Ontario
Cancer Care Ontario
Action Cancer Ontario

Evidence-Based Series Special Report 17-2 Version 2

A Quality Initiative of the
Program in Evidence-based Care (PEBC), Cancer Care Ontario (CCO)

Hepatic, Pancreatic, and Biliary Tract (HPB) Surgical Oncology Standards

The Expert Panel on HPB Surgical Oncology

A Special Project of the Surgical Oncology Program, Cancer Care Ontario and
The Program in Evidence-Based Care, Cancer Care Ontario
Developed by the Expert Panel on HPB Surgical Oncology

An assessment conducted in January 2023 placed Guideline 17-2 Version 2 IN REVIEW. This means that it is undergoing a review for currency and relevance. It is still appropriate for this document to be available while this updating process unfolds. The PEBC has a formal and standardized process to ensure the currency of each document (PEBC Assessment & Review Protocol)

EBS 17-2 is comprised of 4 sections. You can access the summary and full report here: https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/546

Section 1: Standards (ENDORSED)
Section 2: Systematic Review
Section 3: Standards Development and External Review - Methods and Results
Section 4: Document Review Summary and Tool

Release Date: December 15, 2015

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Guideline Report History

GUIDELINE VERSION	SYSTEMATIC REVIEW		PUBLICATIONS	NOTES and KEY CHANGES
	Search Dates	Data		
Original June 2006	1990 through September 2006	Full Report	Peer review publication Web publication	NA
Current Version 2 December 2015	2006 to May 2015	New data found in Section 4: Document Review Summary and Review Tool	Updated web publication	2006 recommendations **ENDORSED**

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Evidence-Based Series #17-2 Version 2: Section 2

Hepatic, Pancreatic, and Biliary Tract (HPB) Surgical Oncology Standards

M. Marcaccio, B. Langer, B. Rumble, A. Hunter,
and the Expert Panel on HPB Surgical Oncology

A Special Project of the Surgical Oncology Program, Cancer Care Ontario and
The Program in Evidence-Based Care, Cancer Care Ontario
Developed by the Expert Panel on HPB Surgical Oncology

Report Date: June 14, 2006

These guideline recommendations have been ENDORSED, which means that the recommendations are still current and relevant for decision making. Please see Section 4: Document Review Summary and Tool for a summary of updated evidence published between 2006 and 2015 and for details on how this Clinical Practice Guideline was ENDORSED.

QUESTION

What is the optimum organization for the delivery of cancer-related hepatic, pancreatic, and biliary tract surgery in Ontario?

SCOPE OF STANDARDS

The following standards, developed by the Expert Panel on HPB Surgical Oncology, apply to hepatic, pancreatic, and biliary tract cancer surgery and include the full spectrum of multidisciplinary assessment and treatment:

- Management of primary and secondary liver cancer by hepatic resection or locally destructive techniques (ablation by any modality, hepatic artery embolization with or without chemotherapy, etc.).
- Management of cancer of the pancreas and peri-ampullary region by pancreatic resection.
- Management of tumours of the biliary tract (including gallbladder) by surgical resection.

The standards cover the full range of resources and expertise needed for the care of these patients and recognize that a multidisciplinary team approach is necessary for optimum

management. Specific criteria relating to the characteristics of surgeons and institutions involved in HPB surgery are described.

SURGEON CRITERIA

General Characteristics

General characteristics for surgeons undertaking the management of patients with HPB cancer are as follows:

- Knowledgeable regarding the biology of HPB cancer, its natural history, appropriate investigation, and the whole range of treatment options.
- Skilled in modern techniques of surgery of the liver, pancreas, and biliary tract, including capability for managing vascular complications and vascular reconstruction.
- Experienced in the management of patients with hepatobiliary and pancreatic diseases, especially the management of early and late postoperative complications.
- Committed to providing excellence in care to patients with HPB diseases and to advancing knowledge in the field in order to improve patient outcomes.
- Committed to participating as a member of a multidisciplinary oncology team.
- Committed to participating in Cancer Care Ontario quality initiatives.

Training

Although there is not a formally recognized subspecialty in HPB surgery, the complex nature of this subspecialty area has lead to the development of training programs designed to provide the kind of expertise and experience necessary to appropriately manage patients with HPB diseases. Thus, appropriate training would include certification by the Royal College of Physicians and Surgeons of Canada in General Surgery (or its equivalent) plus the completion of a period of advanced training in HPB surgery designed to attain a high level of proficiency in the management of the complex surgical problems found in this patient population. The training program should specifically focus on the management of malignant disease and result in the trainee acquiring competence to manage not only routine cases but also those requiring more complex resection and reconstruction. Thus, surgeons practicing HPB surgery should have completed one of the following:

- A specific formal Fellowship in HPB surgery, or
- A Fellowship in liver transplant that includes a major focus in non-transplant HPB cases, or
- A Surgical Oncology Fellowship with a major emphasis on HPB surgery

Surgeons that trained prior to the existence of HPB or Surgical Oncology Fellowships may have received such training in less formal ways, such as extended post-residency training in a busy HPB service or mentoring and progressive experience in the early years of their staff appointment in a hospital where a busy HPB service was present. The increasing complexity of HPB surgery and the development of excellent quality formal fellowship training supports the use of the new standard for surgeons now entering the system.

All surgeons should maintain their expertise and knowledge through continuing professional development programs and a commitment to a career focussed on HPB surgery.

HOSPITAL CRITERIA

General Characteristics

A tertiary care HPB surgical centre should be capable of managing the full range of surgical care for patients with diseases of the liver, pancreas, and biliary tract, from the most complex to the most common, in a single hospital. A minimum of two HPB surgeons should be on staff in order to provide intraoperative assistance and continuous preoperative and postoperative care, while allowing for appropriate personal and professional leave. The hospital should have an

affiliation with a Regional Cancer Program, and the HPB Program should include teaching, research, quality improvement, and program advancement elements.

Hospitals that do not have tertiary HPB services will provide care for patients with common HPB conditions. They should have an established relationship with a tertiary care HPB Centre to facilitate consultation and the referral of common and uncommon cases through a regional care network such as the Local Health Integrated Networks (LHINs), so that all patients may have access to high-quality care in the appropriate setting. These hospitals and their professional staff would also play an important role in the initial diagnostic investigation and surgical follow-up of patients with complex problems. Participation in such a regional care network should lead to both better access to and quality of care.

The capability to provide optimal HPB care requires that an institution ensure the availability of the appropriate physical, fiscal, and human resources needed for the complete spectrum of patient care, from early diagnosis to long-term management and supportive care. A hospital should have a definable system of care for HPB patients that is integrated with the other components of the broader cancer care system.

Specific System Requirements

- Formal acknowledgement by the hospital that it is a Centre for HPB Surgery and therefore has a distinct HPB Surgery Program with definable leadership structure and accountability.
- A commitment to provide HPB surgery in a timely manner, including the support of and commitment to the targets set by the provincial wait-time strategy.
- A system of patient care that ensures multidisciplinary management, including Multidisciplinary Cancer Conferences (i.e., tumour boards) involving the appropriate health care professionals to ensure that patients receive the most appropriate treatment. This is essential for the achievement of optimal patient outcomes.
- A system for the regular review of the program, including clinical and educational rounds, morbidity and mortality review, and quality assurance, including a system for regular tracking of patient outcomes. This includes participation in all quality improvement programs of Cancer Care Ontario.
- Participation in regional cancer programs and the planning processes of the LHINs.
- Infrastructure support for participation in local and national clinical research studies.

Physical Resources

- Appropriately equipped operating rooms available 24 hours a day, seven days a week. This includes the capability for intraoperative imaging (fluoroscopy and ultrasound) and appropriate adjunctive therapy (e.g., radiofrequency ablation).
- Full range of diagnostic imaging ability, including ultrasound (all modalities, including Doppler), computerized tomography (CT) scan, magnetic resonance imaging (MRI), angiography, and interventional radiology, with the appropriate staff skilled in HPB interventions.
- Diagnostic and therapeutic Interventional Endoscopy available 24 hours per day, seven days per week.
- An appropriately equipped intensive care unit (ICU) capable of providing the appropriate range of ventilation modalities, dialysis, and the physical facilities for management of complex infectious problems.
- A fully developed nutrition service, including total parenteral nutrition (TPN).

Human Resources

HPB services are optimally delivered in a multidisciplinary team setting and require a full range of skilled health care professionals for optimum outcomes. These include:

- Qualified HPB surgeons (see Surgeon Criteria and Training).
- Radiologists with appropriate expertise across the full range of angiography, biliary tree imaging, abscess management, and ablative techniques.
- Dedicated, certified critical care physicians.
- An endoscopy service with advanced skills in biliary therapeutic endoscopy.
- Nursing personnel experienced in the management of complex abdominal surgical problems, particularly HPB diseases, abdominal sepsis, and fistulae.
- Medical and radiation oncology services available for consultation and interdisciplinary decision making.
- Supportive care, including pain management, psychosocial support, and palliative care.
- Allied health professionals, including nutritional care, occupational, and physical therapists.
- A pathologist with a special interest in HPB diseases and a commitment to developing the appropriate expertise.
- Administrative support, including a system of data management to meet the needs of the HPB Service.
- Availability of an appropriate spectrum of physician subspecialties to provide the required support to HPB patients, especially infectious disease practitioners.
- Anaesthesiologists with expertise in managing long complex operations in which patients may potentially become unstable and in patients with impaired liver function.

Volume of HPB Surgery

The hospital with an HPB Service should have an adequate volume of index cases to maintain the skills of the multidisciplinary team, function as a tertiary referral centre, justify the resource investment required, and assure that optimum outcomes are achieved.

An HPB Centre should carry out a minimum of 50 index HPB cases per year (index cases include formal anatomic resection of one or more liver segments, all Whipple and total pancreatic resections, and all resections with reconstruction of the biliary tract). The volume should include at least 20 pancreatic resections.

OUTCOME MEASURES, BENCHMARKS, AND QUALITY ASSURANCE

The following outcomes are considered reasonable and achievable at HPB Centres across Ontario:

- A mortality rate (30-day plus in hospital) of less than 5% for major pancreatic resection
- A mortality rate (30-day plus in hospital) of less than 3% for anatomical liver resection.

DEVELOPMENT OF THE STANDARDS DOCUMENT

Evidence on HPB cancer surgery was gathered through a systematic search of the literature and a scan of documents from organizations concerned with quality practice in HPB surgery. Evidence was reviewed by members of the Expert Panel on HPB Surgical Oncology (see Appendix 1, Section 3) investigating the delivery of cancer-related HPB surgery in Ontario. The Panel included HPB surgeons, general surgeons, a medical oncologist, a radiation oncologist, a hospital chief executive officer, a Cancer Care Ontario regional vice president, a pathologist, a radiologist, and methodologists. The members came from across the province and provided appropriate regional representation.

