

Appendix 1 Database search strategy

PubMed

((“Pancreatic Neoplasms”[MeSH] OR “Pancreatic Cancer” OR “Locally Advanced Pancreatic Cancer” OR “LAPC” OR “Unresectable Pancreatic Cancer” OR “Borderline Resectable Pancreatic Cancer”) AND (“Neoadjuvant Therapy”[MeSH] OR “Neoadjuvant” OR “Induction Chemotherapy” OR “Chemoradiotherapy”)) OR ((“Pancreatic Neoplasms”[MeSH] OR “Pancreatic Cancer”) AND (“Surgical Procedures, Operative”[MeSH] OR “Surgery” OR “Pancreatectomy” OR “Distal Pancreatectomy” OR “Pancreaticoduodenectomy” OR “Whipple Procedure”)) AND (“Meta-Analysis”[Publication Type] OR “Systematic Review”[Publication Type])

Embase

1	'Pancreatic neoplasms'/exp OR 'pancreatic cancer' OR 'locally advanced pancreatic cancer' OR 'LAPC' OR 'unresectable pancreatic cancer' OR 'borderline resectable pancreatic cancer'
2	'Neoadjuvant therapy'/exp OR 'neoadjuvant' OR 'induction chemotherapy'/exp OR 'chemoradiotherapy'/exp
3	'Surgical procedures, operative'/exp OR 'surgery'/exp OR 'pancreatectomy'/exp OR 'distal pancreatectomy'/exp OR 'pancreaticoduodenectomy'/exp OR 'whipple procedure'
4	'Meta-analysis'/exp OR 'systematic review'/exp
5	(1 AND 2 AND 4) OR (1 AND 3 AND 4)

MEDLINE (Ovid)

1	exp Pancreatic Neoplasms/ OR Pancreatic Cancer OR Locally Advanced Pancreatic Cancer OR LAPC OR Unresectable Pancreatic Cancer OR Borderline Resectable Pancreatic Cancer
2	exp Neoadjuvant Therapy/ OR Neoadjuvant OR Induction Chemotherapy OR Chemoradiotherapy
3	exp Surgical Procedures, Operative/ OR Surgery OR Pancreatectomy OR Distal Pancreatectomy OR Pancreaticoduodenectomy OR Whipple Procedure
4	Meta-analysis/ OR Systematic Review/
5	(1 AND 2 AND 4) OR (1 AND 3 AND 4)

Cochrane Library

1	MeSH descriptor: [Pancreatic Neoplasms] explode all trees
2	MeSH descriptor: [Neoadjuvant Therapy] explode all trees OR Neoadjuvant OR Induction Chemotherapy OR Chemoradiotherapy: ti, ab, kw
3	MeSH descriptor: [Surgical Procedures, Operative] explode all trees OR Surgery OR Pancreatectomy OR Distal Pancreatectomy OR Pancreaticoduodenectomy OR Whipple Procedure: ti, ab, kw
4	MeSH descriptor: [Meta-Analysis] explode all trees OR Systematic Review: ti, ab, kw
5	(1 AND 2 AND 4) OR (1 AND 3 AND 4)

Table S1 Summary of included meta-analyses evaluating neoadjuvant therapy, surgical techniques, and overall survival in locally advanced pancreatic cancer

