SUPPLEMENTARY MATERIALS

Supplementary Table S1. Database Search Strategies and Results

Date	Database	Search Query	Hits
2025-04-02	PubMed	("Negative-Pressure Wound Therapy"[Mesh] OR "negative pressure wound therapy"[tiab] OR "NPWT"[tiab] OR "vacuum assisted closure"[tiab] OR "VAC"[tiab] OR "vacuum therapy"[tiab] OR "topical negative pressure"[tiab] OR "negative pressure dressing"[tiab] OR "negative pressure therapy"[tiab] OR "wound VAC"[tiab] OR "vacuum sealing"[tiab] OR "vacuum closure"[tiab]) AND ("Pancreaticoduodenectomy"[Mesh] OR "pancreaticoduodenectom*"[tiab] OR "pancreatoduodenectom*"[tiab] OR "Whipple"[tiab] OR "pancreatic resection"[tiab] OR "PD"[tiab] OR "pancreatic surgery"[tiab] OR "pancreatic operation"[tiab]) AND ("Surgical Wound Infection"[Mesh] OR "surgical site infection*"[tiab] OR "SSI"[tiab] OR "wound infection*"[tiab] OR "postoperative infection*"[tiab] OR "post-operative infection*"[tiab] OR "wound complication*"[tiab] OR "surgical wound complication*"[tiab] OR "wound healing"[tiab] OR "infection prevention"[tiab] OR "infection control"[tiab] OR "wound management"[tiab])	19
2025-04-02	Scopus	TITLE-ABS-KEY(("negative pressure wound therapy" OR "NPWT" OR "vacuum assisted closure" OR "VAC" OR "vacuum therapy" OR "topical negative pressure" OR "negative pressure dressing" OR "negative pressure therapy" OR "wound VAC" OR "vacuum sealing" OR "vacuum closure") AND ("pancreaticoduodenectom*" OR "pancreatoduodenectom*" OR "Whipple" OR "pancreatic resection" OR "pancreatic surgery" OR "pancreatic operation") AND ("surgical site infection*" OR "SSI" OR "wound infection*" OR "postoperative infection*" OR "post-operative infection*" OR "wound complication*" OR "surgical wound complication*" OR "wound healing" OR "infection prevention" OR "infection control" OR "wound management"))	27
2025-04-02	BASE	("negative pressure wound therapy" OR "NPWT" OR "vacuum assisted closure" OR "VAC" OR "vacuum therapy" OR "topical negative pressure" OR "negative pressure dressing" OR "negative pressure therapy" OR "wound VAC" OR "vacuum sealing" OR "vacuum closure") AND ("pancreaticoduodenectomy" OR "pancreaticoduodenectomies" OR "pancreatoduodenectomy" OR "pancreatoduodenectomies" OR "Whipple" OR "pancreatic resection" OR "pancreatic surgery" OR "pancreatic operation") AND ("surgical site infection" OR "surgical site infections" OR "SSI" OR "wound infection" OR "wound infections" OR "postoperative infection" OR "postoperative infections" OR "post-operative infection" OR "post-operative infections" OR "wound complication" OR "wound complications" OR "surgical wound complication" OR "wound healing" OR "infection prevention" OR "infection control" OR "wound management")	28
2025-04-02	Cochrane CENTRAL	("negative pressure wound therapy" OR "vacuum assisted closure") AND (Whipple OR pancreaticoduodenectom*) AND "surgical site infection*"	5
2025-04-02	ClinicalTrials.gov	("negative pressure wound therapy" OR "NPWT" OR "vacuum assisted closure" OR "VAC" OR "vacuum therapy") AND ("pancreaticoduodenectomy" OR "Whipple" OR "pancreatic surgery") AND ("surgical site infection" OR "wound infection" OR "SSI")	2

Supplementary Table S2. Detailed Inclusion and Exclusion Criteria

Included Studies (n=9)