The Expert Panel developed the standards, using a combination of evidence-based analysis, recommendations from other jurisdictions, and their own expert opinion based on experience. The Panel analyzed data on the current distribution of HPB cancer surgery across Ontario to inform the process, and in particular to assist in developing the volume standards. The standards proposed represent a consensus of the Expert Panel, and are intended to accommodate the long-range needs of the province, including the ability to manage the

projected increase in demand for HPB cancer surgical care over the next decade due to the growing and aging population.

Funding

The PEBC is supported by Cancer Care Ontario (CCO) and the Ontario Ministry of Health and Long-Term Care. All work produced by the PEBC is editorially independent from its funding agencies.

Contact Information

For information about the PEBC and the most current version of all reports,
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What is the optimum organization for the delivery of cancer-related hepatic, pancreatic, and biliary tract surgery in Ontario?

INTRODUCTION

Malignant diseases of the liver, pancreas, and biliary tract are complex problems that require multidisciplinary assessment and care in order to achieve optimum outcomes. At present, surgical resection remains the only realistic hope for long-term control of these tumours, yet outcomes for surgical resection are still far less than ideal. The surgical procedures themselves, along with the required preoperative investigation and perioperative care, are complex, resource intensive, and not without significant risk. While surgical treatment will benefit many, the combination of complexity and risk in the face of less than desirable tumour control requires that the highest possible standard of care be delivered in order to ensure that an appropriate ratio of benefit and risk can be obtained. Many patients with advanced disease will not benefit from aggressive surgical resection. Management of all patients, including those who are resectable and those who are not, requires a multidisciplinary team with the knowledge and tools to provide a full array of surgical intervention and systemic and radiation treatments. Additionally, supportive and palliative care is essential and will ultimately be needed by the majority of patients.

The Canadian Institute of Health Information (CIHI) data show that approximately 600 major liver, biliary tract, and pancreas resections were performed for cancer in Ontario in 2004/2005. The incidence of hepatic, pancreatic, and biliary malignancies is increasing at over 3% per year, as a function of our growing and aging population. The natural history of these cancers is dismal, with survival rates for pancreas cancer being less than 30% at one year and less than 5% at five years and for liver and biliary tract being less than 30% at five years. While there is demonstrable survival benefit from appropriate surgical and other treatment, the amount of benefit achievable is considerably less than in many other types of cancer. These results have aroused intense interest in finding new management strategies that will improve outcomes. There is a need for HPB Centres that have a focused interest in these disorders and a commitment to innovation and clinical research, in order to both provide appropriate and up to date care and to develop the new therapies that will improve outcomes.

A comprehensive approach to the investigation of these patients is required in order to establish a correct diagnosis at the earliest possible time. Sophisticated technology and diagnostic expertise, especially in imaging and pathology, may not be widely available but is often required to sort out the more difficult cases. Accurate tumour staging forms an essential part of most treatment decisions and is critical in selecting appropriate patients for surgical resection.

The surgery itself requires judgment, experience, and technical skill to ensure proper preoperative planning, determine the appropriate extent of resection, exercise correct intraoperative decision making, and recognize and manage postoperative problems, including reoperative surgery when required. There is increasing evidence that larger volumes of surgery are associated with better outcomes for many kinds of surgical procedures, including liver and pancreatic resections. This relationship applies to both the individual surgeon and to the hospital. Although there may be many individual surgeon and hospital factors that underlie this effect, volume alone has been a consistent surrogate.

In 1999, a research project conducted under the auspices of the Institute of Clinical Evaluative Sciences was published in the *Canadian Medical Association Journal* (1). It reported wide variations in postoperative mortality among Ontario hospitals over a seven-year period, and noted the relationship between increased volume and better outcomes for complex resections involving the head of the pancreas. In response to this report, Cancer Care Ontario (CCO) convened an Expert Panel to discuss strategies to improve the care of these patients. A standards document (2) was developed that described the Panel's opinion with respect to the characteristics of surgeons and institutions involved in the care of these patients that would lead to optimum outcomes. The Panel also recommended a minimum volume threshold for hospitals of 10 major pancreatic resections and 25 total major liver, biliary, and pancreatic resections per year, and suggested that a benchmark mortality rate for major pancreatic resection of less than 5% was achievable. The guidelines were endorsed by the Board of CCO and widely disseminated, including direct delivery to all hospital Chief Executive Officers and Chiefs of Staff/Chiefs of Surgery.

In 2001, a CCO Surgical Oncology Program working group carried out a qualitative study of the effect of the guidelines on the delivery of complex pancreatic resection for cancer. The review revealed that many hospitals had made changes in their practices, including some that had discontinued these operations and others that had reorganized their care. A more recent review showed that there are significantly fewer hospitals performing pancreatic cancer surgery, the proportion of patients receiving these operations in hospitals doing more than 10 cases per year has increased, and the provincial mortality rate has fallen, compared to the period of study in the 1999 report, but is still higher than 5%. These statistics, however, also show that there are still a significant number of hospitals providing these complex resections but performing fewer than 10 pancreatic resections and 25 complex HPB resections per year.

As one of its initiatives in the area of quality improvement, CCO has initiated the development of standards to guide the evolution of our cancer care system. It was felt timely to

review the previous pancreatic cancer surgery standards document and update and incorporate it into a standards document applicable to cancer of the liver, pancreas, and biliary tract, which recognizes the interrelated nature of these diseases. An Expert Panel was therefore convened by the Surgical Oncology Program (SOP) of CCO, in cooperation with the Program in Evidenced-Based Care (PEBC), and charged with the task of developing these standards, utilizing the successful document development process of the PEBC.

METHODS

This report, produced by the SOP and the PEBC, is a convenient and up-to-date source of the best available evidence on volume-related outcomes associated with hepatic, pancreatic, and biliary (HPB) surgery, developed through a systematic review of the available evidence, using the methods of the PEBC Practice Guidelines Development Cycle (3). Members of both the SOP and the PEBC disclosed any potential conflicts of interest. The SOP and the PEBC are both editorially independent of CCO and the Ontario Ministry of Health and Long-term Care (MoH&LTC).

Literature Search Strategy

The MEDLINE database (dB) was searched from 1966 to the second week of September 2005. The EMBASE dB was also searched from 1980 to week 39 2005. Appendix 2 details the MEDLINE search strategy; the EMBASE strategy was comparable but customized for the EMBASE terms. The search terms used covered the appropriate diseases, interventions, settings, and outcomes. Additional articles not located through the formal literature review were provided by some of the authors. A systematic review (4), not found in the formal search as the publication date was too recent to be captured by the review, was also obtained. Relevant articles and abstracts were selected by one reviewer, and data extraction was performed independently by two reviewers, with discrepancies resolved by consensus.

Inclusion Criteria

Articles were selected for inclusion in the systematic review of the evidence if they were fully published English language reports reporting volume-outcome measurements, for either surgeons or hospitals/institutions, in hepatic, pancreatic, or biliary cancer. Ideally, reports would provide both surgeon and hospital/institution volume-outcome measurements. The types of studies eligible for inclusion were randomized controlled trials (RCT), retrospective studies, and case-series reports (with at least 10 patients).

Outcomes of interest

The primary volume-outcome measurements that were of interest included short-term mortality/survival, adverse effects, hospital length of stay, and long-term survival (five-year optimal). Secondary outcomes of interest included costs (as reported in the jurisdiction where the trial was run), physician training, hospital/institutional requirements, and any diagnostic procedures used.

RESULTS

Literature Search Results

A total of 12 trial reports were obtained (1,5-15). None of the trial reports obtained were RCTs; all were retrospective in study design. The data on the relationship between volume categories and mortality, postoperative complications, length of stay, and cost are presented in Table 1 *(Mortality by surgeon-volume, pancreatic resections*), Table 2 (*Mortality by hospital-volume, pancreatic resections*), and Table 3 (*Mortality by hospital-volume, hepatic resections*). The three trials that provided volume-outcome data on surgeons for pancreatic resections (5-7) also provided volume-outcome data on hospitals. Additionally, another 11 trials provided volume-outcome data on hospitals for pancreatic resections only (1,5-14). A single trial reported volume-outcomes for hospitals for hepatic resections (15).

Synthesizing the Evidence

As none of the trials obtained were RCTs, no pooling was possible. Instead, mean cases per hospital per year or mean cases per surgeon per year were calculated and used as the unit of comparison both between trials and between volume categories within trials.

Table 1. Surgeon-Volume measures [3 studies].

Study	Study type	Disease site	Type of intervention	Volume categories (per surgeon per year)	Total No. of surgeons over study period N (%)	Total No. of patients over study period N (%)	Mortality N (%)	Compli-cations (%)	Length of stay d	Cost ($)	Notes
Edge et al, 1993 [USA] (5) Jan 1, 1989 to Dec 31, 1990 [2 years]	Retro-spective audit of discharge coding data	Pan-creas, ampulla of Vater	Pancreaticoduodenectomy, N=168; Total pancreatectomy, N=11; Distal pancreatectomy, N=30; Islet tumour resection, N=14 Total # surgeons: 91 Total # patients: 223	0-0.9	51 (56)	51 (23)	2 (3.9)	14 (27) (major)	17	No compl. $15,424 Minor $21,607 Major $44,899 all per two year	Surgeons performing 0.5-1.5 resections had significantly more minor and major complications than those performing ≥2 (p=0.011)
				1-1.9	22 (24)	50 (22)	5 (10.0)	12 (24) (major)	14.5		
				≥2 Mean = 3.4	18 (20)	122 (55)	6 (4.9)	20 (16) (major) p=0.0163 for 0.5-1.5 cases vs. ≥2 cases	15		
Lieberman et al, 1995 [USA] (6) 1984 to 1991 [8 years]	Retro-spective audit of discharge abstracts from the NY State Depart-ment of Health	Pan-creas, biliary tree, ampulla of Vater	Resections for: Pancreatic ductal adenocarcinomas, 55%; Tumours affecting the Ampulla of Vater, 16%; Distal bile duct adenocarcinoma, 8%; Duodenal adenocarcinoma, 8%; Islet cell tumours, 3% Total # surgeons: 748 Total # patients: 1972	<1.13	687	1321 (67)	172 (13) [a]	NR	34 (a)	NR	Standardized mortality rates reported; Surgeon's experience not significantly related to perioperative deaths when hospital volume is controlled
				1.13-5.13	57	355 (18)	34 (9.7) [b]		26 (b)		
				>5.13 Mean = 9.3	4	296 (15)	18 (6) [c] X^2 p<0.001 for a vs. b, c		27 (c) X^2 p<0.05 for a vs. b, c		
Nordback et al, 2002 [Finland] (7) Study period: 1990 to 1994 [5 years]	Retro-spective study on National Hospital Discharge database	Pancreas (resec-tion of the head of the pan-creas)	Resections for: Multiple indications, 292 pts of 374 pts total required resection for malignancy Standard resection of the head of the pancreas, including partial gastric resection, N=270/350, 77% Pylorus-preserving resection of the head of the pancreas, N= 76/350, 22% Duodenum-preserving resection (Berger's resection), N=4/350, 1% Total # surgeons: 98 Total # patients: 350	0-1.1	74 (75.5%)	NR	Low (<1) 18/125 (14%)	Low (<1) 53/125 (42%)	Low (<1) 24 (range 9-70)	NR	Pancreatic resections performed in high-volume hospitals by high-volume surgeons was associated with decreased postop morbidity, mortality, and hospital stay, and the authors recommend that pancreatic head surgery be limited to only a few hospitals and only a few surgeons.
				1.2-2	20 (20%)	NR	Medium (1-3) 16/164 (10%)	Medium (1-3) 68/164 (41.4%)	Medium (1-3) 23 (range 7-100)		
				2.2-3	1 (1%)	NR	High (>3) 2/61 (3%)	High (>3) 15/61 (24.6%)	High (>3) 18 (range 8-63)		
				3.2-4	2 (2%)	NR					
				4.2-6	1 (1%)	NR					

Abbreviations: compl., complications; d, day; NR, not reported; vs., versus; yr, year; N, number; NA, not applicable.

