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Original Article

Say it ain't *Steno*: a microbiology nudge comment leads to less treatment of *Stenotrophomonas maltophilia* respiratory colonization

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Abstract

Objective: To describe the effect of a *Stenotrophomonas maltophilia* (SM) respiratory culture nudge on antibiotic use in colonized patients.

Design: IRB-approved quasi-experiment.

Setting: Five acute-care hospitals in Michigan.

Patients: Adult patients with SM respiratory culture between 01/01/2022 and 01/27/2023 (pre-nudge) and 03/27/2023–12/31/2023 (post-nudge). Patients with active community/hospital/ventilator-acquired pneumonia or who received SM-targeted antibiotics at the time of culture were excluded.

Methods: A nudge comment was implemented 02/2023 stating: "*S. maltophilia* is a frequent colonizer of the respiratory tract. Clinical correlation for infection is required. Colonizers do not require antibiotic treatment." The primary outcome was no treatment with SM-therapy; secondary outcomes were treatment with SM-therapy ≥72 hrs, length of stay, and in-hospital, all-cause mortality. Safety outcomes included antibiotic-associated adverse drug events (ADEs).

Results: 94 patients were included: 53 (56.4%) pre- and 41 (43.6%) post-nudge. Most patients were men (53, 56.4%), had underlying lung disease (61, 64.8%), and required invasive ventilatory support (70, 74.5%). Eleven (11.7%) patients resided in a long-term care facility. No treatment with SM therapy was observed in 13 (23.1%) pre- versus 32 (78.0%) post-nudge patients (P <0.001). There were no differences in secondary outcomes. Antibiotic-associated ADEs were common (33/41, 76%) in patients who received ≥72hrs of SM-therapy: fluid overload (18, 44%), hyponatremia (17, 42%), elevated SCr (12, 29%), hyperkalemia (5, 12%). After adjustment for confounders, post-nudge was associated with 11-fold increased odds of no treatment with SM-therapy (adjOR, 11.72; 95%CI, 4.18–32.83).

Conclusions: A targeted SM nudge was associated with a significant reduction in treatment of colonization, with similar patient outcomes. SM-treated patients frequently developed antibiotic-associated ADEs.

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Background

Stenotrophomonas maltophilia is a nosocomial aerobic Gram-negative bacillus with intrinsic resistance against common antibacterial agents that frequently colonizes the respiratory tract.[1] Up to 50% of *S. maltophilia* isolates obtained from respiratory cultures are thought to represent colonization and do not require additional treatment.[2,3] The 2024 guidance on the treatment of antimicrobial-resistant Gram-negative infections state, "For . . . *S. maltophilia* in particular, a distinction between bacterial colonization and infection is important because unnecessary antibiotic therapy will only further the development of resistance and may cause unnecessary antibiotic-related harm to patients.[4]" The decision to withhold antibiotic therapy in patients colonized with *S. maltophilia* can be challenging and frequently result in unnecessary treatment, facilitating antimicrobial resistance or other antibacterial-associated harms.[5,6]

Behavioral antimicrobial stewardship interventions, such as nudging clinicians with purposeful microbiology comments, have been shown to improve optimal antibiotic prescribing and reduce patient harms while maintaining prescriptive autonomy.[7–10] While nudge interventions have primarily focused on successful antibiotic de-escalation,[7,10] there are limited data-evaluating nudges as an effective strategy in avoiding treatment of colonization. Often, prescribers are inclined to treat the growth of any organism, including colonizers or growth from an inappropriately collected specimen, as pathogenic.[11] This inclination to treat is often attributed to the "because it is there" mentality

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and is more easily prevented by the establishment of effective microbiology stewardship strategies compared to after the fact.[11]

As providers frequently face clinical uncertainty in appropriate management of colonization, the Henry Ford Health (HFH) antimicrobial stewardship program (ASP) implemented a targeted *S. maltophilia* microbiology nudge to provide guidance and avoid unnecessary treatment of colonization. The study purpose was to describe the effect of a targeted *S. maltophilia* respiratory culture nudge on antibiotic use in patients with colonization.

Methods

Study design

This was a single center, pre-, and post-test quasi-experiment conducted at HFH, a five-hospital health-system with a centralized clinical microbiology laboratory located in metropolitan Detroit, MI, USA. This study received institutional review board approval with a waiver of consent.

