

# Novel Preoperative Patient-centered Surgical Wellness Program Impacts Length of Stay Following Pancreatectomy

MAZHAR SOUFI<sup>1,2\*</sup>, DANIELLE K. DEPERALTA<sup>1\*</sup>, RACHEL SIMPSON<sup>1,2</sup>, KATELYN FLICK<sup>1,2</sup>,  
MICHELE T. YIP-SCHNEIDER<sup>1,2,3,4</sup>, CHRISTIAN M. SCHMIDT II<sup>1,2</sup>, MOLLY KILBANE<sup>5</sup>,  
CAMERON COLGATE<sup>1</sup>, KRISTEN E. KELLEY<sup>5</sup>, WILLIAM WOODEN<sup>1</sup>, EUGENE P. CEPPEA<sup>1,2</sup>,  
MICHAEL HOUSE<sup>1</sup>, NICHOLAS ZYROMSKI<sup>1</sup>, ATILLA NAKEEB<sup>1</sup> and C. MAX SCHMIDT<sup>1,2,3,4</sup>

<sup>1</sup>Department of Surgery, Indiana University School of Medicine, Indianapolis, IN, U.S.A.;

<sup>2</sup>Indiana University Health Pancreatic Cyst and Cancer Early Detection Center, Indianapolis, IN, U.S.A.;

<sup>3</sup>Walther Oncology Center, Indianapolis, IN, U.S.A.;

<sup>4</sup>Indiana University Simon Cancer Center, Indianapolis, IN, U.S.A.;

<sup>5</sup>Infection Prevention, Indiana University Health, Indianapolis, IN, U.S.A.

**Abstract.** *Background/Aim:* We created a novel, preoperative wellness program (WP) that promotes recovery. This study assessed its impact on patient outcomes after pancreatectomy. *Patients and Methods:* Pancreatoduodenectomies (PD) and distal pancreatectomies (DP) performed from 2015 to 2018 were reviewed using our institutional NSQIP database. Patients in the WP had their medical conditions optimized and were provided with the following: chlorhexidine, topical mupirocin, incentive spirometer, and immune-nutrition supplements. *Results:* Out of a total of 669 pancreatectomy patients (411 PD, 258 DP), 308 were enrolled in the WP (188 PD, 120 DP). In the PD subgroup, on multivariable analysis (MVA), the WP patients had shorter lengths of hospital stay (LOS) (12 vs. 10 days,  $p < 0.001$ ). On MVA, WP patients had less post-op transfusion (20 vs. 10%,  $p = 0.027$ ). For the combined groups on MVA, LOS continued to be significant ( $OR = 0.89$ ,  $95\% CI = 0.82-0.97$ ,  $p < 0.007$ ). *Conclusion:* A preoperative patient centered WP may reduce the length of stay.

Pancreaticoduodenectomy (PD) is a high-risk procedure. In 1935, Whipple *et al.* reported the first case series, describing a two-stage procedure, with associated morbidity of 90% and

mortality rate approaching 29% (1). The safety profile of PD has dramatically improved with high-volume centers reporting morbidity rates of 40-60% and mortality rates of 2-4% (2-4). Beyond allocation of complex pancreatic surgery to high-volume centers, several interventions have proven effective in reducing morbidity associated with pancreatectomy.

Healthcare associated infections (HAIs) affect 4% of hospitalized patients (5, 6), of which 20% are surgical site infections (SSIs). SSI is the most common surgical complication, with an incidence of 2-5% following inpatient operations (6), and up to 28% following complex gastrointestinal procedures (3-5). SSI is associated with increased length of stay (LOS), readmission, and an estimated national financial burden of 3-10 billion dollars (6, 7). SSIs are thought to be preventable in up to 60% of cases with adherence to current guidelines (6, 8, 9). These include the use of surgical clippers, chlorhexidine scrub, preoperative antibiotics, and nutritional optimization. Methicillin resistant staph aureus (MRSA) is the most common pathogen involved in SSIs from non-colorectal surgical procedures. Preoperative decolonization with topical mupirocin and chlorhexidine gluconate bath scrub decreases MRSA-associated SSI (6, 8, 9).