Table 2. Hospital-Volume measures (pancreatic) [11 studies].

Study	Study type	Disease site	Type of intervention	Volume categories (per hospital per year)	Total No. of hospitals over study period N (%)	Total No. of patients over study period N (%)	Mortality N (%)	Compli-cations	Length of stay d	Cost ($)	Notes
Edge et al, 1993 [USA] (5) Jan 1, 1989 to Dec 31, 1990 [2 years]	Retro-spective audit of discharge coding data	Pan-creas, ampulla of Vater	Pancreaticoduodenectomy, N=168; Total pancreatectomy, N=11; Distal pancreatectomy, N=30; Islet tumour resection, N=14 Total # hospitals: 26 Total # patients: 223	0-0.9	10 (38)	27 (12)	2 (7.4)	7 (25.9) (major)	15	No compl. $15,424 Minor $21,607 Major $44,899 all per two year	Morbidity and mortality did not correlate with caseload
				1-1.9	9 (35)	78 (35)	5 (6.4)	15 (19.2) (major)	16		
				≥ 2 Mean = 8.4	7 (27)	118 (53)	6 (5.1)	24 (20.3) (major)	15		
Lieberman et al, 1995 [USA] (6) 1984 to 1991 [8 years]	Retro-spective audit of discharge abstracts from the NY State Depart-ment of Health	Pan-creas, biliary tree, ampulla of Vater	Resections for: Pancreatic ductal adenocarcinomas, 55%; Tumours affecting the Ampulla of Vater, 16%; Distal bile duct adenocarcinoma, 8%; Duodenal adenocarcinoma, 8%; Islet cell tumours, 3% Total # hospitals: 184 Total # patients: 1972	<1.25	124 (67)	473 (24)	11 (18.9) [a]	NR	35 (a)	NR	Standardized mortality rates reported; Increased hospital volume associated with decreased mortality and length of stay
				1.25-6.25	57 (31)	1065 (54)	16 (11.8) [b]		32 (b)		
				6.38-10	1 (<1)	59 (3)	1 (12.9) [c]		22 (c)		
				≥10.13 Mean = 23.4	2 (1)	375 (19)	3 (5.5) [d]		27 (d)		
							X^2 test p<0.001 for a vs. b, d and a, b vs. d		X^2 test p<0.05 for a, b vs. c, d		
Glasgow et al, 1996 [USA] (8) 1990 to 1994 [5 years]	Retro-spective audit of discharge abstracts	Pancreas, biliary tree, ampulla of Vater, duo-denum, islet cells	Pancreaticoduodenectomy, 83.5%; Proximal subtotal pancreatectomy, 9.3%; Total pancreatectomy, 7.2% Total # hospitals: 298 Total # patients: 1705	<1	210 (70)	510 (30)	72 (14.1)	NR	22.7	$87,857	Men (p=0.006) and older patients (p<0.0001) had significantly higher operative mortality; High volume centres had reduced resource-demand scale scores
				1.2-2	53 (18)	395 (23)	41 (10.4)		22.7	$76,593	
				2.2-4	20 (7)	258 (15)	23 (8.9)		22.9	$78,003	
				4.2-6	9 (3)	228 (13)	13 (5.7)		20.2	$70,959	
				6.2-10	4 (1)	171 (10)	14 (8.2)		23.9	$111,497	
				>10 Mean = 14.3	2 (1)	143 (8)	5 (3.5)		20.5	$71,588	
							p<0.0001		p=ns	p=ns	
Imperato et al, 1996 [USA] (9) 1991 to 1994	Retrospec tive audit of claims reports from Medicare database	Pancreas	Pancreaticoduodenectomy, 100% Total # hospitals: 117 Total # patients: 579	Regional hospital	2 (2)	138 (24)	3 (2.2)	NR	22.4	NR	A single provider was responsible for all cases in the 5.25-6.25 group; In-hospital mortality and length of stay significantly less at the high-volume regional
				Other hospital	115 (98)	441 (76)	54 (12)		32.9		
							p=0.0002		p<0.001		
				0-1.25	89 (76)	2.2 (mean/ hospital)	12.7 (14.3)		NR		

[4 years]							(RR= 6.87)				hospitals when compared with the low-volume hospitals
				1.5-2.5	19 (16)	7.2 (mean/ hospital)	2.2 (11.7) (RR= 5.08)				
				2.75-3.75	4 (3)	12.0 (mean/ hospital)	<1 (6.3) (RR= 3.08)				
				4-5	2 (2)	19.5 (mean/ hospital)	<1 (5) (RR= 2.09)				
				5.25-6.25	1 (1)	21.0 (mean/ hospital)	<1 (19) (RR= 9.46)				
				>6.25 Mean = 17.2	2 (2)	69.0 (mean/ hospital)	<1 (2.17) (RR= 1.0)				
Gordon et al, 1998 [USA] (10) Jan 1984 to Dec 1995 [12 years]	Retrospective audit of hospital discharge data	Pan-creas	Open Pancreaticoduodenectomy for cancer treatment (Whipple procedure): 100% Total # hospitals: 43 Total # patients: 795	<20 surgeries/yr for 6 of 12 yrs on study	42 (98)	458 (58)	65 (14.2)	NR	NR	NR	Only one hospital met inclusion criteria for high-volume; One pancreaticoduo-denectomy required for inclusion in study; Concluded that regionalization of surgery could lower overall in-hospital mortality rate
				≥20 Mean = 28	1 (2)	337 (42)	6.1 (1.8)				
Sosa et al, 1998 [USA] (11) 1990 to 1995 [6 years]	Retrospective cross-sectional	Pan-creas	<u>Pancreatic resections:</u> Pancreaticoduodenectomy – 36.3% Total pancreatectomy – 3.8% <u>Palliative bypass:</u> Gastrojunostomy Biliary-enteric bypasses such as cholecysto-, choledocho-, and hepaticojejunostomy (all three, 21%), double-bypass (22.8%), stent (16%). Total # hospitals: 48 Total # patients: 1236 (1306 resections)	<5	40 (83)	438 (43)	Resec-tions: 99.3 (18.8)	NR	Resec-tions: 23.6	Resec-tions: US 33,249	Patients appear to benefit from referral to a high-volume provider
							Bypass-es: 80.8 (15.3)		Bypass-es: 19.6	Bypass-es: US 17,483	
							Stents: 51.7 (9.8)		Stents: 11.4	Stents: US 9,564	
							p<0.05		p<0.05	p<0.05	
				5-19	7 (14.6)	270 (21.8)	Resec-tions: 18.6 (6.9)		Resec-tions: 21.1	Resec-tions: US 26,053	
							Bypass-es: 28.4 (10.5)		Bypass-es: 17.2	Bypass-es: US 15,654	

							Stents: 29.4 (10.9)		Stents: 8.6	Stents: US 9,760	
							p<0.05		p<0.05	p<0.05 (med vs. low)	
				≥20 Mean = 88	1 (2)	528 (42.7)	Resec-tions: 4 (0.9)		Resec-tions: 18.2	Resec-tions: US 22,379	
							Bypass-es: 18.4 (4.2)		Bypass-es: 15.1	Bypass-es: US 17,377	
							Stents: 7 (1.6)		Stents: 7.6	Stents: US 8,373	
							p=ns		p<0.05	p=ns	
Simunovic et al, 1999 [Canada] (1) 1988-89 to 1994-95 [6 years]	Retro-spective chart audit	Pancreas	Total pancreatectomy Radical Pancreaticoduodenectomy Total # hospitals: 68 Total # patients: 842	<3.7	56 (82)	354 (42)	5.7 (11.3)	NR	30.5	NR	Outcomes reported without readmissions; Odds of dying from pancreatic resection were 5.1 and 4.5 times greater (p<0.01) and average length of stay for patients 7.7 d and 9.2 longer (p<0.01) in low-volume vs. high-volume and medium-volume vs. high-volume centres respectively
				3.7-7	10 (15)	282 (33)	5 (12.4)		33.5		
				>7 Mean = 17.2	2 (3)	206 (24)	<1 (3.4)		25.3		
							p<0.01		p<0.05		
Gouma et al, 2000 [Nether-lands] (12) Jan 1994 to Dec 1998 [part B] [5 years]	Retrospec tive audit of National Medical Registry	Pancreas	Open pancreaticoduodenectomy; cancer and non cancer treatment Total # hospitals: NR Total # patients: 1124	<1	NR	463 (41)	15 (16)	NR	NR	NR	Average number of resections per year increased from 17 to 50 over the study period; Compared with low-volume hospitals, both relative risk and absolute risk were significantly lower in high-volume hospitals
				1-1.8		205 (18)	5 (13)				
				2-4.8		235 (21)	4 (8)				
				≥5		223 (20)	<1 (1)				
							p<0.05, (<5) vs. (10-24) and (<5) vs. (≥25)				
Birkmeyer et al, 2002 [USA] (13) 1994 to 1999 [6 years]	Retrospec tive audit of Medicare database	Pancreas	Pancreatic resection Total # hospitals: 1868 Total # patients: 10530	<1	1027 (55)	1563 (15)	275 (17.6)	NR	NR	NR	Veterans Affairs Outcome Group study; Included patients between 65-99 years of age covered by fee-for-service
				1-2	560 (30)	2757 (26)	425 (15.4)				
				3-5	168 (9)	1885 (18)	219 (11.6)				

