

# The Impact of Standardized Infectious Diseases Consultation on Postsplenectomy Care and Outcomes

Andrew J. Hale,<sup>1,✉</sup> Benjamin Depo,<sup>1</sup> Sundas Khan,<sup>2</sup> Timothy J. Whitman,<sup>1</sup> Sean Bullis,<sup>1</sup> Devika Singh,<sup>1</sup> Katherine Peterson,<sup>1</sup> Peter Hyson,<sup>1</sup> Laura Catoe,<sup>1</sup> Bradley J. Tompkins,<sup>1</sup> W. Kemper Alston,<sup>1</sup> and Jean Dejean<sup>1</sup>

<sup>1</sup>University of Vermont Medical Center, Larner College of Medicine at the University of Vermont, Burlington, Vermont, USA, and <sup>2</sup>Lankenau Medical Center, Wynnewood, Pennsylvania, USA

**Background.** Patients who receive splenectomy are at risk for overwhelming postsplenectomy infection (OPSI). Guidelines recommend that adult asplenic patients receive a complement of vaccinations, education on the risks of OPSI, and on-demand antibiotics. However, prior literature suggests that a majority of patients who have had a splenectomy receive incomplete asplenic patient care and thus remain at increased risk. This study assessed the impact of standardized involvement of infectious diseases (ID) providers on asplenic patient care outcomes in patients undergoing splenectomy.

**Methods.** A quasi-experimental study design compared a prospective cohort of patients undergoing splenectomy from August 2017 to June 2021 who received standardized ID involvement in care of the asplenic patient with a historic control cohort of patients undergoing splenectomy at the same institution from January 2010 through July 2017 who did not. There were 11 components of asplenic patient care defined as primary outcomes. Secondary outcomes included the occurrence of OPSI, death, and death from OPSI.

**Results.** Fifty patients were included in the prospective intervention cohort and 128 in the historic control cohort. There were significant improvements in 9 of the 11 primary outcomes in the intervention arm as compared with the historic controls. Survival analysis showed no statistically significant difference in the incidence of OPSI-free survival between the groups ( $P = .056$ ), though there was a trend toward improvement in the prospective intervention arm.

**Conclusions.** Standardized involvement of an ID provider in the care of patients undergoing splenectomy improves asplenic patient care outcomes. Routine involvement of ID in this setting may be warranted.

**Keywords.** asplenia; asplenic; asplenic sepsis; overwhelming postsplenectomy sepsis; postsplenectomy.

The spleen is a crucial component of the hematologic and immune systems that helps protect the host from infection [1, 2]. In the United States, every year ~25 000 patients have their spleens removed for traumatic, hematologic, or cancer-related reasons. Patients who have had a splenectomy face significantly increased risk of morbidity and mortality from overwhelming postsplenectomy infection (OPSI) [2, 3]. Data from the 1980s and 1990s demonstrated that mortality from OPSI was in excess of 50% per episode [4, 5], and death can occur just hours after symptom onset [6]. The incidence of OPSI was estimated to be as high as 7.0 cases per 100 person-years, with an estimated lifetime risk of 3%–5% for splenectomized patients [4, 7].

Currently, comprehensive care of the asplenic patient, entailing patient education on the risks of postsplenectomy sepsis, antibiotic prophylaxis, and a series of vaccinations, has improved outcomes in this population, though the risks of OPSI remain high [1, 8, 9]. Vaccines have proven to be a highly effective tool in preventing OPSI. After the advent of the heptavalent pneumococcal conjugate vaccine (PCV7) in 2000, PCV-7-type invasive pneumococcal disease (IPD) in all children decreased 94% [10], with significant reductions in IPD-related OPSI in children and adults [11–13]. PCV7 was replaced by the 13-valent pneumococcal conjugate vaccine (PCV13) in 2010, further reducing rates of asplenic sepsis [1]. Thus, vaccination for patients who have had a splenectomy is crucial for infection and OPSI prevention. The protective benefits of patient education on OPSI outcomes have not been well evaluated in the literature, though education remains an established aspect of care for asplenic patients, and 1 study demonstrated superior OPSI outcomes in patients with more knowledge about OPSI than not [1, 14, 15]. The value of antibiotic prophylaxis in postsplenectomy patients has also not been well evaluated. For children <5 years old with functional asplenia from sickle cell anemia, daily prophylactic penicillin has been demonstrated to reduce the risk of OPSI [16, 17], though daily prophylactic antibiotics are not generally recommended in asplenic adults. Instead,

Received 28 April 2022; editorial decision 25 July 2022; accepted 28 July 2022; published online 30 July 2022

Correspondence: A. J. Hale, MD, University of Vermont Medical Center, Infectious Disease Unit, 111 Colchester Avenue, Mailstop 115 SM2, Burlington, VT 05401 ([andrew.hale@uvmhealth.org](mailto:andrew.hale@uvmhealth.org)).