Smoking cessation has also been associated with decreased SSI and post-operative pulmonary complications (10). Other simple measures include incentive spirometry, ambulation, and increased physical activity in the peri-operative period (11, 12). Finally, poor nutritional status is associated with increased post-operative complications, poor wound healing and decreased functional quality of life (13). Nutritional optimization in the preoperative setting can replenish micronutrient deficiencies, provide a positive nitrogen balance, and optimize the immune response (14, 15).

At a single high-volume academic medical center, a preoperative patient-centered surgical wellness program (WP)

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\*These Authors contributed equally to this work.

*Correspondence to:* C. Max Schmidt, MD, Ph.D., MBA, FACS, Department of Surgery, Indiana University School of Medicine, 545 Barnhill Drive, Emerson Hall 129, Indianapolis, IN 46202, U.S.A. Tel: +1 3179488358, e-mail: maxschmi@iupui.edu

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was launched. This program was part of an institutional initiative to improve postoperative patient outcomes. The objective of this study was to assess the impact of the WP on patient outcomes following pancreatic resection.

**Patients and Methods**

*Description of the intervention.* As part of an effort to improve surgical outcomes, a WP was launched in January 2016. Prior to its launch, patient feedback was an important element in designing clear and concise instructions for the WP. The WP typically starts with a patient’s referral by their surgeon. The WP consists of a visit to the preadmission testing (PAT) Clinic where acute/chronic medical conditions are identified, and referrals are made for testing or to medical subspecialty clinics where indicated. Patients are also educated on the benefits of increasing daily baseline physical activities, smoking/alcohol cessation, and the following bundled components: mupirocin topically for the nares, chlorhexidine bath scrub, an incentive spirometer, and immune-nutrition supplements [Impact Advanced Recovery® (AR) drink]. These components were bundled into a sporty, red, roller bag provided to patients without cost. Patients who did not get referred for the WP, did not visit PAT Clinic and did not receive the red roller bag with bundled components. These patients were the control group. Approximately 46% of patients that underwent pancreatic resection were enrolled in the WP. The PAT visit took place between 3-40 days prior to surgery (average 2 weeks).

*Patient population.* Between June 2015-June 2018, a total of 669 patients underwent pancreatectomy (411 PD, 258 DP). Of these, 46% (n=308; 188 PD, 120 DP) were enrolled in the WP. Using the institutions prospectively gathered National Surgical Quality Improvement Program (NSQIP) database, a retrospective review was performed. Patients were categorized into 2 groups: those enrolled in the WP and those who were not (control group). Patient demographics, comorbidities, and outcomes including complications were noted.

*Variables of interest.* Outcomes data were collected from medical records, patient surveys, as well as staff feedback. Outcome variables of interest included surgical site infection SSI, clinical documented improvement (CDI), ventilation associated events (VAE), MRSA, postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE), as well as patient safety indicators PSI-90. PSI-90 is a nationally recognized quality measure. Although some of the PSI-90 variables were irrelevant to the study (incidental puncture, laceration, pneumothorax), they constituted only a small percentage of the data presented, with most of the cases coming from relevant indicators such as post-operative respiratory failure, sepsis, wound infection, and acute kidney injury. The international study group of pancreatic surgery (ISGPS) updated 2016 criteria, were used to define DGE and POPF, respectively (16, 17). Outcomes per individual wellness component compliance were not analyzed due to lack of quality data and inadequate statistical power. The Indiana University Institutional Review Board approved the conduct of this study, and data storage was compliant with the Health Insurance Portability and Accountability Act.

*Compliance.* All patients enrolled in the WP were referred and seen in the PAT Clinic, underwent a medical evaluation and received

Table I. Comparison of demographics and perioperative variables for PD patients with and without enrollment in the WP program.