				6-16	93 (5)	2166 (21)	163 (7.5)				
				>16 Mean = 18.9	19 (1)	2159 (21)	82 (3.8)				
Nordback et al, 2002 [Finland] (7) Study period: 1990 to 1994 [5 years]	Retro-spective study on National Hospital discharge database	Pancreas (resec-tion of the head of the pan-creas)	Resections for: Multiple indications, 292 pts of 374 pts total required resection for malignancy Standard resection of the head of the pancreas, including partial gastric resection, N=270/350, 77% Pylorus-preserving resection of the head of the pancreas, N= 76/350, 22% Duodenum-preserving resection (Berger's resection), N=4/350, 1% Total # hospitals: 33 Total # patients: 350	0-5	13 (39%)	NR	Low (<1) 26/201 (13%)	Low (<1) 82/201 (40.7%)	Low (<1) 23 (range 8-100)	NR	Pancreatic resections performed in high-volume hospitals by high-volume surgeons was associated with decreased postop morbidity, mortality, and hospital stay, and the authors recommend that pancreatic head surgery be limited to only a few hospitals and only a few surgeons.
				6-10	11 (33%)						
				11-15	4 (12%)		Medium (1-3) 8/93 (7%)	Medium (1-3) 38/91 (40.8%)	Medium (1-3) 23 (range 7-81)		
				16-20	1 (3%)						
				21-30	1 (3%)		High (>3) 2/56 (4%)	High (>3) 16/50 (28.6%)	High (>3) 18 (range 8-58)		
				31-40	2 (6%)						
				41-50	0						
				>50	1 (3%)						
Ho et al, 2003 [USA] (14) Study period: 1988 to 1998 [11 years]	Retro-spective hospital discharge claims for California and Florida	Pancreas	Pancreaticoduodenectomy (Whipple procedure) Total # hospitals: 500 Total # patients: 6652	1	NR	1197 (18)	159 (13.3)	NR	NR	NR	Higher-volume hospitals reported lower mortality rates, and high-volume was a more reliable predictor of decreased mortality than increased experience was.
				2-3	NR	1996 (30)	236 (11.8)				
				4-9	NR	1929 (29)	170 (8.8)				
				>10	NR	1530 (23)	63 (4.1)				

Abbreviations: d, day; NR, not reported; ns, not significant; OR, odds ratio; RR, relative risk; vs., versus; yr, year

Table 3. Hospital-Volume measures (liver) [1 study].

Study	Study type	Disease site	Type of intervention	Volume categories (per yr)	Total No. of surgeons over study period (%)	Total No. of patients over study period (%)	Mortality N (%)	Compli-cations	Length of stay d	Cost ($)	Notes
Choti et al, 1998 [USA] (15) Jan 1990 to June 1996 [7 years]	Retro-spective hospital discharge data from 52 acute-care hospitals (non-federal)	Liver	Partial hepatectomy Hepatic lobectomy Total # hospitals: 52 Total # patients: 606	Low-volume: ≤15/year High-volume: >15/year Mean = 37.7	35 (97) 1 (3)	342 (56) 264 (44)	4 (7.9) 3.9 (1.5) p<0.01		Low-volume: 13.2 High-volume: 12.7 p=ns	Minor: $17,923 Major: $22,485 p=ns	RR for mortality was 5.2 times higher at low-volume centres compared with high-volume centres (p<0.01). Average costs were higher at low-volume centres for major resections ($21,090 versus $30,000; p<0.05)

The Impact of Surgeon-Volume on Outcomes [Pancreatic]

Three trials were obtained that described the relationship between surgeon volume and patient outcomes (5-7). All three of these trials only included patients undergoing pancreatic resections. The types of procedures used and the reasons for the resection are given in Table 1, along with all reported outcomes. The number of patients included in these trials ranged from a low of 223 (5) to a high of 1,972 (6). All of the trials (5-7) reported mortality rates stratified by surgeon volumes, and in two of the trials (6,7), a trend of lower mortality was observed related to higher surgeon volumes. This trend was not observed in one trial (5), possibly resulting from the volume categories not being wide enough to detect subtle differences, as this trial had a very narrow range with an upper limit of ≥two per year, while the other two trials had upper limits of ≥5.13 per year (6) and 4.2-six per year (7).

Two of these trials (5,7) also provided data on postoperative complications stratified by surgeon volume. A similar trend was observed for postoperative complications, with higher surgeon volume categories being associated with a low incidence of complications.

All of the trials obtained (5-7) provided data on hospital length of stay stratified by surgeon volumes. A similar trend was observed for hospital length of stay, with higher surgeon volume categories being associated with a shorter hospital stay.

The observed trends in these trials provide some evidence that surgeons who perform a greater volume of pancreatic resections per year are also able to provide their patients with benefits in survival, postoperative complication rates, and shorter lengths of stay.

The Impact of Hospital-Volume on Outcomes [Pancreatic]

Eleven trials were obtained that described the relationship between hospital-volumes and patient outcomes in pancreatic resections (1,5-14). Types of procedures used and the reasons for the resection are given in Table 2 along with all outcomes. The number of patients included in these trials ranged from a low of 223 (5) to a high of 10530 (13).

All eleven trials described the relationship between volume categories and mortality. In five studies, overall reductions in mortality were reported from the low to the highest volume category and also between the volume categories within each study itself (5,7,12-14). Another five studies, while reporting variances in the trend towards lower mortality between volume categories within each trial itself, did show overall trends towards lower mortality from the lowest to the highest volume category (1,6,8-10). The trial by Sosa et al (11) showed a trend toward lower mortality between >5 and 5-16 procedures volume categories for resections (<5 volume category, 18.8% versus 5-16 volume category, 6.9%) Five of the eleven studies reported that the observed mortality reductions were statistically significant from low-volume to high-volume centres, either for all volume categories or from the lowest to the highest volume category (1,6,8,11,12).

The data strongly suggests that hospitals with high volumes of pancreatic resections have lower operative mortality rates than those with low volumes. The five studies in which hospitals in high-volume categories achieved postoperative mortality rates below 5% (1,8,9,11,13) had analysis thresholds of 6.25, 10, 16, 17, and 20, respectively. The mean hospital volume/year in those hospitals were 17.2, 14.3, 18.9, 17.2, and 88. It is not possible to calculate an exact threshold that represents a minimum volume to result in a mortality rate of less than 5%, but it is likely that it lies somewhere between 15 and 25 cases per year.

Only three trials reported outcomes on postoperative complications stratified by hospital-volumes (5,7,13). In these trials, the relationship between higher hospital volumes and postoperative complications was not as clear as the relationship between hospital volumes and mortality, as none of the three trials shows a clear association between higher volumes and better outcomes. However, in all three cases, the highest hospital-volume categories reported fewer postoperative complications than the lowest hospital-volume categories.

Nine of the trials reported comparable outcomes on the relationship between hospital volumes and in-hospital length of stay (1,5-9,11,14,15). In these trials, the relationship between higher hospital volumes and in-hospital length of stay was not as clear as the relationship between hospital volumes and

mortality. Four trials (7,9,14,15) reported a clear trend with higher hospital volumes being associated with a shorter in-hospital length of stay, and four trials (1,5,6,8) did not.

The Impact of Hospital-Volume on Outcomes [Hepatic]
One trial was obtained that examined the relationship between hospital volumes and mortality in hepatic resections (15). In this study, a statistically significant reduction in mortality was detected for institutions that performed more than 15 hepatic resections per year compared with institutions that performed fewer than 15 hepatic resections per year ($p<0.01$). No difference was detected for comparisons of length of stay between high- and low-volume centres.

Systematic Reviews
In the one systematic review obtained (4), the relationship between hospital volume and mortality following pancreatic resection was explored. A total of 12 retrospective trials involving a total of 19,688 patients were obtained and included in that systematic review, all of which are included in this report (1,5-14). As the trials were too heterogeneous to allow pooling of data, a qualitative analysis was performed. Analysis using two arbitrarily defined cut-off points for clinical importance (a low value of five per year and a high value of 24 per year), found that centres that performed fewer than five pancreatic resections per year reported hospital mortality rates ranging from 13.8% to 16.5%, and in contrast to this, centres that performed 24 or more pancreatic resections per year reported hospital mortality rates ranging from 0% to 3.5%. The authors of that review state that this qualitative analysis provides convincing evidence for an inverse relationship between hospital mortality and hospital volume and are advocating for the centralization of services to provide pancreatic resections.

Environmental Scan Strategy
A Web search of provincial, national, and international surgery associations, including those dedicated to HPB surgery, was conducted between September and November 2005. As well, unpublished sources were sought by contacting surgical opinion leaders in each region and through direct contact with known leaders in the field of HPB surgery. Sources 1 and 2 from the practice organization document list below were forwarded from Expert Panel members.

Environmental Scan Results
Six practice organization documents were located through the search strategy:

1. British Association for the Study of the Liver. National Plan for Liver Services UK. 2004 (18).
2. Cancer Care Ontario Pancreatic Task Force. Criteria for Delivery of Pancreatic Cancer Surgery. 1999 (2).
3. New York State Committee on Quality Improvement in Living Liver Donation. A report to: New York State Transplant Council and New York State Department of Health 2002 (19).
4. Department of Health; National Cancer Guidance Steering Group. Guidance on Commissioning Cancer Services: Improving Outcomes in Upper Gastro-Intestinal Cancers: The Manual. 2001 (20).
5. Guidelines for Resection of Colorectal Cancer Liver Metastases. 2005 (21).
6. The Leapfrog Group. Evidence-Based Hospital Referral Fact Sheet. 2004 Apr 7 version (22).

All of the practice organization documents were developed through expert consensus and were generally similar in that they recognized the need for the regionalization of these complex services in order to concentrate experience in dedicated institutions with dedicated health professionals. Those from the United Kingdom, where there is a more regional approach to healthcare planning, were the most comprehensive.

The recommendations addressed aspects of care that were felt to be important in determining quality and outcomes in this complex area of surgical practice. The necessary components include the formal surgeon and institutional focus on HPB cancer surgery; a comprehensive array of physical and human resources with the training and experience to provide for the most complex patient care situations; a formal organizational structure with administrative leadership and accountability; a

commitment to clinical care, education, and innovation; and an adequate volume of procedures (based on either a defined number of index procedures or the size of population served). A summary of key elements from the HPB practice documents are shown in Table 4.

Table 4. Recommendations from HPB practice organization documents.

