25; range 0–7) (Fig. 2).

Intravenous fluids were only continued in 14 patients (14%) in total, however 11 of these were in the group who also received continued antibiotics (11/36 (31%); 95% CI 0.18–0.47 vs 3/64 (5%); 95% CI 0.02–0.13) showing an in between-group difference of 26% (95% CI 0.10–0.42; $p = 0.001$) indicating an association between continued antibiotic and intravenous fluid treatment.

Discussion

The main finding of this study is that 36% of inpatients continued to receive antibiotics after EOL discussion, indicating that antibiotic therapy was frequently maintained even after a transition to symptom-oriented care

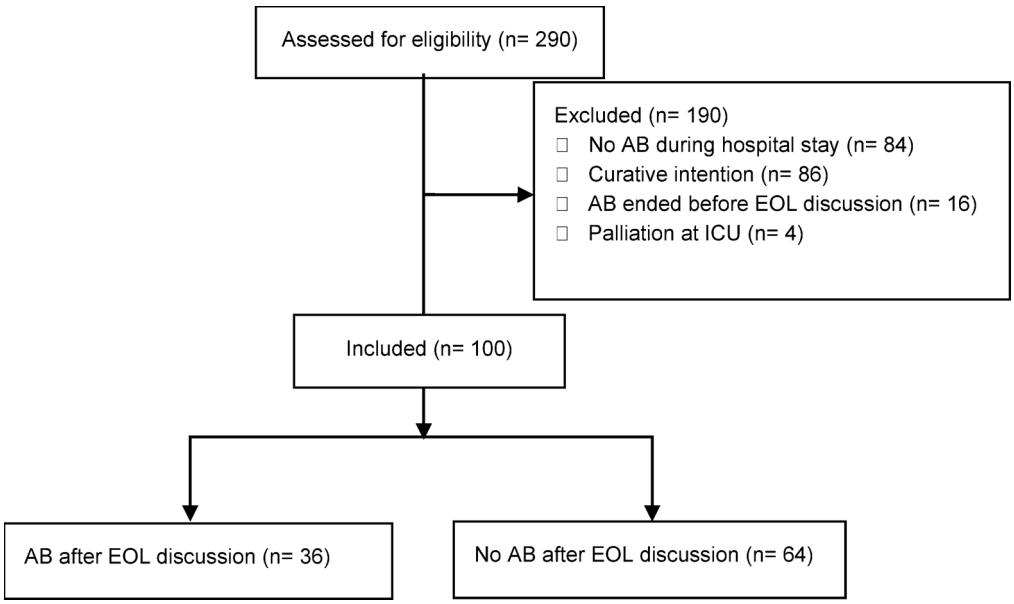

Fig. 1. Flow chart of included and excluded patients.

Characteristics	Antibiotics after EOL discussion (n = 36)	No antibiotics after EOL discussion (n = 64)	p-value
Age, range(mean) [SD], y	34–94 (77.1) [11.9]	45–98 (81.6) [11.1]	(t-test) 0.064
Median (IQR)	77.5 (72–85)	84.5 (76–89)	
Sex, no (%)			(Chi^2) 0.528
Female	13 (36)	28 (44)	
Male	23 (64)	36 (56)	
Specialty unit no. (%)			(Chi^2)
Gynaecology	1 (3)	3 (5)	0.545
Infectious Disease	2 (6)	15 (23)	0.022
Surgical	8 (22)	10 (16)	0.410
Medical	18 (50)	33 (52)	0.881
Orthopaedics	2 (6)	1 (2)	0.294
Cardiology	5 (14)	1 (2)	0.022
Ear Nose Throat	0 (0)	1 (2)	1
Days admitted, mean (SD)	11.5 (11.6)	9.3 (8.5)	(t-test) 0.288
Median (IQR)	8 (4–12.75)	7 (3–12.25)	
Documented EOL discussion, no. (%)			(Chi^2) 0.747
Documented in medical journal	25 (69)	41 (64)	
ICD Diagnosis	1 (3)	1 (2)	
Both	10 (28)	22 (34)	
Documented Care limitation plan, no. (%)			(Chi^2) 0.617
Yes	34 (94)	62 (97)	
No	2 (6)	2 (3)	
Relevant Comorbidity, no. (%)			(Chi^2)
Malignancy	10 (53)	27 (42)	0.496
Dementia	1 (3)	10 (16)	0.092
COPD	7 (19)	10 (16)	0.626
CVD	13 (36)	24 (28)	0.890
CKD	14 (39)	29 (45)	0.533
Stroke	9 (25)	10 (16)	0.251

Table 1. Baseline demographics.

and death was anticipated. Antibiotic use varied by specialty and infection site and appeared higher among patients with a palliative diagnosis at admission, although no data were collected to confirm this observation. The study population represents a selected cohort of patients, at a single regional hospital, who received antibiotics during hospitalisation and had a documented EOL discussion. As such, the reported proportion of antibiotic continuation describes local prescribing patterns within this specific population rather than antibiotic use at the end of life in general, and caution is warranted when generalising these results to other hospitals or healthcare systems. Nevertheless, the observed patterns are broadly consistent with previous studies regarding the frequency of antibiotic use, infection site and antibiotic choice at EOL [5,16].