First author	Year	Journal	Neoadjuvant treatment	Main surgical technique	OS for LAPC with resection (month), median (range/interquartile range)	OS for LAPC without resection (month), median (range/interquartile range)
Comparative meta-analysis						
Brown (26)	2022	<i>British Journal of Surgery</i>	NAC, NACRT	PD, DP, DP-CAR, TP	30.0 (20.9, 33.0)	14.6 (12.8, 16.4)
Dong (27)	2022	<i>European Review for Medical and Pharmacological Sciences</i>	NAC	PD, DP, TP	–	–
Gong (28)	2016	<i>Medicine</i>	–	DP, DP-CAR	DP: 14.1; DP-CAR: 14.9	6.4
Gurusamy (29)	2014	<i>Cochrane Database of Systematic Reviews</i>	–	TP, PD, DP	0–60	0–24
Single-arm meta-analysis						
Xue (30)	2023	<i>Internal Journal of Surgery</i>	NAC, NACRT	DP-CAR	17–44.9	–
Eshmuminov (31)	2023	<i>Annals of Surgical Oncology</i>	NACRT	PPPD, PD, DP, DP-CAR, TP	FOLFIRINOX: 33.4 (29.0, 36.3); Gem/nab: 27.9 (22.7, 38.8); GemX: 33.7 (25.3, 73.3); Gem-mono: 23.0 (17.6, unknown)	FOLFIRINOX: 15.7 (14.7, 17.0); Gem/nab: 11.8 (10.0, 13.8); GemX: 11.1 (10.4, 12.1); Gem-mono: 9.0 (7.7, 10.0)
Damm (32)	2021	<i>Cancers</i>	NAC, NACRT	PD, DP, DP-CAR, TP	19.8–43.6	10.2–16.0
Chen (33)	2020	<i>Medicine</i>	NAC, NACRT	PD, DP, DP-CAR, TP	14.0 (10.0, 32.7)	
Suker (34)	2016	<i>The Lancet Oncology</i>	NAC, NACRT	PD, DP, DP-CAR, TP	24.2 (21.6, 26.8)	

LAPC, locally advanced pancreatic cancer; NAC, neoadjuvant chemotherapy; NACRT, neoadjuvant chemoradiotherapy; DP, distal pancreatectomy; DP-CAR, distal pancreatectomy with celiac axis resection; PD, pancreaticoduodenectomy; PPPD, pylorus-preserving pancreaticoduodenectomy; TP, total pancreatectomy; OS, overall survival.

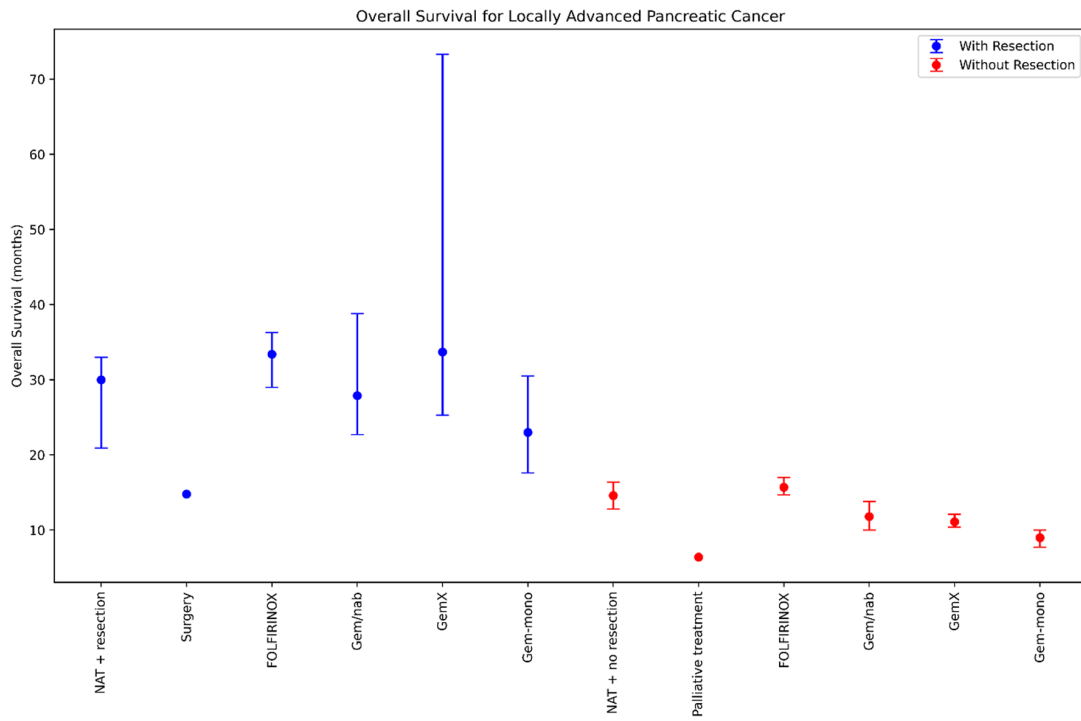


Figure S1 Overall survival by resection status and treatment strategy in locally advanced pancreatic cancer.