SURGEON CRITERIA
National Plan for Liver Services UK (2004) ▪ Sufficient complement of HPB consultant surgeons able to provide continuous 24 hour coverage throughout the year, who are supported by specialist registrars ▪ Each hepatology centre should be able to provide training in HPB surgery. This is essential to maintain the flow of qualified clinicians in this subspecialty
CCO – Criteria for the Delivery of Pancreatic Cancer Surgery (1999) ▪ Completion of training in general surgery plus a period of advanced training in HPB and pancreatic surgery ▪ Competency to manage routine cases and complex resections and reconstructions of biliary tract, intestine, pancreas and vascular structures ▪ Ideally, there should be more than one surgeon
NY State Committee on Quality Improvement in Living Liver Donation (2002) ▪ All surgeons should be board certified in general surgery and have demonstrated experience in liver transplant surgery ▪ Two surgeons should have demonstrated experience in live donor hepactomy (15 procedures) or major hepatobiliary resectional surgery (20 procedures) or surgical fellowship at an American Society of Transplant Surgeons approved liver transplant fellowship program with demonstrated experience (15 procedures)
Guidelines for Resection of Colorectal Cancer Liver Metastases (University of Edinburgh, 2005) ▪ At least two specialist surgeons trained in, and maintaining a special interest in liver resection surgery, and who can demonstrate a high level of skill and training in this area.
HOSPITAL CRITERIA
National Plan for Liver Services UK (2004) Volume: ▪ Each centre should serve a population of 2-4 million Physical Resources: ▪ Appropriately equipped facilities (including CUSA dissector, harmonic scalpel, intra-operative ultrasonography, argon beam coagulator, laparoscopic equipment, ablation treatment equipment, etc) ▪ Sufficient ICU beds to accommodate at least 95% of hepatology/HPB emergencies ▪ High quality diagnostic facilities (US, CT, MRI, PET) 7 days a week ▪ Diagnostic and therapeutic endoscopy and ERCP 24 hours a day ▪ Coverage in hepatology, hepatobiliary surgery and intensive care medicine to provide service 365 days a year Human Resources: ▪ Nurse specialists to coordinate the care of patients and to facilitate communication and provide psychological, spiritual, social and palliative care ▪ Medical support from consultation hepatologists or gastroenterologists with HPB interest able to provide continuous 24 hour coverage ▪ Interventional radiologist, ideally available 365 days a year ▪ Specialized liver pathologist onsite ▪ Intensivist/anaesthetist with interest in hepatology or HPB should be available ▪ Oncology team - Palliative care professionals, Pharmacist with interest in liver disease, Data Manager Organization ▪ Group (10-15) of managed clinical network providing liver services across UK. ▪ Managed networks responsible for: o Targeting resources where most needed o Agreeing to common protocols and service patterns o Monitoring clinical outcomes of treatment pathways • Patient pathways to be determined by National and International guidelines • Meetings weekly with HPB surgery, hepatology, pathology, oncology, radiology and specialist nurses. Innovation: ▪ Networks should have clinical trials facility and an active research programme ▪ MCNs (Multicare Networks) should actively participate in clinical research that aims to improve the management of liver and HPB surgery patients. ▪ Participation in multi-centre trials…should be a priority.
CCO – Criteria for the Delivery of Pancreatic Cancer Surgery (1999) Volume: ▪ Surgical volumes in the range of 25 cases per year (including 10 major pancreatic resections) should be minimum targets,

with 50 cases per year an optimum volume for HPB service

Physical Resources:

- Fully equipped; Available 24/7; Capability for intraoperative ultrasound and fluoroscopy; With ventilator capacity; Ultrasound, Colour Doppler, CT, MRI (may be offsite), Angiography, PTC, All available 24/7; Dialysis, PTN
- Infectious disease

Human Resources:

- Ideally more than 1 surgeon involved
- A sufficient complement of HPB consultant surgeons able to provide continuous 24 hour cover throughout the year. The consultants should be supported by specialist registrars.
- Radiologists skilled in angiography, embolization, transhepatic stenting, abscess drainage
- Anesthesiologist with capability to manage long and complex operations
- Dedicated trained critical care physicians
- Endoscopists: Physicians with capability to perform endoscopic diagnosis (ERCP) and treatment (papillotomy, endoscopic stenting)
- Nursing care, experienced in management of complex abdominal surgical problems, particularly HPB and pancreatic diseases, abdominal sepsis and fistulas
- Medical and radiation oncologists to consult for pre and post operative interdisciplinary decision making
- Supportive care, including pain management, psychosocial support and palliative care

Organization

- Team approach, including surgical and non-surgical specialists
- Regular review of patient management (educational round, morbidity and mortality review, formal ongoing outcome measurement and quality assurance)
- Information system in place to support quality assurance and to facilitate interface with Cancer Care Ontario, education, consultation and management programs

Innovation

To advance knowledge in the field to improve patient outcomes

NY State Committee on Quality Improvement in Living Liver Donation (2002)

Human Resources:

- Two liver transplant attending surgeons, one present for entire procedure and both present for critical portions
- A third should be present in recipient operating room
- Two separate anesthesia attending physicians and teams for donor and recipient operations
- 24/7 coverage of transplant service by general surgery residents at year 2 level or higher, transplant fellows or physician extenders (nurse practitioners or physician assistants)
- Nursing staff, with ongoing education and training in live donor transplantation nursing care.
- Radiologist with experience in evaluation of liver transplant patients
- Interventional radiologists

NHS Executive: Improving outcomes in upper gastro-intestinal cancers (2001)

Volume:

- Cancer centres should draw patients from catchment areas of with populations of 2-4 million
- Minimum acceptable population size is 1 million for sparsely populated areas
- Team could expect at least 200 new patients requiring specialist treatment per year

Physical Resources:

- Provision of adequate and appropriate facilities for surgery and post-operative care
- Availability of EUS, spiral CT facilities, MRCP and ERCP at Cancer Centres

Human Resources:

- All members should be specialists in management of pancreatic cancer
- A designated lead clinician (physician or surgeon) who will take overall responsibility for assessment and treatment of patients
- Team Members include: Specialist HPB surgeons, Gastroenterologist, Anesthetist/intensivist, Radiotherapy specialist (clinical oncologist), Chemotherapy specialist with expertise in treatment of upper GI cancers, Radiologist with GI sub-specialty interest and expertise in interventions, Histopathologist, Cytopathologist, Dietitian, Clinical nurse specialist, Palliative care specialist, One or more members should be trained in endoscopic ultrasonography, Gastroenterologist with interest in upper GI cancers, Clinical nurse specialist with knowledge of upper GI cancer, Endoscopist with expertise in stenting, Interventional radiologist

Organization:

- Cancer Network in which roles of hospitals which offer upper GI services are specified
- Systems to link and coordinate activities of the hospitals within the Network
- Adequate systems and support for rapid communication between teams within the Network
- Evidence-based assessment, treatment and referral guidelines agreed by specialist teams throughout the network
- Systems for Network-wide audit of procedures and outcomes
- Evidence of regular team meetings at Cancer Units and Centres

Guidelines for Resection of Colorectal Cancer Liver Metastases (University of Edinburgh, 2005)

Volume:

- Liver resection should be based in a cancer centre serving a population of at least two million

Human Resources: ▪ At least two specialist surgeons trained in, and maintaining a special interest in liver resection surgery, and who can demonstrate a high level of skill and training in this area. Organization ▪ Consideration of patients for resection of liver metastases should be carried out in a single high volume centre ▪ Patients under consideration of treatment for hepatic metastases should be discussed at a multidisciplinary meeting ▪ The team should also include an oncologist, diagnostic and interventional radiologist with an expertise in hepatobiliary disease, histopathologist, and clinical nurse specialist.
The Leapfrog Group: Evidence-Based Hospital Referral Fact Sheet (2004) Volume: ▪ Evidence-based hospital referral Safety Standard indicates that the volume of surgery procedures for pancreatic resection is > 11/year

Abbreviations: NHS, National Health Service; NY, New York; UK, United Kingdom

DISCUSSION

The Expert Panel on HPB Surgical Oncology used the evidence that was available from the published literature, standards from other jurisdictions, data on provincial activity, and their own expert opinion to reach consensus on standards for HPB cancer surgery in Ontario. They also took into account issues of population distribution in Ontario, current regional service organization, distribution of HPB surgery volumes and the educational and research mandates of the various stakeholders.

The body of evidence on the optimum organization for delivery of HPB cancer surgery in the published and unpublished literature is quite limited. Most studies are focused on the volume-outcome relationship. As indicators of performance in an individual institution, the studies have significant limitations, including the inherent risk of referral bias and potentially confounding co-interactions. The published studies are also limited by a lack of standardization in their reporting of outcomes and in the methodology used to define high- and low-volume centres. They also tended to focus on single procedures or types of procedures rather than the full range of HPB cancer surgery. The Panel considered trying to plot a volume-outcomes curve from raw data in the studies but this proved to not be feasible.

Notwithstanding these limitations, the Panel noted that all the studies did show a definite trend for improved outcome with increasing volume, both for surgeons and hospitals. There was consensus for the concept that these patients present very complex oncological problems and require an integrated approach by a dedicated team with access to advanced levels of expertise, system resources, and integrated care, in order to achieve the best possible outcomes. The Panel felt quite strongly that carrying out isolated surgical procedures in the absence of a comprehensive system of care is not likely to result in appropriate outcomes. There was consensus that, in keeping with the current trend within Ontario, the centralization of complex surgical procedures should continue and that the development of integrated regional networks of care will allow appropriate participation in HPB cancer care by the remaining institutions. This will assist in the goal of providing appropriate care as close to home as possible, whenever possible.

The Expert Panel on HPB Surgical Oncology discussed the issue of volume standards and, while acknowledging the previously discussed problems in the available literature, did reach consensus on this issue. The Panel agreed that the specific structural or process factors that influence the volume-outcome relationship were not discernable from the current literature. They felt that the predominant focus at this time should be on the institution as a whole and, therefore, felt it most appropriate to define an overall volume for an institution rather than define an individual surgeon volume. The Panel also felt it appropriate to consider the major hepatopancreaticobiliary surgical procedures, for both benign and malignant disease, as part of the institutional volume. This opinion is based on the similarities in the surgical management of these patients and the fact that the volume-outcome data is often based on all procedures rather than only cancer procedures. The procedures are resection of the pancreatic head (or total pancreatectomy) with duodenum, anatomic resection of the liver, and resection and reconstruction of the biliary tract. The Panel also felt that, in developing the volume standard of the number of index surgical procedures per institution, there should be some consideration also of the size of the population served, the optimum utilization of specialized hospital resources, and the need to maintain expertise and skills in the entire interdisciplinary team. This recognizes the realities of population distribution and

current health care organization in the province of Ontario, and the Panel felt that the number of index cases would serve as an adequate surrogate for the volumes of the other components of comprehensive cancer care.

After due deliberation, the Expert Panel reached consensus that a minimum institutional volume of 50 index HPB surgery cases per year is required to maintain the skills of the multidisciplinary team, provide the regional consultation and referral service, and achieve appropriate outcomes in Ontario. The Panel also concluded that the evidence demonstrated better outcomes with increasing volume at all volume levels. The Panel recognized that applying a criterion based on this finding would result in a relatively small number of institutions providing complex HPB cancer surgery and that the development of regional networks of care will be critical to providing optimum integrated care across the province. It is also recognized that some regions do not currently have the case volume to support the recommended targets. Additionally, some major University Centres, where participation in complex HPB surgery is important to the broader institutional educational mandate, will also face challenges in meeting the volume targets. However, the Panel believes that the combination of further regional consolidation and the increasing volume of care required by a growing and aging population will provide solutions to these difficult issues and that it will be possible to provide both excellent care and meet regional and institutional needs with the standards described.