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<https://doi.org/10.1093/ofid/ofac380>

on-demand antibiotics, to be taken with fever or first signs of OPSI, have been recommended in asplenic adults [1], though data are lacking on the efficacy of this approach.

Despite recommendations to provide care for asplenic patients with the 3-pronged approach of patient education, antibiotic prophylaxis, and vaccination [1], delivery has traditionally been lacking [14]. Ample literature from a variety of settings worldwide have consistently demonstrated low-rates of compliance with asplenic patient care recommendations. Vaccination rates have been the most routinely assessed, with asplenic vaccine delivery rates ranging from 3% to 55% [5, 18–27]. Rates of patient education on OPSI and on-demand antibiotic prescription rates in adults have been poorly assessed, but available literature suggests it likely that a significant majority of asplenic patients have received neither [22, 28]. There is thus a need for improvement in the delivery of care for asplenic patients.

Potential barriers to this care delivery include provider lack of knowledge, complexity of vaccine regimens, disparate medical record systems, and confusion about which health care provider is responsible [22, 29, 30]. Minimal literature exists regarding formal interventions to improve rates of guideline-based care for asplenic patients. One study demonstrated that outpatient follow-up of postsplenectomy patients to a travel clinic significantly increased vaccination rates, though only a minority of the total asplenic cohort participated [31]. Others have demonstrated that an intensive patient outreach model in a general medicine clinic improved comprehensive care for asplenic patients [22] and that patients are receptive to educational interventions [32]. However, these prior interventions retrospectively captured patients who had had a splenectomy, sometimes years prior, which is important because OPSI is most common in the first year postsplenectomy [1, 33]. Interventions to prospectively identify postsplenectomy patients in the pre- or perioperative period and provide them guideline-based care are thus a health care priority in this population.

Infectious diseases (ID) physicians may be in a unique position to improve outcomes in postsplenectomy patients. In addition to specializing in the treatment and prevention of infection, ID clinicians are vaccine experts and typically see patients both inpatient and outpatient [34]. We hypothesized that the standardized inclusion of an ID physician in the care of patients undergoing splenectomy would increase rates of asplenic guideline compliance and decrease morbidity and mortality from OPSI in this population.

## METHODS

### Study Design, Setting, Population, and Ethical Approval

We conducted a quasi-experimental study comparing a prospective intervention group with a historic control group. The study took place at the University of Vermont Medical Center (UVMMC), Burlington, Vermont. UVMMC is a

tertiary care academic medical center with 620 licensed beds that serves an urban and rural population in Vermont and New York of ~1 million persons; it is the only level 1 trauma center in the region.

The historic control group included all patients aged 18 and older who received a splenectomy at UVMMC from January 1, 2010, until July 31, 2017. The prospective intervention group included all patients aged 18 and older who received a splenectomy at UVMMC from August 1, 2017, until June 30, 2021. The intervention in our study was prospective, standardized consultation with an ID provider regarding care for the asplenic patient for patients planning to receive (for elective) a splenectomy or status (for urgent) postsplenectomy. The intervention was implemented on August 1, 2017. ID consultation occurred preoperatively in the outpatient setting for elective splenectomies and postoperatively in the inpatient setting for urgent, unplanned splenectomies. ID trained faculty, fellows, and nurse practitioners provided consultations. Surgeons who perform splenectomies were educated about the intervention via active outreach to ensure that they were partners in this process. We also created an automated daily report in the electronic medical record to alert us when a splenectomy was performed to ensure that ID became involved. Patients with incomplete medical records were excluded. The study was approved by the UVM Institutional Review Board.