Study	Design	Population	Intervention	Primary Reason for Inclusion
Andrianello et al. (2020) [10]	Prospective RCT	95 patients, major pancreatic resections	PICO NPWT vs standard dressing	High-quality RCT with SSI as primary outcome, high-risk population
Burkhart et al. (2017) [5]	Retrospective cohort	436 patients, pancreaticoduodenectomy	iVAC NPWT vs standard care	Large cohort with risk-stratified analysis, clear NPWT comparison
Greene et al. (2023) [2]	Historical cohort	175 patients, high-risk pancreaticoduodenectomy	Prevena NPWT vs conventional dressing	Recent study targeting high-risk patients, clear methodology
Gupta et al. (2017) [4]	Retrospective cohort	61 patients, Whipple procedure	NPWT vs traditional dressing	Direct NPWT comparison, pancreaticoduodenectomy-specific
Javed et al. (2019) [11]	RCT	123 patients, high-risk pancreaticoduodenectomy	PREVENA NPWT vs standard closure	High-quality RCT, industry-independent analysis, clear outcomes
Kuncewitch et al. (2019) [12]	Prospective RCT	73 patients, major pancreatectomy	NPWT vs standard dressing	RCT design with long-term follow-up, wound-specific outcomes
Lawrence et al. (2019) [13]	Prospective cohort	300 patients, pancreaticoduodenectomy	Bundle including PICO NPWT	Large prospective study, before-after design with clear methodology
O'Neill et al. (2019) [14]	RCT	40 patients (18 pancreatic)	PICO NPWT vs island dressing	Randomized design with pancreatic subgroup analysis
Shen et al. (2017) [1]	RCT	265 patients (pancreatic subset)	Polyurethane foam NPWT vs standard	Well-designed RCT with identifiable pancreatic surgery subgroup

Excluded Studies (n=14)

Study	Primary Reason for Exclusion	Detailed Justification
Zhang et al. (2022) [7]	Secondary research	Systematic review and meta-analysis, not primary research
Fowler & Barry (2020)	Wrong population	Mixed abdominal surgeries, insufficient pancreaticoduodenectomy-specific data
Zuckerman & Hallet (2021) [8]	Wrong study design	Editorial comment, not primary research
Woo et al. (2015)	Wrong population	Pilonidal sinus wounds, unrelated to pancreatic surgery
Tomita et al. (2018)	Wrong intervention	Sutures vs staples comparison, not NPWT evaluation
Mori et al. (2018)	Wrong population	Peritoneal dialysis exit sites, unrelated to pancreaticoduodenectomy
Poruk et al. (2016) [6]	Wrong intervention	SSI risk score development, no NPWT intervention
Leenen et al. (2018)	Wrong population	Peritoneal dialysis complications, unrelated to pancreatic surgery
Hut'an et al. (2014)	Wrong study design	Case report, insufficient evidence level
Lin et al. (2017)	Wrong population	Animal study on burn wounds, not clinically relevant
Magistri et al. (2016) [3]	Wrong intervention	Islet autotransplantation focus, incidental wound management mention
DeLeon et al. (2024)	Methodological concerns	High risk of selection bias, database coding issues
Lenet et al. (2022) [9]	Secondary research	Meta-analysis, included in background discussion
Kim et al. (2019)	Insufficient information	Abstract only, full methodology unavailable

Supplementary Table S3. Detailed Study Protocols and Co-interventions

Study	Patient Population	NPWT Protocol	Control Protocol	Co-interventions	Duration
Andrianello [10]	95 patients undergoing major pancreatic resections for periampullary neoplasms; High-risk criteria: BMI ≥30, diabetes, neoadjuvant therapy, ASA ≥3, Charlson ≥1, surgery >360 min, blood loss >1L	PICO portable NPWT device (Smith & Nephew); First dressing until POD3, second dressing until POD7; Continuous negative pressure	Sterile gauze initially, then OPSITE Post-Op Visible (Smith & Nephew) after POD3	Ampicillin 2g + sulbactam 1g at induction, repeated q3h; Antiseptic shower; 5% iodine povidone/chlorhexidine skin prep	POD 7
Burkhart [5]	436 patients undergoing pancreaticoduodenectomy over 21 months; Risk stratification based on preoperative factors	iVAC therapy (specific settings not detailed)	Standard wound closure and dressing (not specified)	Standard perioperative protocols (not detailed)	Not specified
Greene [2]	175 high-risk patients undergoing pancreaticoduodenectomy; High-risk defined by institutional criteria	Prevena Incision Management System (Acelity); Prevena Peel & Place for incisions ≤20cm; Prevena Customizable for longer incisions; 125 mmHg continuous pressure	Conventional pad film dressing with nonadherent pad, removed POD2	Preop antibiotics (cefazolin + metronidazole or pip/tazo if biliary stent); Chlorhexidine skin prep; Alexis wound protector; Hypothermia prevention; Glycemic control	7 days
Gupta [4]	61 patients undergoing Whipple procedure; Single surgeon, single institution	NPWT device (brand not specified) applied immediately post-closure	Traditional wound dressing (specific type not detailed)	Standard SSI reduction: wound protector, glove change before closure, perioperative antibiotics	7-10 days
Javed [11]	123 high-risk patients undergoing pancreaticoduodenectomy; High-risk: preop biliary drainage, neoadjuvant therapy	PREVENA Peel & Place Dressing (Acelity); Applied immediately after closure	Standard wound closure technique with conventional dressing	Preoperative antibiotic prophylaxis; Intraoperative forced air warming; Tight perioperative glycemic control	4 days
Kuncewitch [12]	73 patients undergoing major pancreatectomy (subset analysis from larger study)	NPWT device (specific brand not specified)	Standard surgical dressing (SSD)	Standard perioperative care protocols	POD 4