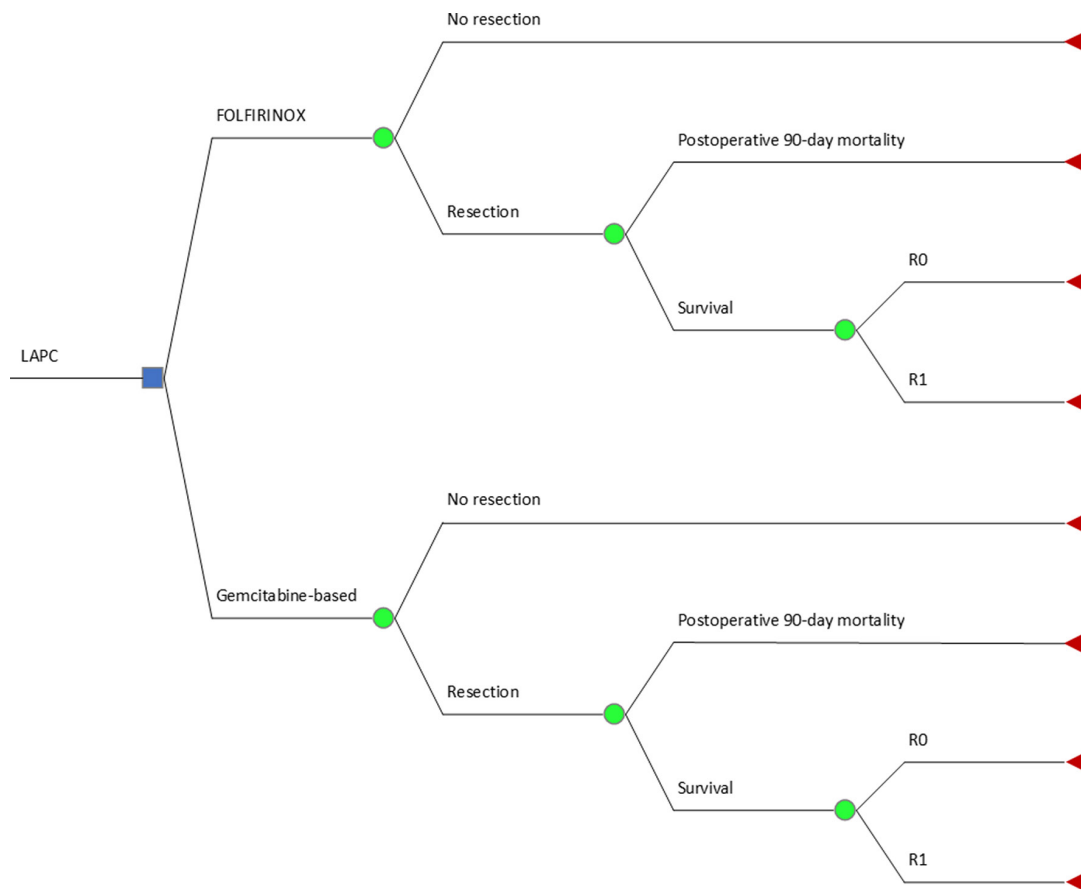


Figure S2 The decision tree model simulated the clinical pathway of patients with LAPC starting at diagnosis. Patients were assigned to either FOLFIRINOX or gemcitabine/nab-paclitaxel regimens. For each regimen, patients could either remain unresectable after induction chemotherapy, leading to palliative care or proceed with surgical resection. The tree structure was identical for both branches. Following resection, patients were further stratified based on the occurrence of postoperative morbidity or mortality. Survived patients were categorized according to their resection status: R0 (complete tumor removal with negative margins) or R1 (microscopic residual disease). LAPC, locally advanced pancreatic cancer; FOLFIRINOX, leucovorin calcium, fluorouracil, irinotecan, and oxaliplatin.