### Care for Asplenic Patient Components and Outcome Measures

We assigned each of 11 components of care for the asplenic patient as primary outcomes: (1) Receipt of PCV13. (2) Receipt of 23-valent pneumococcal polysaccharide vaccine (PPSV23). (3) Correct timing of PCV13 and PPSV23 in relation to each other; asplenic guidelines recommend that PCV13 be given first, followed by PPSV23 no sooner than 8 weeks later. If PPSV23 is given first, then PCV13 should be delayed for 1 year [8]. (4) Receipt of first dose of meningococcal serotype ACWY vaccination. (5) Receipt of second dose of meningococcal serotype ACWY vaccination. (6) Correct timing of PCV13 and meningococcal serotype ACWY vaccination. Certain meningococcal serotype ACWY vaccines should be delivered at least 4 weeks after PCV13 because of potential for interference with PCV13 immune response [35]. (7) Receipt of *Haemophilus influenzae* serotype B vaccination (HiB). (8) Receipt of annual influenza vaccination a majority of follow-up years. (9) Correct timing of all vaccines in relation to the splenectomy. Studies suggest inferior immune response if vaccines are given within 14 days before or after splenectomy; thus it is recommended to complete (if elective) or start (if urgent) asplenic vaccinations 14 days before or after splenectomy, respectively [36–38]. (10) Prescription written for on-demand antibiotics for fever or first signs of OPSI, either levofloxacin 750 mg or amoxicillin/clavulanic acid 875/125 mg. (11) Documentation within the medical record of patient education on OPSI

prevention and recognition. We created a composite score of the 11 primary outcomes, with 1 point for each outcome achieved, to help quantify the overall quality of care for the asplenic patient delivered, though we recognize that comparative data on the relative value of each primary outcome are lacking. Secondary outcomes included the occurrence of OPSI, death, and death from OPSI. OPSI was defined as a clinical episode wherein a patient had evidence of sepsis and was ill enough to warrant hospitalization. Data were obtained by medical record review. Primary care provider offices were contacted if there were gaps in medical records, and the Vermont Immunization Registry was cross-referenced for accuracy regarding receipt of vaccinations. Patients with incomplete data were excluded.

### Statistics

Comparisons between the historic and prospective groups were made using Wilcoxon rank-sum tests for continuous variables and chi-square analysis for categorical variables. The Fisher exact test was substituted for chi-square when cell sizes were small ( $n < 5$ ). Logistic regression was used to assess for any correlation between composite score and risk of OPSI and sepsis-free survival. Because the control group was historic and thus had a longer follow-up time, making it more likely to achieve a secondary outcome, we performed a survival analysis and generated Kaplan-Meier survival estimates. For all outcomes, a  $P$  value  $< .05$  was considered significantly different. All analyses were performed using Stata, version 16.0 (StataCorp LLC, College Station, TX, USA).

## RESULTS

### Patient Characteristics

There were 130 patients in the historic control group. Two of these patients were missing data for the primary outcomes and were excluded, leaving 128 historic control patients. Fifty patients were included in the prospective intervention group, with no exclusions, and all received ID consultation. Baseline characteristics between the control and intervention groups, respectively, were age: mean (SD), 56.2 (17.7) years and 58.1 (19.3) years ( $P = .40$ ); and female gender: 48.4% and 48.0% ( $P = .96$ ).

### Outcomes

Comparison between groups of all primary and secondary outcomes is shown in Table 1. There were statistically significant improvements in 9 of the 11 primary outcomes (no significant improvements in receipt of first meningococcal serotype ACWY or Hib vaccination) in the intervention arm as compared with the historic controls. There was a statistically significant decrease in the rate of OPSI in the intervention group (27% vs 6.0%;  $P = .01$ ), though not in OPSI-related death