The study was performed over two time periods: a pre-intervention (pre-nudge) period from January 1st, 2022 to January 27th, 2023, and the corresponding post-intervention (post-nudge) period from March 27th, 2023 to December 31st, 2023. Hospitalized patients were included if they were ≥18 years old, had a positive respiratory culture with *S. maltophilia*, and met the study definition for colonization. Patients were excluded if they met criteria for an active community/hospital/ventilator acquired pneumonia, if they had microbiological culture data from outside institutions, if they died within 72 hours of culture result, received comfort/hospice care at the time of culture, or received active *S. maltophilia* therapy prior to culture result. Only the index respiratory culture of *S. maltophilia* was included in patients with multiple encounters.

Intervention

Prior to comment implementation, the nudge comment was proposed, discussed, and voted for approval in person with members of the health system critical care council and antimicrobial stewardship subcommittee to establish stakeholder buy-in. On February 27th, 2023, an automated microbiology comment on positive *S. maltophilia* respiratory cultures was implemented that reported: *"S. maltophilia is a frequent colonizer of the respiratory tract. Clinical correlation for infection is required. Colonizers do not require antibiotic treatment."* Prior to the intervention, culture results stated the organism alone and without an interpretative comment. The HFH ASP developed a one-page educational handout (Supplement 1) provided to the pharmacy department in the form of a weekly email for the month prior to and after the implementation of the nudge comment from January to March 2023. This education was also shared with providers on the day of implementation through electronic communication. Target audiences included pulmonary and critical care leadership, chief medical residents, infectious diseases providers, and clinical pharmacists.

Key definitions and data

The primary outcome was the proportion of patients who did not receive treatment with *S. maltophilia* therapy within 72 hours of final culture result in colonized patients. Respiratory cultures included sputum, tracheal aspirate, and/or bronchoalveolar lavage samples. *S. maltophilia*-active therapy was defined as trimethoprim-sulfamethoxazole, minocycline, levofloxacin, ciprofloxacin, eravacycline, cefiderocol, ceftazidime-avibactam, and aztreonam in response to the culture result.

Colonization was defined as a positive respiratory culture and the absence of clinical criteria for an active pneumonia, including community-acquired (CAP), hospital-acquired (HAP), and ventilator-associated pneumonia (VAP). The criteria were defined using the National Healthcare Safety Network reporting definitions. CAP/HAP were defined as having new or worsening infiltrate on chest radiography with two of the following signs/symptoms: shortness of breath and/or hypoxia, productive cough, or tachypnea. VAP was defined as at least three of the following criteria: new or worsening infiltrates on chest radiography, maximum temperature >38.1°C, purulent and/or increased respiratory secretions, and/or increasing oxygen requirements.

Secondary outcomes included antibiotic-related adverse drug events in those receiving active *S. maltophilia* therapy for 72 hours or more. Adverse drug events, assessed at 72 hours of therapy, were defined as fluid overload as documented on exam, change in serum creatinine (SCr) by ≥0.3 mg/dL, serum sodium ≤135 mEq/L, serum potassium ≥5 mEq/L, and *Clostridioides difficile* toxin positive stool sample. A nonequivalent dependent variable of appropriate deep-vein thrombosis (DVT) prophylaxis was used to evaluate the standard of care over the study period and was defined as the use of heparin, low molecular weight heparin, fondaparinux, or sequential compression devices unless on therapeutic anticoagulation or with documented problem of bleeding.

Other key definitions included underlying lung conditions, defined as chronic obstructive pulmonary disease, asthma, lung cancer, pulmonary edema, pulmonary hypertension, bronchiectasis, and a history of airway stents. Ventilatory support was categorized as invasive and non-invasive. Invasive ventilatory support included tracheostomy and endotracheal intubation; non-invasive ventilatory support included nasal cannula, nonrebreather, high-flow nasal cannula, continuous positive airway pressure, and bilevel positive airway pressure. Immunosuppression was defined as a history of transplant, active malignancy, chemotherapy or radiotherapy within the past 90 days, CD4 cell count <200 cells/mm^3, or receiving a steroid equivalent of prednisone 20 mg for at least 30 days.

Data collection and statistical analysis

Patient data were acquired for screening using Microsoft SQL Server Management Studio (Microsoft, Redford, WA, USA) based on positive *S. maltophilia* respiratory culture results. Patients were subsequently screened for inclusion; patents that met inclusion criteria had demographic and outcome data manually collected from the electronic health record using a standardized case report form. Data collected included patient and demographic information, microbiology culture data, antibiotic treatment, and patient outcomes.