In our cohort, piperacillin-tazobactam was the most frequently prescribed antibiotic, while only 40% of patients had a confirmed infection. This reflects the diagnostic uncertainty that accompanies infection management at the end of life. In Sweden, piperacillin-tazobactam is commonly used as empiric broad-spectrum therapy in severely ill patients with suspected infections, particularly when the infectious focus is unclear or when healthcare-associated infection is suspected. Symptoms such as fever, fatigue, or respiratory distress in this patient population may result from either infection or progression of the underlying disease, which complicates clinical decision-making regarding antibiotic therapy. Currently, no general guidelines exist for antibiotic treatment at EOL, neither in Sweden nor internationally. In this study, there was an observed difference between speciality units where infectious disease specialists were more likely to discontinue antibiotics after EOL discussions, whereas cardiology specialists tended to continue therapy. Determining when antibiotic use becomes futile is challenging, and uncertainty regarding ethical and legal responsibilities may influence physicians' decision. Physicians must balance clinical judgement with effective communication with patients and their families. Considerations such as antibiotic resistance often receive low-priority in EOL care, and limited awareness of potential adverse effects may lead physicians to prioritise perceived patient-centred benefits over antimicrobial stewardship[7,17].

Continuation of antibiotics after EOL discussion was associated with *Clostridioides difficile* infection, likely because diarrhea is the cardinal, and sometimes the only, symptom, and treatment can relieve symptoms within 3–5 days[18]. However, the sample size was small and our findings do not allow confirm conclusions regarding appropriateness of antibiotic use in this context.

Variable	Antibiotics after EOL discussion (n = 36)	No antibiotics after EOL discussion (n = 64)	p-value (chi^2-test)
Infection site, no (%)			
UTI	8 (22)	11 (17)	0.538
Pulmonary	15 (42)	30 (47)	0.615
Gastrointestinal or Hepatobiliary	4 (11)	8 (13)	1
Skin or soft tissue	2 (6)	7 (11)	0.482
Clostridioides difficile	4 (11)	1 (2)	0.055
Unknown	3 (8)	5 (8)	1
Other (neutropenic fever, endocarditis)	0 (0)	2 (3)	0.535
Suspected or confirmed infection		0.396	
Confirmed	12 (33)	28 (44)	
Suspected	24 (67)	36 (56)	
Antibiotic (multiple allowed)			
Piperacillin-Tazobactam	14 (39)	23 (36)	0.769
Cefotaxime	10 (28)	22 (34)	0.497
Meropenem	1 (3)	8 (13)	0.151
Metronidazole	5 (14)	2 (3)	0.095
Vancomycin	1 (3)	3 (5)	1
Pivmecillinam	2 (6)	1 (2)	0.294
Trimethoprim Sulpha	1 (3)	2 (3)	0.294
Clindamycin	1 (3)	2(3)	1
Quinolones	4 (12)	1 (2)	0.055
Ceftriaxone	0 (0)	2 (3)	0.535
Flu- or cloxacillin	0 (0)	2 (3)	0.535
Cefadroxil	0 (0)	1 (2)	1
PCG or PCV	0 (0)	1 (2)	1
Doxycycline	0 (0)	1 (2)	1

Table 2. Infection characteristics.

Similarly, patients with a palliative diagnosis at admission appeared more likely to receive prolonged antibiotics. In terminally ill patients, antibiotics may be perceived as easier to prescribe than withhold. Perceived improvements in symptom management or survival may influence prescribing decisions, despite evidence suggesting that infections do not significantly affect survival in these patients[5,17].

Strengths of the present study include the use of detailed, patient-level clinical data from a hospital cohort, allowing accurate assessment of documented EOL discussions, treatment decisions, and infection characteristics. Patients were randomly sampled from all in-hospital deaths during the study period, reducing the risk of systematic selection bias and strengthened the validity of observed prescribing patterns. Furthermore, evaluating antibiotics alongside infection site, survival time, and fluid therapy provided a more comprehensive understanding of decision-making at the EOL than is typically available, helping identify clinically relevant patterns that may support future antibiotic stewardship efforts and guideline development.