**Table 1. Comparison of Primary and Secondary Outcomes for the Historic Control and Prospective Intervention Groups**

Primary Outcomes	Historic Control Group (n = 128), No. (%)	Prospective Intervention Group (n = 50), No. (%)	P Value
PCV13 <sup>a</sup>	58 (45)	49 (98)	<.001
PPSV23 <sup>b</sup>	117 (91)	50 (100)	.036
PCV13/PPSV23 timing <sup>c</sup>	39 (31)	46 (92)	<.001
Meningococcal #1 <sup>d</sup>	111 (87)	48 (96)	.103
Meningococcal #2	23 (18)	43 (86)	<.001
Meningococcal/PCV13 timing <sup>e</sup>	24 (19)	43 (86)	<.001
Hib <sup>f</sup>	109 (85)	47 (94)	.132
Annual influenza <sup>g</sup>	49 (39)	49 (98)	<.001
Pill-in-pocket Rx <sup>h</sup>	2 (2)	47 (94)	<.001
Infection risk education <sup>i</sup>	26 (20)	50 (100)	<.001
±14 d from splenectomy <sup>j</sup>	70 (55)	46 (92)	<.001
Secondary Outcomes	No. (%)	No. (%)	P Value
Postsplenectomy sepsis	34 (27)	3 (6)	.010
Death	35 (27)	5 (10)	.016
Death due to postsplenectomy sepsis	7 (6)	0 (0)	.193

<sup>a</sup>PCV13: 13-valent pneumococcal conjugate vaccine.

<sup>b</sup>PPSV23: 23-valent pneumococcal polysaccharide vaccine.

<sup>c</sup>Correct timing of PCV13 and PPSV23 in relation to each other. Asplenic guidelines recommend that PCV13 be given first, followed by PPSV23 no sooner than 8 weeks later. If PPSV23 is given first, then PCV13 should be delayed for 1 year.

<sup>d</sup>Meningococcal serotype ACWY vaccine, which is typically a 2-dose series.

<sup>e</sup>Correct timing of PCV13 and meningococcal serotype ACWY vaccination. Certain meningococcal serotype ACWY vaccines should be delivered at least 4 weeks after PCV13 because of potential for interference with PCV13 immune response.

<sup>f</sup>Hib: *Haemophilus influenzae* serotype-B vaccination.

<sup>g</sup>Annual influenza vaccination provided a majority of follow-up years.

<sup>h</sup>Prescription written for on-demand antibiotics for fever or first signs of OPSI, either levofloxacin 750 mg or amoxicillin/clavulanic acid 875/125 mg.

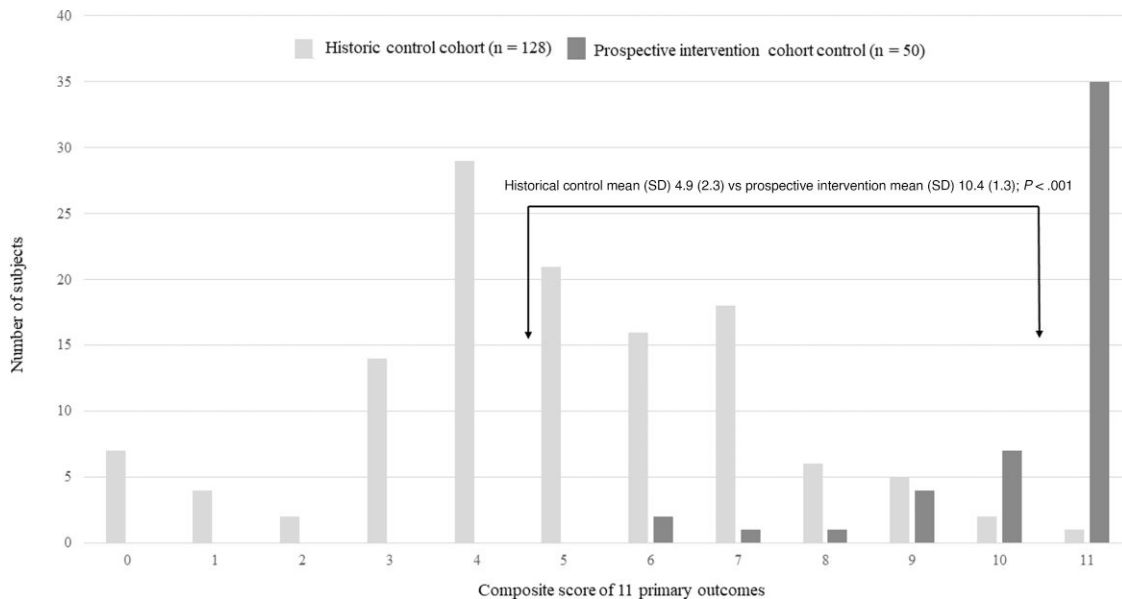
<sup>i</sup>Documentation of patient education on asplenic care and infection prevention.