This study was designed to detect a difference in *S. maltophilia* antibiotic treatment in patients with colonization. A sample size of 168 patients was calculated using a two-sided α of 0.05, β of 0.8, and an anticipated effect size of 20% decrease in antibiotic use at three days following comment implementation based on previously published nudge data.[12]

Descriptive statistics (proportion [%], median [IQR]) were used to describe patients in the pre- and post-intervention groups. Bivariate analyses were used to compare groups; continuous data were analyzed using Mann–Whitney U test and categorical data were compared using the Pearson X^2 or Fisher's exact tests. To

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Table 1. Baseline characteristics of patients before and after implementation of a *Stenotrophomonas maltophilia* microbiology nudge

Variable (*n*, % or median, IQR)	Pre-nudge (*n* = 53)	Post-nudge (*n* = 41)	*P* value
Age, years	66 (56–75)	63 (56–75)	0.649
Female sex	22 (42%)	19 (46%)	0.639
Charlson Comorbidity Index	6 (4–8)	7 (4–9)	0.845
Underlying Lung Condition	34 (64%)	27 (66%)	0.864
Immunosuppression	11 (21%)	13 (32%)	0.227
Ventilation – Invasive	41 (77%)	29 (71%)	0.465
Prior to Admission – Home	37 (70%)	25 (61%)	0.37
Prior to Admission – LTCF	5 (9%)	6 (15%)	0.525
Prior to Admission – OSH	12 (23%)	9 (22%)	0.936
Polymicrobial Infection	36 (68%)	27 (66%)	0.832
Concurrent Infection	21 (40%)	12 (30%)	0.337
ID Consult	23 (43%)	18 (44%)	0.961
Control – DVT Prophylaxis	50 (94%)	39 (95%)	1.00

LCTF, long-term care facility; OSH, outside hospital; ID Consult, Infectious Diseases Consult; DVT Prophylaxis, deep-vein thrombosis prophylaxis.

determine variables independently associated with treatment of *S. maltophilia* colonization, variables associated with the primary outcome (P <0.2) from bivariate analysis were entered into a multivariable logistic regression model using a backward, stepwise approach. Variables included in the model were selected based on clinical rationale, the absence of variable colinearity, and were restricted to an event-to-variable ratio of 10:1; model fit was performed using the Hosmer–Lemeshow goodness-of-fit test. Categorical variables were assessed for colinearity using the Pearson X^2 test. For all analyses, P values <0.05 were considered statistically significant. All statistical tests were performed using SPSS Statistics, version 29 (IBM Corp., Armonk, NY, USA).

Table 2. Outcomes of patients colonized with *Stenotrophomonas maltophilia* before and after a microbiology nudge

Variable (*n*, % or median, IQR)	Pre-nudge (*n* = 53)	Post-nudge (*n* = 41)	*P* value
Hospital Length of Stay, days	24 (10–49)	16 (8–29)	0.370
ICU Length of Stay, days	15 (2–35)	11 (3–25)	0.404
In-Hospital All-Cause Mortality	11 (21%)	7 (18%)	0.694
S. maltophilia Therapy Present >72 Hours	36 (90%)	8 (89%)	1.00

ICU, intensive care unit.

Results

There were 94 patients included: 53 (56%) patients in the pre-nudge comment group and 41 (44%) in the post-nudge comment group. 237 patients were initially screened for inclusion; 143 patients did not meet inclusion criteria and were excluded most commonly due to active *S. maltophilia* infection (31%), outpatient cultures (35%), or death within 72 hours of culture result (24%). Baseline characteristics of the pre- and post-group patients are provided in Table 1. Most patients had an underlying lung condition (61, 65%) and required mechanical ventilatory support at the time of *S. maltophilia* culture (70, 74%).

The primary outcome, the proportion of patients who did not receive *S. maltophilia* therapy within 72 hours of culture result, was observed in 13 patients (23%) in the pre-nudge comment group and in 32 patients (78%) in the post-nudge comment group (P <0.001). Secondary outcomes are presented in Table 2.