Covariate	PD Patients only		p-Value
	Non-WP (n=223) n (%) or mean (SD)	WP (n=188) n (%) or mean (SD)	
Age	65.33 (13.16)	63.65 (12.15)	0.158
BMI	27.01 (6.06)	27.79 (5.63)	0.116
Gender (male)	111 (49.8)	90 (47.9)	0.770
Race (non-white)	20 (9)	15 (8)	0.731
Diabetes	54 (24.2)	55 (29.3)	0.263
Hypertension	131 (58.7)	105 (55.9)	0.619
Steroid/Immunosuppressant use	3 (1.3)	6 (3.2)	0.311
Weight loss >10%	44 (19.7)	42 (22.3)	0.545
Received preop transfusion(s)	5 (2.2)	0 (0)	0.066
Open operative approach	223 (100)	185 (98.4)	0.093
Soft gland	109 (52.2)	82 (44.6)	0.154
Pancreatic duct size			0.209
<3 mm	35 (15.7)	39 (20.7)	
3-6 mm	149 (66.8)	111 (59.0)	
>6 mm	26 (11.7)	30 (16.0)	
Preop obstructive jaundice	80 (35.9)	59 (31.4)	0.350
Preop biliary stenting	114 (51.1)	106 (56.4)	0.320
Preop chemotherapy	30 (13.5)	39 (20.7)	0.058
Preop radiation therapy	3 (1.3)	3 (1.6)	1.000
Albumin	3.7 (0.58)	3.84 (0.56)	0.024
Bilirubin	1.94 (3.12)	1.92 (3.72)	0.494
Hematocrit	36.64 (5.72)	38.39 (5.11)	0.007
INR	1.11 (0.15)	1.12 (0.24)	0.586
Procedure duration (min)	283.61 (92.92)	283.73 (84.1)	0.534

SD: Standard deviation; BMI: body mass index; INR: international normalized ratio.

instructions about preoperative wellness. Overall patient reported compliance (partial or full) with the individual wellness components of the WP among both PD and DP groups was 55%, and one third of patients completed all components of the WP. A nurse in the preoperative holding area handed out a sheet to the patients to self-report compliance with each of the individual components of the bundle. Unfortunately, there were several barriers to receiving this information from patients the day of surgery. Moreover, the small sample of patients included in this study along with the insufficiently powered data were limiting factors to report a meaningful analysis of the effect of each individual component.

*Statistical analysis.* Chi-squared and t-tests were used to examine potential differences in perioperative variables. Potential confounders were included in multivariable logistic regression and Poisson regression (for modeling length of stay) models.

**Results**

*Pancreatoduodenectomy (PD).* Baseline characteristics were comparable between the groups (Table I). Enrollment in the WP was associated with a significant reduction in LOS from

Table II. Post-operative course and outcomes for PD patients with and without enrollment in WP - univariable analysis.

Covariate	PD Patients only		p-Value
	Non-WP (n=223) n (%)	WP (n=188) n (%)	
Deep SSI	5 (2.2)	0 (0)	0.094
Superficial SSI	4 (1.8)	4 (2.1)	0.816
DGE	42 (18.8)	30 (16)	0.448
Death	6 (2.7)	3 (1.6)	0.473
Organ SSI	26 (11.7)	19 (10.1)	0.619
Percutaneous drain(s) placed	12 (5.4)	14 (7.4)	0.401
Pneumonia	6 (2.7)	6 (3.2)	0.771
Septic shock	9 (4)	5 (2.7)	0.459
Needed postop transfusions	69 (30.9)	44 (23.4)	0.090
UTI	5 (2.2)	4 (2.1)	0.940
Vein thrombosis	9 (4)	5 (2.7)	0.459
Had related readmission	34 (15.2)	18 (9.6)	0.090
LOS [days, mean (SD)]	12 (10)	9.6 (8.0)	<b>&lt;0.001</b>

SSI: Surgical site infection; UTI: urinary tract infection; LOS: length of stay. p-Values were obtained using logistic regression and negative binomial regression (for length of stay). Bold values indicate statistical significance.