This study has several potential limitations. Its retrospective design relies on the accuracy and detail of physician documentation regarding EOL discussions and treatment decisions. Judgement of EOL was subjective and not standardised, and motivations for continuing antibiotics could not be fully assessed. Occasional documentation noted reasons such as allowing family time to arrive for final goodbyes. Other influencing factors, including patient and family preferences, psychosocial dynamics, and healthcare professional biases could not be captured in medical records. Symptom burden, patient or family preferences, and physician rationale at the time of the EOL discussion was not systematically documented in the medical records and could therefore not be reliably assessed in this retrospective study. Statistical analyses were limited by the relatively small sample size, resulting in reduced precision, small cell counts, and wide confidence intervals. This limited the reliability of subgroup analyses and increases the risk of chance findings, particularly as multiple comparisons were performed without adjustment. Consequently, subgroup results should be interpreted as exploratory. Furthermore, the observed differences in survival between groups cannot be interpreted as a causal effect of antibiotic treatment as treatment decision may reflect clinical judgement regarding prognosis and infection severity. Despite these limitations, this retrospective cohort study contributes to the limited body of research on antibiotic use at EOL and generates hypotheses for future work. The findings highlight the complexity of antibiotic decision-making at the end of life and the need for clearer guidance to support physicians in decision-making, reduce unnecessary antibiotic use, excess costs and minimise patient suffering. Antibiotic stewardship rounds are conducted in most wards at Blekinge Hospital, although not within the cardiology department. While subgroup findings should be interpreted cautiously due to the small sample size, the observed variation between specialties highlights how prescribing practices may differ between clinical disciplines and suggests that targeted antibiotic stewardship interventions and training could support more consistent decision making in end-of-

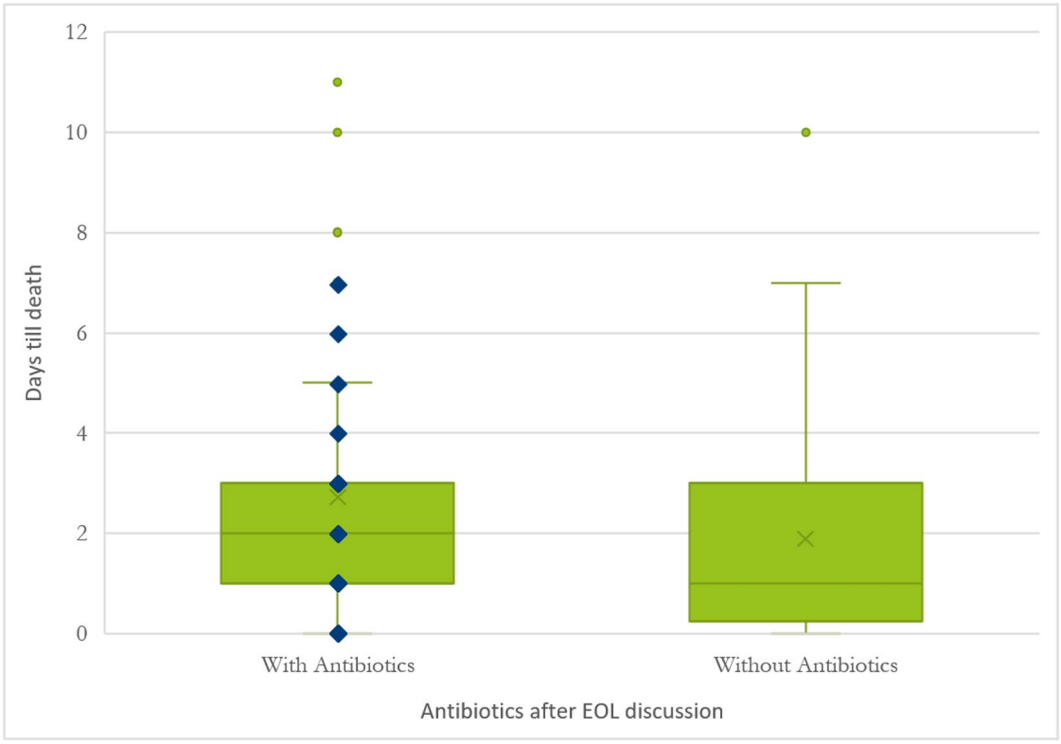

Fig. 2. Time from end-of-life discussion to death and number of days with continued antibiotics. Box plot of time from EOL discussion to death (days). Mean(SD) 2.7(2.6) with antibiotics vs. 1.9(2.0) without antibiotics. Median(IQR) 2(1–3) with antibiotics vs. 1(0.75–3) without antibiotics. Individual points of the number of days with continued antibiotics past EOL discussion is also shown.

life care. Careful identification of infection sites may help physicians recognise situations in which symptom relief justifies antibiotic treatment, such as in UTIs and potentially *C. difficile*, balancing patient comfort with antimicrobial stewardship.

In conclusion, more than one third of inpatients who died at Blekinge Hospital between January 2022 and February 2024 received antibiotics after EOL discussions. The appropriateness of continued antibiotic therapy cannot be determined by our data. However, continued antibiotic use may not always provide clinical benefits, and may contribute to antimicrobial resistance at a population level. Differences between infectious disease specialists and other physicians suggest that antibiotic stewardship programs may help improve treatment quality and reduce potentially avoidable antibiotic use. Evidence-based guidelines could help physicians make consistent, ethically sound decisions regarding antibiotic use when death is imminent. In the absence of robust evidence, a restrained, goal-directed approach may best align with patient comfort, antimicrobial stewardship principles and high-value care.

Data availability

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

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Author contributions
Study conception and design (KS, ME); data collection (KS); statistical analysis (KS); first draft (KS); interpretation, revision of the manuscript and approval of the final version to submit (KS, ME).

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Declarations

Competing interests
The authors declare no competing interests.

Ethics approval and consent to participate
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Additional information
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