In patients who were initiated on *S. maltophilia* treatment within 72 hours of culture results (n = 49), the proportion who had *S. maltophilia* treatment discontinued was 36/40 (90%) in pre-nudge group versus 8/9 (89%) in the post-nudge group (P = 1.00). Within this population, the primary agent used was trimethoprim-sulfamethoxazole (36, 82%) and 41 (93%) patients received *S. maltophilia*-active treatment for 72 hours or more. Antibiotic-associated adverse drug events were common (33/41, 76%) among the patients who received at least 72 hours or more of *S. maltophilia*-active treatment: fluid overload (18, 44%), hyponatremia (17, 42%), elevated SCr (12, 29%), and hyperkalemia (5, 12%). A nonequivalent dependent variable of appropriate DVT prophylaxis was observed in 50 (94%) patients in the pre-nudge group and 39 (95%) in the post-nudge group (P = 1.00).

The results of bivariate analyses and clinical rationale dictated the variables selected for inclusion into a multivariable logistic regression model: admission from a long-term care facility, invasive ventilatory support, and post-group patients with a targeted *S. maltophilia* comment (Table 3). Other variables (i.e., immunosuppressed status, underlying lung condition, pulmonary edema) were excluded from the model due to unmet statistical criteria, to preserve the event to variable ratio, or to prevent inclusion of colinear variables. In the final parsimonious model, patients in the post-intervention group had 11-fold increased odds of not receiving *S. maltophilia* therapy within 72 hours of culture result (adjOR, 11.72; 95%CI, 4.18–32.83).

Discussion

This study demonstrated that a *S. maltophilia* respiratory microbiology nudge was associated with significantly reduced unnecessary antibiotic treatment in colonized patients, including a high proportion of patients who required invasive mechanical ventilation. Among patients who received treatment for *S. maltophilia* colonization, antibiotic courses were frequently

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Table 3. Variables associated with no treatment with *Stenotrophomonas maltophilia* therapy within 72 hours of final culture result in colonized patients

Variable	*n* (%)	Unadjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)
S. maltophilia Nudge	41 (44%)	10.94 (4.15–28.8)	<0.001	11.72 (4.18–32.83)
Residence at LTCF	11 (12%)	5.88 (1.20–28.88)	0.016	6.07 (1.05–35.10)
Pulmonary Edema*	16 (17%)	0.43 (0.14–1.36)	0.14	Not tested
Invasive Ventilatory Support	70 (74%)	0.35 (0.13–0.94)	0.03	0.34 (0.11–1.09)
Immunosuppressed Status*	24 (25%)	1.40 (0.55–3.56)	0.47	Not tested
Underlying Lung Condition*	61 (65%)	1.40 (0.59–3.29)	0.43	Not tested

LTCF, long-term care facility.
Hosmer–Lemeshow goodness-of-fit test result: 0.55.
*Pulmonary edema, immunosuppressed status, and underlying lung condition were excluded from the final model due to unmet statistical criteria and/or colinearity.

prescribed for greater than 72 hours and antibiotic-associated harms were common. In the 2024 update to the guidance on the treatment of antimicrobial-resistant Gram-negative infections, it is noted that *S. maltophilia* frequently presents as a colonizing organism and colonization does not require treatment.[4] This recommendation also emphasizes the timeliness and necessity of diagnostic stewardship initiatives, such as microbiology nudges, to preserve novel therapies for true infections and serve providers in executing evidence-based care.

The findings of the present study add to the growing body of evidence that suggest microbiology nudge comments are successful, lean-process interventions that improve antibiotic optimization.[7–10] However, there are few data that describe successful microbiology nudges that result in withholding treatment in colonized patients. Schartz and colleagues performed a quasi-experiment that evaluated the impact of an asymptomatic candiduria nudge comment on *Candida* spp. treatment in hospitalized patients.[10] This intervention provided therapy indications for *Candida* urine cultures that showed normal flora, resulting in a significant reduction in antifungal administration within 72 hours (48.1% vs 34.0%; $P = 0.02$).[10] Asymptomatic urinary cultures may represent a more widely accepted condition for opting to not treat, whereas the current study elucidates that patient characteristics pose continued uncertainty in management of respiratory culture results. While Schartz and colleagues focused their comment template on colonization management, they also provided clinical guidance highlighting indications for antifungal use in key patient populations, including high-risk patients or those undergoing a urologic procedure. In contrast, the current intervention clearly states that colonization does not require treatment, which further refines the utility of nudge interventions. Furthermore, the study contributes to the evolving field of colonization management by clearly defining that asymptomatic respiratory cultures similarly do not require treatment.