<sup>j</sup>Correct timing of all vaccines in relation to the splenectomy. Studies suggest an inferior immune response if vaccines are given within 14 days before or after splenectomy; thus it is recommended to complete (if elective) or start (if urgent) asplenic vaccinations 14 days before or after splenectomy.

(6.0% vs 0.0%;  $P = .19$ ), in unadjusted head-to-head comparisons.

The distribution of care for the asplenic patient composite scores, with values ranging from 0 to 11 based on achieving each primary outcome, is shown in Figure 1. The intervention group had a statistically significantly higher composite score than the historic controls (mean [SD], 10.4 [1.3] vs 4.9 [2.3];  $P < .001$ ). Only 1 of the 128 (0.8%) control patients had a perfect composite score of 11, whereas 35 of 50 (70%) of the intervention patients received a perfect score ( $P < .001$ ). We found across all participants that a higher composite score was significantly associated with a lower risk of OPSI (odds ratio [OR], 0.81; 95% CI, 0.74–0.95;  $P = .006$ ) and OPSI-related death (OR, 0.53; 95% CI, 0.36–0.77;  $P = .001$ ).

Although OPSI and OPSI-associated death were more frequent in the control group, there were 1004 person-years of follow-up in the historic group vs 90 person-years of follow-up



**Figure 1.** Composite scores of the 11 primary outcomes on care for the asplenic patient. The 11 primary outcomes of care for the asplenic patient were combined into a single composite score. The number of patients in the prospective intervention and historic control groups achieving each composite score, with a range of 0 to 11, is shown. The prospective intervention group had a higher mean (SD) composite score (10.4 [1.3]) than did the historic control group (4.9 [2.3];  $P < .001$ ), suggesting that they received more complete asplenic patient care. The proportion of patients receiving “perfect” care for the asplenic patient, defined as achieving all 11 of the primary outcomes, increased from 0.8% to 70% ( $P < .01$ ).

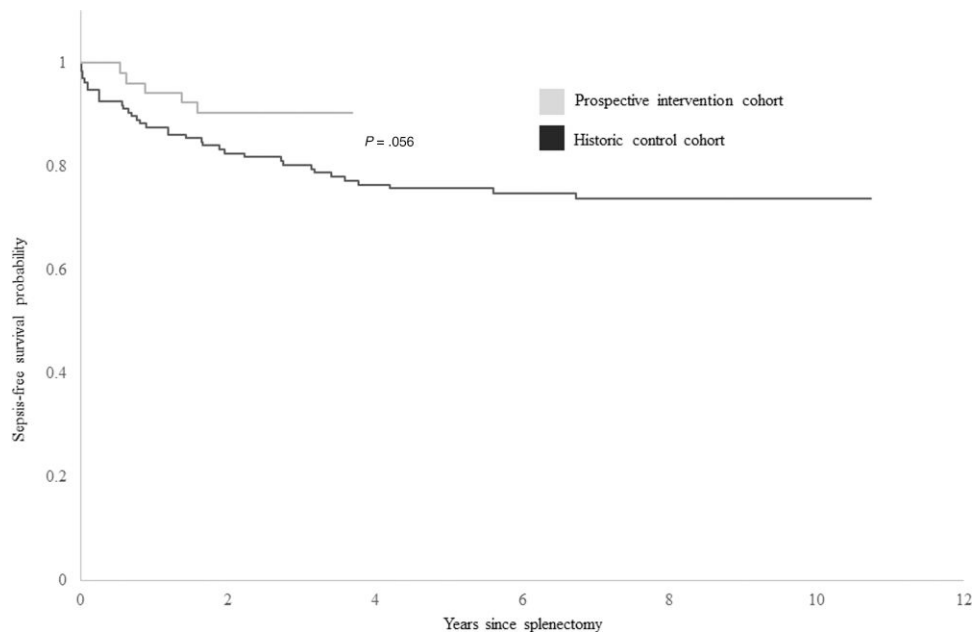
in the prospective intervention group, a consequence of the quasi-experimental study design, making these outcomes more likely in the controls. A survival analysis (Figure 2) showed no statistically significant difference in incidence of OPSI-free survival between the groups ( $P = .056$ ), though there was a trend toward improvement in the prospective intervention arm.