CONCLUSIONS

Based on its study of the available evidence and the consensus process, the Expert Panel on HPB Surgical Oncology have identified several characteristics that institutions and surgeons providing care for patients with cancer of the liver, pancreas, and biliary tract should have in order to achieve the best possible outcomes for this patient population.

Surgeon Criteria

General characteristics for surgeons undertaking the management of patients with HPB cancer include knowledge of the biological behaviour and natural history of and range of treatment options for these patients. The surgeons are to be skilled in modern techniques of HPB surgery, and knowledgeable about the management of the early and late postoperative complications. They are committed to providing excellence in care, and to advancing knowledge in the field. They support and participate actively as a member of a multidisciplinary team and are committed to advancing knowledge to improve the care of these patients. They are also committed to participation in quality assurance initiatives.

Surgeons carrying out complex operations will have advanced training in HPB surgery and provide consultation services, leadership, and professional development support to other surgical providers who also have an important role in the care of patients with hepatopancreaticobiliary disorders including cancer.

Hospital Criteria

Institutions providing complex surgical procedures for HPB cancer require a comprehensive range of fiscal and human resources in order to meet the needs of this patient population. Organizationally, institutional commitment to multidisciplinary care that includes regular case conferencing, quality assurance activities (including regular outcomes review), and an information management system to provide the necessary data is a key requirement. Such institutions must be committed to working in a system of regional care, including a linkage with a regional cancer centre, and have a commitment to evidence-based practice, including the use of appropriately developed guidelines.

They will have the human resources required to provide the full range of necessary care on a continuous basis. This includes a minimum of two surgeons with specific training in HPB surgery and access to all necessary medical specialists, specifically including focused expertise in diagnostic and interventional radiology, HPB pathology, anaesthesiology, medical oncology, and radiation oncology.

They will have the physical resources necessary, including fully equipped and available operating rooms that have intraoperative imaging and adjunct modalities such as radiofrequency ablation, technologies for liver parenchymal division, and technologies for minimally invasive surgery. They will

have appropriate facilities for postoperative care (ward and ICU) that are able to deal with the common postoperative problems, including renal failure. Imaging services for both diagnostic and interventional purposes need to be available on a continuous basis and to include a full array of technologies.

An HPB Surgical Centre needs to have a critical mass of patients in order to achieve appropriate outcomes. The recommendation is that they carry out at least 50 major HPB cases annually, including at least 20 pancreatic resections.

Overall, the Expert Panel on HPB Surgical Oncology believes that the benefits associated with the implementation of these standards would result in improvements in patient outcomes, including lower operative mortality rates, the reduced frequency of serious complications, better disease-free and overall survival, and improved quality of life for HPB cancer patients. The Expert Panel feels that these standards will provide useful guidelines to those responsible for the organization of health care, including governments, Cancer Care regional vice presidents, regional planning authorities (LHINs), hospital CEOs, surgeons, and other health care professionals, in the planning of integrated regional and provincial cancer services.

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Evidence-Based Series #17-2 Version 2: Section 3

Hepatic, Pancreatic, and Biliary Tract (HPB) Surgical Oncology Standards: Standards Development and External Review—Methods and Results

M. Marcaccio, B. Langer, B. Rumble, A. Hunter,
and the Expert Panel on HPB Surgical Oncology

A Special Project of the Surgical Oncology Program, Cancer Care Ontario and
The Program in Evidence-Based Care, Cancer Care Ontario
Developed by the Expert Panel on HPB Surgical Oncology

Report Date: June 14, 2006

These guideline recommendations have been ENDORSED, which means that the recommendations are still current and relevant for decision making. Please see Section 4: Document Review Summary and Tool for a summary of updated evidence published between 2006 and 2015 and for details on how this Clinical Practice Guideline was ENDORSED.

THE SURGICAL ONCOLOGY PROGRAM AND THE PROGRAM IN EVIDENCE-BASED CARE COLLABORATION

The Surgical Oncology Program (SOP) and the Program in Evidence-Based Care (PEBC) are initiatives of Cancer Care Ontario (CCO). The mandate of the SOP is to improve the delivery of cancer surgery in Ontario through initiatives designed to increase access to care, improve the quality of care, support the recruitment and retention of cancer surgeons, support knowledge transfer and evidence-based practice, and foster research and innovation. The mandate of the PEBC is to improve the lives of Ontarians affected by cancer, through the development, dissemination, implementation, and the evaluation of evidence-based products designed to facilitate clinical, planning, and policy decisions about cancer care. The SOP and the PEBC have worked collaboratively on a number of occasions to develop evidence-based materials relevant to the surgical community in Ontario, which includes the creation of HPB surgical oncology standards.

The PEBC is best known for producing high-quality evidence-based practice guideline reports, using the methods of the Practice Guidelines Development Cycle (1,2). A typical PEBC report consists of the comprehensive systematic review of the clinical evidence on a specific

cancer-related topic, the interpretation of and consensus agreement on that evidence, the resulting clinical recommendations, and the results of an external review by Ontario clinicians for whom the topic is relevant. The PEBC has a formal standardized process to ensure the timeliness of each clinical practice guideline report, conducting routine periodic reviews and evaluations of the scientific literature and, where appropriate, integrating that literature with the original practice guideline report information.

As part of its quality improvement mandate, the SOP convenes expert panels for the selection of quality indicators and the development of clinical guidelines and organizational standards. The panels are comprised of surgeons, other clinicians, health care administrators, other health care professionals, and methodologists and are established on an as-needed basis for specific quality initiatives, such as the development of the HPB surgical oncology standards. In this instance, the SOP coordinated the development of the Expert Panel on HPB Surgical Oncology, and the PEBC contributed methodological expertise. The PEBC process and report format has been adapted for this HPB standards document.

The Evidence-Based Series

This Evidence-Based Series is comprised of the following three sections:

- *Section 1: Standards* This section contains the standards derived by the Expert Panel on HPB Surgical Oncology through systematic review, an environmental scan, interpretation of the clinical and scientific literature, and consensus process, as well as through a formalized external review by Ontario practitioners and administrators.
- *Section 2: Systematic Review* This section presents the comprehensive systematic review of the clinical and scientific research, the environmental scan, and the Panel discussion on the topic and the conclusions drawn by the Expert Panel on HPB Surgical Oncology
- *Section 3: Methodology of the Standards Development and External Review Process* This section summarizes the standards development process and the results of the formal external review by Ontario practitioners and administrators of the draft version of the HPB surgical oncology standards and systematic review.

DEVELOPMENT OF THE EVIDENCED-BASED SERIES

Developing the Draft Systematic Review and Standards

This Evidence-Based Series was developed by the Expert Panel on HPB Surgical Oncology. The series is a convenient and up-to-date source of the best available evidence on hepatic, pancreatic, and biliary tract surgical oncology standards, developed through systematic review, evidence synthesis, and input from practitioners and health care administrators in Ontario. Section 2 contains the systematic review of the evidence on outcomes related to the optimum delivery of cancer-related HPB surgery. The draft recommendations derived from the interpretation of that evidence by members of the Expert Panel are detailed in Section 1. Sections 1 and 2, along with Section 3, were circulated to Ontario practitioners and administrators for their feedback. Section 3 presents the feedback process results and any changes made to the draft document. This series represents the third collaboration between Cancer Care Ontario's SOP and PEBC.

Expert Panel Consensus Process

The recommendations were based on available information regarding surgeon and other team member training and experience, resource requirements, centre organization, and the relationship of volumes to outcomes. Information from the environmental scan plus the experience of panel members led to a consensus on all issues but the volume thresholds. The literature search showed a consistent relationship between centre volume and postoperative mortality for radical pancreatic resection but not as consistent a relationship for liver resection.

Members of the Expert Panel agreed with this interpretation of the evidence, and the main discussion within the Expert Panel focused on what would be a reasonable minimum volume to set as the provincial standard, given the limitations of the data reviewed. Members of the Expert Panel reached consensus on the volume numbers as stated.

External Review by Ontario Clinicians

Following the review and discussion of Sections 1 and 2 of this evidence-based series, the Expert panel on HPB Surgical Oncology circulated the clinical practice guideline and systematic review to clinicians, hospital administrators, and other stakeholders within the Province of Ontario for review and feedback. Box 1 summarizes the draft standards and supporting evidence developed by the panel.

BOX 1:
DRAFT RECOMMENDATIONS
(approved for external review March 20, 2006)

SURGEON CRITERIA

General Characteristics

The general characteristics for surgeons undertaking the management of patients with HPB cancer are as follows:

- Knowledgeable regarding the biology of HPB cancer, its natural history, appropriate investigation and the whole range of treatment options.
- Skilled in modern techniques of surgery of the liver, pancreas, and biliary tract, including the capability for managing vascular complications and vascular reconstruction.
- Experienced in the management of patients with hepatobiliary and pancreatic diseases, especially the management of early and late postoperative complications.
- Committed to providing excellence in care to patients with HPB diseases and to advancing knowledge in the field in order to improve patient outcomes.
- Committed to participating as a member of a multidisciplinary oncology team.
- Committed to participating in Cancer Care Ontario (CCO) quality initiatives.

Training

Although there is not a formally recognized subspecialty in HPB surgery, the complex nature of this subspecialty area has lead to the development of training programs designed to provide the kind of expertise and experience necessary to appropriately manage patients with HPB diseases. Thus, appropriate training would include certification by the Royal College of Physicians and Surgeons of Canada in General Surgery (or its equivalent) plus the completion of a period of advanced training in HPB surgery designed to reach a high level of proficiency in the management of the complex surgical problems found in this patient population. The training program should focus specifically on the management of malignant disease and result in the trainee acquiring competence to manage not only routine cases but also those requiring more complex resection and reconstruction. Thus, surgeons practicing HPB surgery should have completed either:

- A specific formal Fellowship in HPB surgery, or
- A Surgical Oncology Fellowship with a major emphasis on HPB surgery

Surgeons who trained prior to the existence of HPB or Surgical Oncology Fellowships may have had such training in less formal ways, such as extended post-residency training in a busy HPB service or mentoring and progressive experience in the early years of their staff appointment in a hospital with a busy HPB service. The increasing complexity of HPB surgery and the development of excellent-quality, formal fellowship training support the use of the new standards for surgeons now entering the system. All surgeons should maintain their expertise and knowledge through continuing professional development programs and a commitment to a career focus on HPB surgery.