This study has several limitations. While robust and objective definitions for colonization were utilized, misclassification is still possible due to the nature of medical record documentation. Additionally, the results may be subject to maturation in practice and are impacted by regression to the mean. The nonequivalent dependent variable of DVT prophylaxis was not significantly different throughout the two intervention periods, but the selection of this variable may represent an unideal measure of secular trends due to practice standards in intensive care units; maturation is also unlikely as the antimicrobial stewardship program had significant reductions in staffing models or practice resources during the study period. While these results suggest the *S. maltophilia* microbiology nudge comment is impactful in preventing colonization treatment and subsequent patient harm, more robust evaluation is warranted due to the limitations of the present study size and analytical approach. Future evaluations should include a larger confirmatory study with additional time-point measurements and with segmented regression analysis to measure the impact of this intervention more accurately. The present study did not assess the failure of the clinician to treat active *S. maltophilia* infection in response to the microbiology nudge and represents a direction for future work. The study design utilized may have overestimated the effect size associated with this intervention. This microbiology nudge comment is part of a series of stewardship efforts at HFH and the generalizability of these findings may be limited to outside institutions.

This study highlights the effectiveness of targeted microbiology interventions in guiding the management of respiratory cultures in patients colonized with *S. maltophilia* and providing antimicrobial stewardship programs with a simple, reproducible method of communication. Future studies should further enhance the effectiveness of nudge interventions in managing colonization and promote the diversification of stewardship programs through the leveraging of electronic health records.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/ice.2024.195.

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Competing interests. None.

References

1. Pathmanathan A., & Waterer GW. Significance of positive *Stenotrophomonas maltophilia* culture in acute respiratory tract infection. *Eur Respir J* 2005;2:911–914.
2. Saugel B, Eschermann K, Hoffmann R, *et al. Stenotrophomonas maltophilia* in the respiratory tract of medical intensive care unit patients. *Eur J Clin Microbiol Infect Dis* 2012;31:1419–1428.
3. del Toro MD, Rodríguez-Bano J, Herrero M, Rivero A, García-Ordoñez MA, Corzo J, Pérez-Cano R. Clinical Epidemiology of *Stenotrophomonas maltophilia* Colonization and Infection: A Multicenter Study. *Medicine (Baltimore)* 2002;81:228–239.
4. Tamma PD, Heil EL, Justo JA, Mathers AJ, Satlin MJ, Bonomo RA. Infectious Diseases Society of America Antimicrobial-Resistant Treatment Guidance: Gram-Negative Bacterial Infections. Infectious Diseases Society of America website. https://www.idsociety.org/practice-guideline/amr-guidance/ Published 2024. Accessed July 31, 2024.

5. Banar M, Sattari-Maraji A, Bayatinejad G, *et al.* Global prevalence and antibiotic resistance in clinical isolates of *Stenotrophomonas maltophilia*: a systematic review and meta-analysis. *Front Med (Lausanne)* 2023;10: 1163439.
6. Vuong L, Davis SL, Jedinak T, *et al.* High frequencies of adverse drug events with intravenous vs oral high-dose trimethoprim-sulfamethoxazole: an opportunity for antibiotic stewardship. *Open Forum Infect Dis* 2021;8:S147.
7. Langford BJ, Leung E, Haj R, *et al.* Nudging in microbiology laboratory evaluation (NIMBLE): a scoping review. *Infect Control Hosp Epidemiol* 2019;40:1400–1406.
8. Arena CJ, Kenney RM, Kendall RE, Tibbetts RJ & Veve MP. Respiratory culture nudge improves antibiotic prescribing for *Moraxella catarrhalis* and *Haemophilus influenzae* lower respiratory tract infections. *Antimicrob Steward Healthc Epidemiol* 2023;3:e23.
9. Musgrove MA, Kenney RM, Kendall RE, *et al.* Microbiology comment nudge improves pneumonia prescribing. *Open Forum Infect Dis* 2018;5:162.
10. Schartz WR, Bennett N, Aragon L, *et al.* (2022). Templated microbiology comments with candiduria to enhance antimicrobial stewardship. *Antimicrob Steward Healthc Epidemiol* 2022;2:e156.
11. Goldstein EJ, Goff DA, Reeve W, *et al.* Approaches to modifying the behavior of clinicians who are noncompliant with antimicrobial stewardship program guidelines. *Clin Infect Dis* 2016;63:532–538.
12. McBride J, Schulz L, Fox B, *et al.* Influence of a "no MRSA, no Pseudomonas" comment to a respiratory culture on antibiotic utilization during the treatment of lower respiratory tract infection. *Open Forum Infect Dis* 2015;2:1500.

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