## DISCUSSION

We report here the effect of standardized, prospective ID physician involvement in care on outcomes of asplenic patients. We found that the intervention resulted in significant improvements to vaccination, patient education, and access to prophylactic antibiotics in the prospective arm, with 9 of 11 of the primary outcomes showing significant improvement in the intervention group as compared with controls. There was a trend toward increased OPSI-free survival in the intervention group that did not reach statistical significance ( $P = .056$ ), likely as a result of the study being underpowered. The proportion of patients receiving “perfect” care for the asplenic patient, defined as achieving all 11 of the primary outcomes, increased from 0.8% to 70% ( $P < .01$ ), and we demonstrated that higher composite scores were associated with significantly decreased risk of OPSI and OPSI-related death across groups.

Our study is one of the first to prospectively capture all patients undergoing splenectomy and ensure that asplenic patient care is started as soon as possible pre- or postoperatively, as well

as to look at a specific intervention’s effect on rates of OPSI and OPSI-related death. This is important because most prior literature on improving care for the asplenic patient has retrospectively identified patients and outcomes tend to include only vaccination rates. Mitchell et al. retrospectively identified 129 asplenic patients in a single center, were able to get 28 (29%) into travel clinic for asplenic patient care, and demonstrated improvement in 3 of 4 vaccine goals for this cohort [31]. In addition, Kim et al. retrospectively identified 113 asplenic patients in a single center and prospectively reached out to them regarding care for the asplenic patient, with asplenic guideline compliance increased from 2.7% to 82.7% ( $P < .01$ ), though sometimes multiple years after the splenectomy had occurred [22]. Finally, Rieg et al. conducted a recent prospective single-center study in Germany looking at the impact of referral to an outpatient clinic dedicated to care for the asplenic patient who had received a splenectomy and showed improvements in pneumococcal vaccination rates, though a sizable portion were not seen for 3 to  $\geq 12$  months postsplenectomy [39]. We have identified in this study that standardized, prospective involvement of an ID physician significantly improves care for the asplenic patient. A benefit of our intervention over prior studies is that an infectious diseases clinician can be involved right away and take immediate responsibility for asplenic patient care, without the need for the patient to wait for outpatient follow-up or for the health care provider to identify such patients retrospectively and then create interventions to catch up. For the ID provider, taking on care for asplenic patients



**Figure 2.** Survival analysis of the prospective intervention and historic control groups. OPSI-free survival probability of the prospective intervention and historic control groups is shown. Because this was a quasi-experimental study design comparing a prospective intervention group vs a historic control group, there was longer-term follow-up for the controls (1004 person-years of follow-up in the historic group vs 90 person-years in the prospective intervention group). There was no statistically significant difference in incidence of OPSI-free survival between the groups ( $P = .056$ ), though there was a trend toward improvement in the prospective intervention arm.

both fulfills the health care needs of a chronically underserved population and may create novel productivity gains. Additionally, as a widely available resource, this use of ID providers is immediately scalable to regional, state, and national asplenic patient care needs [40–42].

Our study has several limitations. This was a single-center study and was likely underpowered to detect actual differences in rates of OPSI and OPSI-related death, though we did show a nonsignificant trend toward benefit. The quasi-experimental design allows for potential unaccounted confounding differences between the prospective intervention group and the historic controls. We did not compare comorbid conditions between groups, allowing for potential confounding. Our composite score of primary outcomes is unvalidated and may over- or underestimate the relative benefit of any individual factor, though it was a useful tool for looking at care for the asplenic patient globally, and further studies may validate a tool to score what interventions truly matter for care for the asplenic patient.

## CONCLUSIONS

Despite widely available guidelines on what care of the asplenic patient should entail, in the real world most studies to date have demonstrated significant deficiencies in its delivery [1]. We have identified that involving ID providers at the outset can markedly improve care for asplenic patient outcomes. While future studies should elucidate more clearly which specific

interventions help improve outcomes in this population, given the critical need to make improvements from the status quo, we believe widespread implementation of this intervention is supported by our data.

## Notes

**Author contributions.** All co-authors have seen and agree with the contents of the manuscript and have contributed significantly to the work.

**Financial support.** The authors received an internal grant from University of Vermont Medical Center department of internal medicine to support this work.

**Patient consent.** The study was approved by the University of Vermont Institutional Review Board (UVM IRB). The patient's written consent was obtained for all patients in the prospective intervention cohort. Written consent was not required by the UVM IRB for patients in the historic control cohort.

**Potential conflicts of interest.** The authors: no reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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