Table S2 Parameters for the decision model

Parameter	Mean	Distribution	Source
Cost (inflation-adjusted to 2023 US dollars)			
Resection			
Pancreaticoduodenectomy for uncomplicated or minor complication resection	\$26,032	Gamma	(20-23)
Pancreaticoduodenectomy for major complication resection with perioperative mortality	\$36,479	Gamma	(20-23)
Neoadjuvant therapy			
FOLFIRINOX (4 cycles)	\$46,437	Gamma	(20-23)
Gemcitabine/Nab-paclitaxel (4 cycles)	\$25,730	Gamma	(20-23)
Adjuvant chemotherapy			
FOLFIRINOX per cycle	\$10,000	Gamma	(20-23)
Gemcitabine/Nab-paclitaxel per cycle	\$6,500	Gamma	(20-23)
Palliative care (total)	\$112,211	Gamma	(20-23)
Probabilities			
Resection rate in FOLFIRINOX group	0.27	Beta	Data from this study
Resection rate in Gemcitabine+ group	0.18	Beta	Data from this study
R0 resection in FOLFIRINOX group	0.80	Beta	Data from this study
R0 resection in Gemcitabine+ group	0.74	Beta	Data from this study
Postoperative mortality	0.05	Beta	Data from this study
Utility			
Overall survival in FOLFIRINOX group with resection (month)	31.7	Weibull	Data from this study
Overall survival in Gemcitabine+ group with resection (month)	27.9	Weibull	Data from this study
Overall survival in FOLFIRINOX group without resection (month)	15.7	Weibull	Data from this study
Overall survival in Gemcitabine+ group without resection (month)	11.8	Weibull	Data from this study
Overall survival in perioperative mortality (month)	3.0	Weibull	Data from this study

FOLFIRINOX, leucovorin calcium, fluorouracil, irinotecan, and oxaliplatin; Gemcitabine+, gemcitabine/nab-paclitaxel.

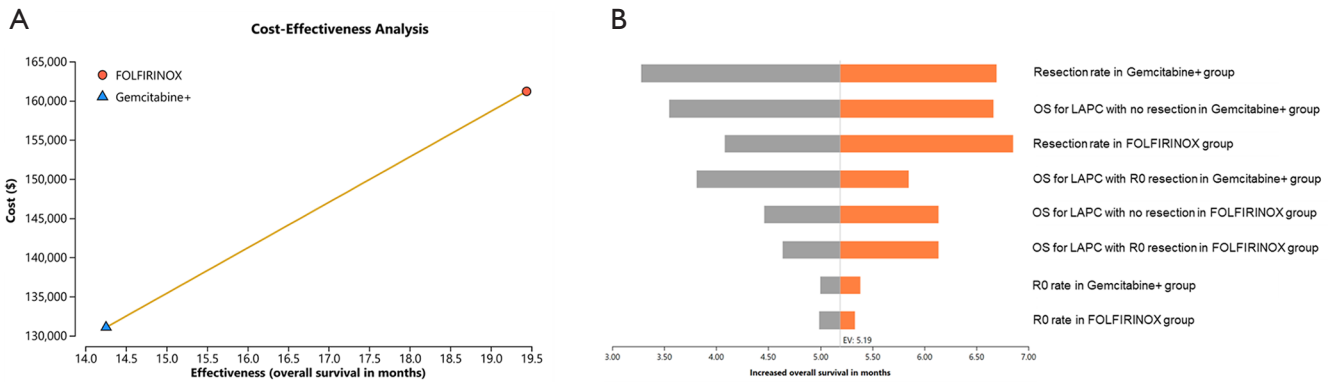


Figure S3 Cost-effectiveness analysis comparing FOLFIRINOX and gemcitabine/nab-paclitaxel in locally advanced pancreatic cancer. (A) Cost-effectiveness analysis plot. The line represents the cost-effectiveness frontier, connecting the two strategies. The vertical distance indicates the incremental cost, and the horizontal distance indicates the incremental effectiveness. The slope of this line corresponds to the ICER. (B) One-way sensitivity analysis. The lower and upper bounds of parameters are shown as deviations in incremental effectiveness from the mean values. ICER, incremental cost-effectiveness ratio; EV, effectiveness; LAPC, locally advanced pancreatic cancer; OS, overall survival; FOLFIRINOX, leucovorin calcium, fluorouracil, irinotecan, and oxaliplatin; Gemcitabine+, gemcitabine/nab-paclitaxel.