Lawrence [13]	300 patients undergoing pancreaticoduodenectomy; 150 pre-bundle vs 150 post-bundle implementation	PICO System (Smith & Nephew) as part of prevention bundle	Standard care protocols (pre-bundle period)	Bundle components: Alexis wound protector, bacitracin irrigation, gown/glove change for closure, NPWT dressing	POD 7 or discharge
O'Neill [14]	40 patients total (18 pancreatic resections); Stratified randomization by organ system	PICO NPWT (Smith & Nephew) applied immediately post-closure	Sterile island dressing	14-point SSI prevention protocol: preop antibiotics, skin prep, normothermia, euglycemia, other standard measures	7 days
Shen [1]	265 patients total including pancreatic resection subset; Mixed gastrointestinal and peritoneal surface malignancies	Polyurethane foam NPWT with 125 mmHg continuous negative pressure	Adhesive Primapore dressing (Smith & Nephew)	Standard perioperative care (not detailed by subgroup)	POD 4

Supplementary Table S4. Complete Patient Demographics and Risk Factors

Study	Sample Size (NPWT/Control)	Age (years)	Male (%)	BMI (kg/m²)	Diabetes (%)	Smoker (%)	Preop Biliary Drainage (%)	ASA Score	Other Risk Factors
Andriani ello [10]	46/49	Balanced between groups	Balanced between groups	High-risk criterion if ≥30	High-risk criterion	Not specified	Balanced between groups	High-risk if ≥3	Charlson index ≥1, surgery >360 min, blood loss >1L, neoadjuvant therapy
Burkhart [5]	120/316	Not specified	Not specified	Not specified	Not specified	Not specified	More common in iVAC group	Not specified	Obese patients more likely to receive iVAC; Prior abdominal surgery associated with complications
Greene [2]	61/114	66/65 (mean)	61%/61%	Not specified	39%/38%	34%/54% (p=0.005)*	79%/53% (p=0.006)*	Not specified	Significantly different smoking and biliary drainage rates between groups
Gupta [4]	25/36	61.1/64.1 (mean)	Not specified	24.0/25.7 (mean)	Not specified	20%/22%	48%/44%	Not specified	No significant baseline differences; Multivariate analysis performed
Javed [11]	62/61	Not specified	Not specified	Not specified	Not specified	Not specified	82.3%/83.6% (p=0.84)	Not specified	High-risk population; More neoadjuvant therapy in NPWT group (70.0% vs 54.1%, p=0.05)
Kuncewitch [12]	36/37	65 (range 35-85), both groups	55% overall	Balanced between groups	Similar between groups	Similar between groups	Not specified	Not specified	No significant differences in baseline characteris

									tics; Long-term follow-up (median 11 months)
Lawrence [13]	150/150 (bundle/pre-bundle)	Not specified directly	Not specified directly	No difference between SSI groups	No difference between SSI groups	No difference between SSI groups	47% overall; Higher in SSI group (76% vs 41%, p<0.001)	Not specified	Bundle vs pre-bundle comparison; Biliary drainage major risk factor for SSI
O'Neill [14]	20/20 (9/9 pancreatic)	60.8±10.3 (overall)	57.5% (overall)	31.7±7.0 (overall)	32.5% (overall)	17.5% (overall)	Not specified	Not specified	Small pancreatic subgroup; Pilot study design
Shen [1]	~36/37 (pancreatic subset)	Not specified by subgroup	Not specified by subgroup	Not specified by subgroup	Not specified by subgroup	Associated with SSI (p=0.017)	Not specified	Not specified	Mixed population; Lower preoperative albumin associated with SSI (p=0.0031)

*Statistically significant difference between groups

Supplementary Table S5. Complete Risk of Bias Assessment

Randomized Controlled Trials (Cochrane Risk of Bias Tool 2.0)