HOSPITAL CRITERIA

General Characteristics

A tertiary care HPB surgical centre should be capable of managing the full range of surgical care for

patients with diseases of the liver, pancreas, and biliary tract, from the most complex to the most common, in a single hospital. A minimum of two HPB surgeons should be on staff in order to provide intraoperative assistance and continuous preoperative and postoperative care, while allowing for appropriate personal and professional leave. The hospital should have an affiliation with a Regional Cancer Program, and the HPB Program should include teaching, research, quality improvement, and program advancement elements.

Hospitals that do not have tertiary HPB services will provide care for patients with common HPB conditions. They should have an established relationship with a tertiary care HPB Centre to facilitate consultation and referral of common and uncommon cases through a regional network of care such as Local Health Integrated Networks (LHINs), so that all patients may have access to high-quality care in the appropriate setting. These hospitals and their professional staff would also play an important role in the initial diagnostic investigation and surgical follow-up of patients with complex problems. Participation in such a regional care network should lead to both better access to and quality of care.

The capability to provide optimal HPB care requires that an institution ensure the availability of the appropriate physical, fiscal, and human resources needed to provide for the complete spectrum of patient care from early diagnosis to long-term management and supportive care. Hospitals should have a definable system of care for HPB patients' that is integrated with the other components of the broader cancer care system.

Specific System Requirements

- Formal acknowledgement by the hospital that it is a Centre for HPB Surgery and, therefore, has a distinct HPB Surgery Program with definable leadership structure and accountability.
- A commitment to provide HPB surgery in a timely manner, including support of and commitment to the targets set by the provincial wait-time strategy
- A system of patient care that ensures multidisciplinary management, including Multidisciplinary Cancer Conferences (i.e., tumour boards) involving the appropriate health care professionals to ensure that patients receive the most appropriate treatment. This is essential for the achievement of optimal patient outcomes.
- A system of regular review of the program, including clinical and educational rounds, morbidity and mortality review, and quality assurance, including a system for the regular tracking of patient outcomes. This includes participation in all quality improvement programs of Cancer Care Ontario.
- Participation in Regional and Provincial Integrated Networks of Care as outlined in the CCO Provincial Cancer Plan (2004), through the LHINs.
- Infrastructure Support for Participation in Local and National Clinical Research Studies

Physical Resources

Appropriately equipped operating rooms available 24 hours a day, seven days a week. This includes the capability for intraoperative imaging (fluoroscopy and ultrasound) and appropriate adjunctive therapy (i.e., radiofrequency ablation).

- A full range of diagnostic imaging ability including ultrasound (all modalities including Doppler), CT scan, MRI, angiography, and interventional radiology with appropriate skills in HPB interventions.
- Diagnostic and therapeutic Interventional endoscopy available 24 hours per day, seven days per week.
- An appropriately equipped intensive care unit (ICU) capable of providing the appropriate range of ventilation modalities, dialysis, and the physical facilities for management of complex infectious problems.
- A fully developed nutrition service including total parenteral nutrition (TPN).

Human Resources

HPB services are optimally delivered in a multidisciplinary team setting and require a full range of skilled health care professionals for optimum outcomes. These include:

- Qualified HPB surgeons (see Surgeon Criteria and Training).
- Radiologists with appropriate expertise across the full range of angiographic, biliary tree

imaging, abscess management, and ablative techniques.
- Dedicated, certified critical care physicians.
- An endoscopy service with advanced skills in biliary therapeutic endoscopy.
- Nursing personnel experienced in the management of complex abdominal surgical problems, particularly HPB diseases, abdominal sepsis, and fistulae.
- Medical and radiation oncology services available for consultation and interdisciplinary decision making.
- Supportive care, including pain management, psychosocial support, and palliative care.
- Allied health professionals including nutritional care and occupational and physical therapists.
- Pathologist with a special interest in HPB diseases and a commitment to developing the appropriate expertise.
- Administrative support, including a system of data management to meet the needs of the HPB Service.
- Availability of an appropriate spectrum of physician subspecialties to provide the required support to HPB patients, especially infectious disease practitioners.
- Anaesthesiologists with expertise in managing long, complex operations in which patients may potentially become unstable and in patients with impaired liver function.

Volume of HPB Surgery

The hospital with an HPB service should have an adequate volume of index cases to maintain the skills of the multidisciplinary team as required in a tertiary referral centre, to justify the resource investment required, and to assure that optimum outcomes are achieved.

An HPB Centre should carry out a minimum of 50 index HPB cases per year (index cases include formal anatomic resection of one or more liver segments, all resections of the head of the pancreas, and all resections with reconstruction of the biliary tract). The volume should include at least 20 pancreatic resections.

OUTCOME MEASURES, BENCHMARKS, AND QUALITY ASSURANCE

The following outcomes are considered reasonable and achievable at HPB Centres across Ontario:
- A mortality rate (30-day plus in hospital) of less than 5% for major pancreatic resection
- A mortality rate (30-day plus in hospital) of less than 3% for anatomical liver resection.

Methods

Feedback was obtained through a mailed survey of 264 clinicians and other relevant stakeholders (see Table 1 for a description of the population surveyed). The survey sample was comprised of 239 clinicians and 25 administrators or other stakeholders. The survey consisted of items evaluating the methods, results, and interpretive summary used to inform the draft standards and whether the draft standards should be approved as a standards document. Written comments were invited. The survey was mailed out on March 20, 2006. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again). The Expert Panel on HPB Surgical Oncology reviewed the results of the survey.

Results

Ninety-one responses were received out of the 264 surveys sent (34.5% response rate; average response rate for PEBC/SOP collaborative reports = 42.4% (n=4)). Responses include returned completed surveys as well as phone, fax, and email responses. Of the practitioners who responded, 55 indicated that the report was relevant to their clinical practice, and they completed the survey. See Table 1 for a breakdown of survey results obtained by respondent category. Key results of the practitioner feedback survey are summarized in Table 2.

Table 1. Description of survey sample population

Category	Sent	Received
Medical oncologists	17	4
Radiation oncologists	13	6
Surgeons	145	53
Pathologists	1	-
Gastroenterologists	1	1
Medical imaging specialists	4	2
LHIN CEOs	7	-
Hospital Chief of Staff	12	3
Hospital Chief of Surgery	16	6
Cancer Surgery Investment personnel	8	3
Head, Surgical Oncology	7	4
Hospital CEO	19	7
Medical School Representative	3	1
Regional Vice-President	6	1
Other (various)	5	-
TOTALS	**264**	**91**

Note: LHIN, Local Health Integration Networks; CEO, Chief Executive Officer.

Table 2. Responses to eighteen items on the external review survey.

Item	Number (%)		
	Strongly agree or agree	Neither agree nor disagree	Strongly disagree or disagree
There is a need for a standards document on this topic	87	11	2
The evidence (literature search and environmental scan) is relevant and complete (e.g., no key information sources or studies missed, nor any included that should not have been)	84	9	7
I agree with the methodology used to summarize the evidence	85	7	7
The draft standards are in agreement with my understanding of the evidence	82	7	11
The draft standards in this report are clear	93	6	2
I agree with the draft standards as stated	75	13	13
The draft standards are suitable for the Ontario context.	67	15	18
The draft standards are too rigid to apply in the Ontario context	40	9	51
When applied, the draft standards will produce more benefits for patients than harms	82	11	7
The draft standards report presents a series of options that can be implemented	59	24	17
To apply the draft standards will require reorganization of services/care in my practice setting	50	13	37
The standards will be associated with more appropriate utilization of health care resources	60	29	11
The draft standards in this report are achievable	76	9	15
The draft report presents standards that are likely to be supported by a majority of my colleagues	69	15	15
The draft standards reflect a more desirable system for improving the quality of patient care than current practice	78	17	6
I would feel comfortable if patients received the care recommended in these draft standards	86	9	5

These draft standards should be formally approved	74	11	15
	Not at all likely or unlikely	**Unsure**	**Very likely or likely**
If these draft standards were to be approved how likely would you be to apply the recommendations to the clinical care or organizational and/or administrative decisions for which you are professionally responsible?	77	9	13

Eighty-seven percent of all respondents agreed that there exists a need for guidance on this clinical topic, 84% agreed that the evidence reviewed was relevant and complete, 85% agreed that the methods used in formulating the standards was correct, and 82% of all respondents were in complete agreement with the draft standards. Seventy-four percent of all respondents supported the draft report being approved as a standards document and stated that they would use the recommended standards in their own practice. The observed discordance between the result for the final question and the preceding 18 questions may be explained by the change in response structure where the previous 18 questions used a consistent scoring method but the final question deviated from this, which may explain the low approval score for the final question. The change in response structure for the final question was intentional to monitor the attentiveness of the respondents. The incongruent result suggests there may be some level of inattentiveness on part of the respondents.

Summary of Written Comments and Expert Panel Responses

Twenty-five of the 55 total respondents (45.5%) provided written comments. The main points contained in the written comments are displayed in the following chart along with the Expert Panel discussion and responses.

Comment 1: SURGEON NUMBERS: Several respondents forwarded concerns regarding the recommendation that a minimum of two HPB surgeons should be on staff in order to provide intra-operative assistance and continuous preoperative and postoperative care, while allowing for appropriate personal and professional leave.
Response: The overall emphasis of the standards reflects the concept of a designated unit, based on at least 2 surgeons for coverage, and continuity of care. Even in smaller tertiary centres, it should be possible to have two surgeons, who have the training described, commit to the level of participation in HPB care required by the standard. *Overall:* Agreed no changes to the HPB Standards document are warranted.
Comment 2: CASE VOLUME: Several respondents raised concern with respect to the validity of the volume target. A question was raised about including a specific target for liver resection.
Response: While, in some of the studies, there may be occasional high-volume centres with a high mortality rate, they are relatively few and do not diminish the consistent and clear evidence of improved outcomes with higher volumes. The Expert Panel reaffirms that using the mean cases per hospital per year or the mean cases per surgeon per year as the unit of comparison, as was performed in this document, is a valid method, given the limitations of the data obtained. Distal pancreatectomies are not considered to be index cases, and the 50-case

minimum refers to procedures listed in the Standards document. There is evidence to support the minimum number of pancreatic resections, but there is very little volume data available for liver resections. The total of 50 HPB cases per year is the number expected to be generated in a population of 1 million and includes 20 pancreatic resections.

Overall: Agreed under Volume of HPB Surgery replace "all resections of the head of the pancreas with "all Whipple and total pancreatic resections".

Comment 3:
IMPACT OF VOLUME TARGET: Several respondents raised concerns that the standards in general, and volume targets in particular, would lead to some institutions and surgeons no longer being able to perform the index procedures.

Response:
In order to meet the volume standards, HPB index cases will be done in a relatively small number of centres. The number reflects the caseload expected to be generated by a referral population of one million and is appropriate for the Ontario situation. Regions will have to support their referral centres, in order to help them achieve the target. For the most part, this has already occurred in Ontario.

Overall: Agreed no changes to the HPB Standards document are warranted.