12 to 9.6 days (Table II), univariable index ratio (IR) of 0.80 (95%CI=0.71-0.91,  $p<0.001$ ). Participation in the program was also associated with trends toward decreased deep SSI (OR=0.1, CI=0.01-1.48,  $p=0.094$ ), post-operative transfusions, (OR=0.68, 95%CI=0.44-1.06,  $p=0.090$ ), and rates of readmission (OR=0.59, 95%CI=0.33-0.99,  $p=0.090$ ) on univariable analysis. On multivariable analysis, only LOS continued to have significance (OR=0.85, 95%CI=0.77-0.94,  $p<0.001$ ).

*Distal pancreatectomy (DP)*. Slight differences in baseline characteristics were noted between cohorts. Patients in the non-intervention group were more likely to have an open procedure (90 vs. 76.7%,  $p=0.003$ ), receive pre-operative chemotherapy (78 vs. 39.3%,  $p<0.001$ ), and radiation therapy (9.7 vs. 0%,  $p=0.024$ ) (Table III). DP patients that received the WP were less likely to receive postoperative blood transfusion (OR=0.45, 95%CI=0.22-0.91,  $p=0.027$ ) (Table IV). This finding-maintained significance on multivariable analysis (OR=0.38, 95%CI=0.19-0.9,  $p=0.027$ ). There was a non-significant trend toward shorter LOS (7.3 vs. 6.5 days) on univariable analysis (OR=0.85, 95%CI=0.77-1.03,  $p=0.11$ ).

*Pancreatoduodenectomy and distal pancreatectomy combined*. On combined assessment of all patients that underwent pancreatic resection, the two groups had comparable demo-

Table III. Comparison of demographics and perioperative variables for DP patients with and without enrollment in the WP.

Covariate	Distal patients only		
	Non-WP (n=138) n (%) or mean (SD)	WP (n=120) n (%) or mean (SD)	p-Value
Age	57.63 (13.79)	58.07 (15.84)	0.427
BMI	28.51 (6.3)	28.55 (6.69)	0.804
Gender (male)	69 (50)	57 (47.5)	0.707
Race (non-white)	13 (9.4)	13 (10.8)	0.838
Diabetes	34 (24.6)	36 (30)	0.400
Hypertension	71 (51.4)	53 (44.2)	0.265
Steroid/Immunosuppressant Use	3 (2.2)	1 (0.8)	0.622
Weight loss >10%	11 (8)	18 (15)	0.078
Received preop transfusion(s)	3 (2.2)	0 (0)	0.251
Open operative approach	125 (90.6)	92 (76.7)	<b>0.003</b>
Soft gland	4 (36.4)	16 (45.7)	0.726
Preop chemotherapy	99 (78)	46 (39.3)	<b>&lt;0.001</b>
Preop radiation therapy	3 (9.7)	0 (0)	<b>0.024</b>
Albumin	3.97 (0.55)	4.01 (0.54)	0.527
Bilirubin	0.53 (0.27)	0.52 (0.26)	0.828
Hematocrit	38.49 (5.87)	39.2 (5.31)	0.337
INR	1.09 (0.15)	1.14 (0.22)	<b>0.009</b>
Procedure duration (min)	189.91 (59.63)	183.24 (64.83)	0.285

BMI: Body mass index; INR: international normalized ratio. Bold values indicate statistical significance.

graphics with regards to gender, age, race, ethnicity, and ASA. In comparison to patients in the WP, controls were more likely to have required pre-operative transfusion (2.2 vs. 0.2 %,  $p=0.013$ ), presented with jaundice (32.1 vs. 22.3%,  $p=0.014$ ), and/ or received pre-operative chemotherapy (36.9 vs. 27.9%,  $p=0.017$ ). On univariable analysis, implementation of the WP was associated with a significant decrease in LOS (10.2 vs. 8.4 days,  $p<0.001$ ), less post-operative transfusion requirements (OR=0.61, 95%CI=0.42-0.88,  $p=0.008$ ), and a trend towards decreased deep SSIs (OR=0.08, 95%CI=0.01-1.12,  $p=0.061$ ) and readmission rates (OR=0.68, 95%CI=0.43-1.08,  $p=0.107$ ). On multivariable analysis, LOS continued to maintain statistical significance (IR=0.89, 95%CI=0.82-0.97,  $p<0.007$ ).