Study	Domain 1: Randomization Process	Domain 2: Deviations from Intended Interventions	Domain 3: Missing Outcome Data	Domain 4: Measurement of Outcome	Domain 5: Selection of Reported Results	Overall Risk of Bias	Comments
Andrianello [10]	Low Risk: Computer-generated randomization sequence; Allocation concealment maintained until intervention assignment	Some Concerns: Participants and personnel not blinded to intervention; May have influenced care decisions	High Risk: Reported dropouts due to relaparotomy (8 NPWT, 1 control) before POD7; Unbalanced missing data	Some Concerns: Subjective wound evaluations (VAS, SBSES) performed by single blinded physician; Potential for measurement bias	Low Risk: All pre-specified outcomes reported; Protocol violations documented	Moderate Risk	Industry provided dressing kits; Good methodology with some methodological concerns
Javed [11]	Low Risk: Simple randomization method with sealed envelope allocation concealment	Low Risk: Principal investigator blinded to group assignment when reviewing medical records for SSI confirmation	Low Risk: Complete outcome data available for all participants; No significant missing data	Low Risk: SSI diagnosis confirmed through blinded medical record review; Objective outcome assessment	Low Risk: All pre-specified outcomes reported; No evidence of selective reporting	Low-Moderate Risk	Industry funding disclosed (KCI/Acelity grant #125164); High-quality methodology
Kuncewitch [12]	Some Concerns: Described as prospective RCT but subset analysis; Allocation concealment method not clearly specified	Some Concerns: Blinding procedures not specified; Unclear if care providers were aware of allocation	Low Risk: Complete follow-up for median 11 months; All participants accounted for	Some Concerns: Outcome assessment procedures not fully detailed; Unclear if assessors were blinded	Low Risk: All pre-specified outcomes reported for the subset	Moderate Risk	Small sample size subset analysis; Limited methodological details provided

Observational Studies (Newcastle-Ottawa Scale)

Study	Selection (4 stars max)	Comparability (2 stars max)	Outcome (3 stars max)	Total Score	Quality Rating	Detailed Assessment
Burkhart [5]	2/4: Retrospective design; Limited representativeness details; No description of non-exposed cohort	1/2: Groups compared on basis of design; No evidence of control for	2/3: Assessment of outcome adequate; Follow-up duration not	5/9	Moderate	HIGH RISK due to limited outcomes reporting and minimal methodological

	selection; Ascertainment of exposure adequate	important confounders	specified; Some loss to follow-up			details in abstract format
Greene [2]	3/4: Historical control design; Exposed cohort representative; Non-exposed cohort drawn from same population; Ascertainment of NPWT adequate	1/2: Groups compared but significant baseline differences noted (smoking, biliary drainage); Limited confounder control	2/3: SSI assessment adequate; Follow-up duration appropriate; Complete follow-up	6/9	Moderate	HIGH RISK due to historical control design and post-hoc power calculation (40%)
Gupta [4]	2/4: Retrospective single-center study; Limited generalizability; Exposed cohort adequately selected; Ascertainment of exposure adequate	2/2: Groups well-balanced at baseline; Multivariate analysis performed controlling for confounders	3/3: Outcome assessment adequate; Follow-up duration sufficient; Complete outcome data	7/9	High	HIGH RISK due to single surgeon, single institution retrospective design limiting generalizability
Lawrence [13]	3/4: Prospective design; Exposed cohort representative; Non-exposed cohort from same institution; Clear intervention definition	1/2: Before-after comparison; Some baseline comparisons but bundle intervention prevents isolation of NPWT effect	3/3: Outcome assessment standardized; Adequate follow-up duration; Complete outcome reporting	7/9	High	HIGH RISK due to bundle intervention preventing isolation of NPWT effect; Cannot determine specific NPWT benefit
O'Neill [14]	3/4: Randomized design stratified by organ system; Representative exposed cohort; Appropriate control selection; Clear exposure definition	2/2: Randomized groups well-balanced; Stratification by organ system controls for important confounder	3/3: Outcome assessment standardized; Follow-up adequate; Complete outcome data for all participants	8/9	High	MODERATE RISK due to small sample size (n=40) and pilot study design; Otherwise well-conducted
Shen [1]	3/4: RCT design with randomization; Representative cohort; Appropriate control group; Clear intervention protocol	2/2: Randomized groups; Block randomization with varying sizes; Baseline characteristics balanced	2/3: Outcome assessment adequate but protocol deviations noted (4.9% early removal, 48.3% missed assessments); 39.2% follow-up outside window	7/9	High	MODERATE RISK due to significant protocol deviations and follow-up issues; Otherwise sound methodology