**Discussion**

Enhanced recovery after surgery (ERAS) protocols are associated with improved outcomes and shorter length of stay (18, 19). The ERAS Group published guidelines for colorectal procedures, which are widely accepted (19) and similar protocols have been applied to other surgical specialties including plastics, orthopedics, gynecologic oncology, foregut, and liver surgery (19-22). A growing body of literature

Table IV. Post-operative course and outcomes for DP patients with and without enrollment in WP - univariable analysis.

Covariate	Distal patients only		p-Value
	Non-WP	WP	
	(n=138) n (%)	(n=120) n (%)	
Deep SSI	2 (1.4)	0 (0)	0.287
Superficial SSI	1 (0.7)	1 (0.8)	0.932
DGE	2 (7.1)	2 (2.6)	0.897
Death	2 (1.4)	2 (1.7)	0.897
Organ SSI	15 (10.9)	8 (6.7)	0.249
Percutaneous drain(s) placed	4 (14.3)	6 (7.9)	0.354
Pneumonia	6 (4.3)	1 (0.8)	0.123
Septic shock	3 (2.2)	2 (1.7)	0.783
Needed postop transfusions	28 (20.3)	12 (10)	<b>0.027</b>
UTI	0 (0)	5 (4.2)	0.058
Had related readmission	20 (14.5)	15 (12.5)	0.645
LOS [days, mean (SD)]	7.3 (6.2)	6.5 (3.9)	<0.111

SSI: Surgical site infection; UTI: urinary tract infection; LOS: length of stay. Bold values indicate statistical significance.

supports implementation of ERAS for pancreatic surgery; however, many pancreatic surgeons have been slow to incorporate these protocols. A prospective trial and meta-analysis with 3,700 pancreatectomy patients reported improved patient outcomes and/or decreased length of stay with implementation of ERAS protocol focused on early alimentation, drain removal, and minimization of narcotics and intravenous fluids (23-27). The effect of the WP has been previously established on a large scale across multiple surgical specialties at our institution; implementation was associated with a reduction in post-operative complications such as SSIs, particularly among patients with ASA score of 3 or higher (28). The present study focused on pancreatic surgery patients in the preoperative settings and demonstrated expedited recovery.

A multimodality pre-operative rehabilitation program assesses patients physiologic reserve through analysis of acute/chronic medical conditions as well as nutritional status. In the present study, acute/chronic medical conditions were identified during the PAT Clinic visit for each patient enrolled in the WP and referrals made to medical subspecialty clinics when needed. In addition, these patients were educated about the importance of increasing daily physical activities, avoiding modifiable risk factors such as smoking/alcohol cessation and individual components of a wellness bundle. Although a bundled approach to quality improvement initiatives is challenged by difficulties in discerning the impact of each component, the educational meeting and referral process likely played very important roles in patient outcome.

Additionally, when considering specific components of the red bag, the immuno-nutrition drink (ID) emerges as a strong candidate in the present study for the following reasons. Malnutrition is prevalent among pancreatic surgery patients and is marked by the presence of dysfunctional T-cells, coagulopathy, as well as deconditioning after surgery. Invasive surgery is associated with suppression of helper T cell activity and cytokine production (14, 29, 30). Supplemental ID has been postulated to modulate post-operative changes, potentially ameliorating the impact of surgical stress on T-cell impairment (14). Several studies have demonstrated improved postoperative outcomes and decreased length of stay with ID (14, 23-27, 31). Furthermore, the immuno-nutrition drink used in the current study contains arginine, a conditionally essential amino acid. Although arginine is synthesized by a variety of body cell types, endogenous synthesis may not meet cellular demand in highly stressful conditions experienced after major surgeries. Arginine supports the immune system by promoting T-cell growth and replication; in addition, it is a precursor for nitrous oxide (NO), which increases gut oxygenation and micro-perfusion (14). Another key ingredient in the immuno-nutrition drink is essential fatty acids such as linoleic and linolenic acid, provided in the form of Omega-3 & 6, respectively. Omega fatty acids preserve intestinal integrity and decrease injury from peritoneal air exposure, which in turn would mitigate the systematic inflammatory response in the post-operative setting. Tan and colleagues established a direct correlation between the duration of peritoneal air exposure and mucosal barrier injury using animal models (32). Finally, the immune-nutrition drink contains nucleotides, which can serve as building blocks for active DNA and RNA replication during cellular regeneration in post-operative periods. There have been multiple studies reporting positive outcomes with nutritional status optimization in pancreatic surgery patients (33-35). However, ERAS Society has rated the level of evidence for the application of immune-nutrition to pancreatic patients as moderate, with a low recommendation to its application (36). The moderate level of evidence leaves the door open for studies such ours to assess the utility of immune-nutrition drinks. The “low” rated recommendation could be explained by the variability of the commercially available products evaluated. The drink used in the present study, to our knowledge, is the only validated drink with the three key ingredients detailed above.

In our study, the WP was extremely cost effective. The cost of the bundled components was estimated at fifty dollars per patient (n=308), bringing the overall cost to \$15,400. A one-day delay in discharge at our institution has an estimated cost of \$1,600. We report that patients who received the WP and underwent PD (n=188) stayed in the hospital on average 2.4 days less. Adjusting the calculations to the nearest

decimal change for an average two days difference brings the total cost savings to approximately \$601,600.

We also analyzed the effect of the WP on major liver resections and observed similar trends (unpublished results). Specifically, we found consistency in the reduction of LOS, as well as post-operative blood transfusion requirements. These results suggest that the WP should also be considered for potential application to hepatobiliary surgeries. In support, a reduction in LOS, as well as overall complications, has been previously reported in a systematic review of the effect of ERAS on liver resections (37).

This study has several limitations. First, intervention and control groups were not randomized nor matched, which introduces the possibility of selection bias. However, the intervention group was characterized as having comorbidities prompting a referral by the operating surgeon to the PAT Clinic. Next, detailed compliance data were not available, limiting our ability to investigate the effect that each individual component had on the outcome. Moreover, the number of patients evaluated would likely limit the statistical power of individual component analysis. Finally, despite collecting data prospectively, our study was non-randomized, retrospective and from a single institution. Understanding these limitations, future goals will be targeted toward achieving more efficient and convenient timing for WP counseling, maximizing delivery of WP instructions to optimize compliance, and developing a more reliable method of reporting compliance.

## Conclusion

Adoption of a novel, preoperative, patient-centered WP can improve outcomes for pancreatic surgery patients by reducing postoperative infectious complications, blood transfusion requirements, as well as LOS. Future efforts should focus on delivering the care within a timeframe that maximizes efficacy, ideally remotely using technology such as video-assistive devices, as well as optimizing compliance among pancreatic surgery patients.

## Conflicts of Interest

The Authors have no conflicts of interest to disclose regarding this study.

## Authors' Contributions

Soufi, DePeralta, Schmidt: conception/design of the work; data acquisition, analysis, interpretation; manuscript drafting/revision/final approval; agreement to accountability. Simpson, Flick, Yip-Schneider, Schmidt II, Kilbane, Kelley, Wooden, Ceppa, House, Zyromski, Nakeeb: Data acquisition, interpretation; manuscript revision/final approval; agreement to accountability. Colgate: Data analysis, interpretation; manuscript revision/final approval; agreement to accountability.

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