Comment 4:
FUNDING: The question of funding being withheld from institutions performing these procedures at low volumes was raised.

Response:
Funding of procedures is a hospital-based decision, and outside the mandate of the PEBC and the Expert Panel.

Overall: Agreed no changes to the HPB Standards document are warranted.

Comment 5:
TEACHING REQUIREMENT: Concern was expressed that the teaching requirement would exclude non-university hospitals

Response:
The teaching requirement is not specifically for undergraduate or postgraduate training in medicine; it reflects the need for education of the team and the broader health care community in the appropriate management of these problems. This is necessary for appropriate quality in both teaching and non-teaching centres.

Overall: Agreed no changes to the HPB Standards document are warranted.

Comment 6:
INFRASTRUCTURE REQUIREMENTS: Clarification was requested with respect to the location and availability of some of the support resources

Response:
The required support services do not necessarily have to be continuously on site, rather they need to be continuously available when required. The wording in the Standards reflects this.

Overall: Agreed no changes to the HPB Standards document are warranted.

Comment 7: TRAINING REQUIREMENTS: Questions were raised with respect to whether transplant training would meet the standard. It was also suggested that more specificity be included with respect to the term "major focus on HPB surgery."
Response: These standards have been modified to reflect that HPB training can be achieved in both transplant and non-transplant programs, as well as surgical oncology fellowships. It is difficult to be more specific in defining the components of training as there are no agreed-upon standards for these training programs at this time. *Overall:* Agreed add a second bullet under Training Requirements "A Fellowship in liver transplant which includes a major focus in non-transplant HPB cases, or…"

Report Approval Panel

The PEBC Report Approval Panel (RAP) reviewed the draft Standards document in an advisory capacity in March 2006. The RAP consists of two members, including an oncologist, with expertise in clinical and methodology issues. Following review, the RAP motioned to fully endorse this document. No comments, requests for clarifications, or revisions were submitted for Expert Panel consideration.

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Appendix 1: Expert Panel on HPB Surgical Oncology members.

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Appendix 2: Literature search (MEDLINE).

exp Liver Neoplasms/su [Surgery]
exp HEPATECTOMY/ 5265
exp Liver Neoplasms/su [Surgery] 5249
hepatic surgery.mp. 180
exp LIVER/su [Surgery] 1430
1 or 2 or 3 or 4 or 5 9268
exp PANCREAS/su [Surgery] 857
exp Pancreatic Neoplasms/su [Surgery] 3132
pancreas surgery.mp. 25
exp PANCREATECTOMY/ 1864
7 or 8 or 9 or 10 4724
exp Biliary Tract Diseases/su [Surgery] 7065
biliary surgery.mp. 195
exp CHOLECYSTECTOMY/ 5855
exp Biliary Tract Surgical Procedures/ 7771
12 or 13 or 14 or 15 11471
6 or 11 or 16 23954
surgery/st 448
surgery/ma 252
surgery/sn 185
surgical procedures, operative/ 6597
surgery department, hospital/ 1062
general surgeon$.tw. 749
general surgery$.ti. 360
exp Colorectal Surgery/ 420
"colon and rectal surgery (specialty)"/ 420
18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 9558
exp Disease-Free Survival/ 14682
exp SURVIVAL/ 1134
exp Survival Rate/ 46033
exp Patient Readmission/ 2044
exp Postoperative Complications/ 101643
"outcome assessment (health care)"/ 18519
exp "outcome and process assessment (health care)"/ 232760
28 or 29 or 30 or 31 or 32 or 33 or 34 354262
exp Patient Admission/ 6118
exp Health Manpower/ 1315
hospital volume$.tw. 233
exp Hospital Mortality/ 6570
surgeon volume$.tw. 95
surgical volume$.tw. 97
exp HOSPITALS/
36 or 37 or 38 or 39 or 40 or 41 or 42
17 and 27 and 35 and 43

Evidence-Based Series #17-2 Version 2: Section 4

Hepatic, Pancreatic, and Biliary Tract (HPB) Surgical Oncology Standards: Standards Development and External Review— Guideline Review Summary and Review Tool

M. Marcaccio, L.D. Durocher-Allen and the Expert Panel on HPB Surgical Oncology

A Special Project of the Surgical Oncology Program, Cancer Care Ontario and
The Program in Evidence-Based Care, Cancer Care Ontario
Developed by the Expert Panel on HPB Surgical Oncology

Review Date: XXX, 2015

The 2006 guideline recommendations are

ENDORSED

This means that the recommendations are still current and relevant for decision making.

The original version of this guidance document was released by Cancer Care Ontario's Program in Evidence-based Care in 2006, and updated in 2015. In September 2014, this document was assessed in accordance with the PEBC Document Assessment and Review Protocol and was determined to require a review. As part of the review, a PEBC methodologist conducted an updated search of the literature. A clinical expert (MM) reviewed and interpreted the new eligible evidence and proposed the existing recommendations could be endorsed. The HPB Surgical Oncology Expert Panel endorsed the recommendations found in Section 1 (Clinical Practice Guideline) in December 1st 2015.

DOCUMENT ASSESSMENT AND REVIEW RESULTS

Questions Considered

1. What is the optimum organization for the delivery of cancer-related hepatic, pancreatic, and biliary tract surgery in Ontario?

Literature Search and New Evidence

The new search (January 2006 to May 2015) yielded a total of 4 systematic reviews and 61 publications of primary studies. The results of the included systematic reviews and primary studies can be found in the Document Review Tool (page 33).

Impact on Guidelines and Its Recommendations

The evidence supports the existing recommendations; specifically, the identified systematic reviews and meta-analysis provide strong evidence of a volume-outcome relationship, for both hospital and surgeon volume, in hepatic, pancreatic, and biliary tract surgical oncology. Both high hospital volume and high surgeon volume are associated with lower 30-day mortality. The evidence shows a weaker link between hospital or surgeon volume and long-term survival.

There is a recent study (Kanhere 2014) that suggests that it is not the volume of any one individual procedure, but the aggregate volume of complex surgical procedures that is the key quality metric. This is not to say that the volume of an individual procedure is not important to outcomes and quality. There are many more dimensions to quality than perioperative mortality. With periampullary cancer/pancreaticoduodenectomy in particular, a potentially much larger influence on quality is the judgement of what is resectable, both on preoperative assessment and in the operating room. It is currently understood that if this could be measured, individual procedure volumes would likely have a major impact.

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Document Review Tool

Number and title of document under review	17-2: **Hepatic, Pancreatic, and Biliary Tract (HPB) Surgical Oncology Standards**
Current Report Date	June 14, 2006
Clinical Expert	Michael Marcaccio
Research Coordinator	Lisa Durocher-Allen
Date Assessed	December 3, 2013
Approval Date and Review Outcome (once completed)	Endorsed December 1 2015

Original Question(s):
What is the optimum organization for the delivery of cancer-related hepatic, pancreatic, and biliary tract surgery in Ontario?

Target Population:
The following standards, developed by the Expert Panel on HPB Surgical Oncology, apply to hepatic, pancreatic, and biliary tract cancer surgery and include the full spectrum of multidisciplinary assessment and treatment:

- Management of primary and secondary liver cancer by hepatic resection or locally destructive techniques (ablation by any modality, hepatic artery embolization with or without chemotherapy, etc.).
- Management of cancer of the pancreas and peri-ampullary region by pancreatic resection.
- Management of tumours of the biliary tract (including gallbladder) by surgical resection.

Study Section Criteria:

Inclusion Criteria

Articles were selected for inclusion in the systematic review of the evidence if they were fully published English language reports reporting volume-outcome measurements, for either surgeons or hospitals/institutions, in hepatic, pancreatic, or biliary cancer. Ideally, reports would provide both surgeon and hospital/institution volume-outcome measurements. The types of studies eligible for inclusion were randomized controlled trials (RCT), retrospective studies, and case-series reports (with at least 10 patients).

Outcomes of interest

The primary volume-outcome measurements that were of interest included short-term mortality/survival, adverse effects, hospital length of stay, and long-term survival (five-year optimal). Secondary outcomes of interest included costs (as reported in the jurisdiction where the trial was run), physician training, hospital/institutional requirements, and any diagnostic procedures used.

Search Details:
2006 – February 2014 (Medline Week 5)
2006- February 2014 (Embase Week 5)
Also searched: Cochrane library via OVID (CDSR [Feb 2014], CCTR [Feb 2014], and DARE [1st quarter, 2014).

Brief Summary/Discussion of New Evidence:
A total of 8,682 citations were identified from MEDLINE, EMBASE, CDSR, CCTR, and DARE via OVID. Of those, 169 were selected for full text review. A total of 72 met the inclusion criteria, 3 publications were

irretrievable, and 94 publications were excluded.
Of the 72 identified publications, there were 4 publications of 4 systematic reviews. The remaining 59 publications were primary studies and 14 abstracts.

The results of the systematic reviews can be found in Table 1. Of the 72 identified publications, 65 publications of primary studies and abstracts that were not included in at least one of the identified systematic reviews (Table 1) can be found in Table 2, 3, and 4. Seven primary studies were included in at least one of the identified systematic reviews; the results of those studies are not reported here. Appendix 1 consists of a bibliography of those studies.

Clinical Expert Interest Declaration: None to declare

Table 1. Systematic reviews meeting inclusion criteria for EBS #17-2

Author, year, reference	Inclusion criteria	Methods	Intervention/ Comparison	Outcomes of interest	Brief results
van Heek 2005 Systematic review; data on Dutch nationwide registry Pancreatic resection for pancreatic and periampullary malignancy	All studies comparing mortality rates of patients w/PR between hospitals w/ diff volumes	**Systematic review:** Medline and Embase: 1966-2004 Cochrane library: 1996-2004 RR calculated for high vs low volume hospitals (using multiple cutoff points as data allowed) **Registry:** Data from 1994-2004, 4 time intervals ('94-'95, '96-'98, '99-'00, '01-'03)	Hospital volume (high vs low) **SR:** Categorized by cutoff values of high/low Four cutoff points defined: I: 2 PR/y II: 5 PR/y III: 10 PR/y IV: 20 PR/y **Registry:** 4 volume categories: <5, 5-9, 10-24, >25 PR/y	Hospital or 30-day mortality	***Systematic review*** 12 included studies, PR from 1984-1998, n=19,688 patients (b/w 130-7229 per study) ***Mortality (high vs low), RR*** Cutoff I: (6 studies) 6.6% vs 19.0%, RR 0.25-1.10 Cutoff II: (9 studies) 5.2% vs 12.6%, RR 0.29-0.76 Cutoff III: (7 studies) 3.8% vs 11.8%, RR 0.21-0.62 Cutoff IV: (2 studies) 2.2% vs 15.4%, RR 0.07-0.15 (12 studies included; 24 total analyses done using as many cutoff points as available data allowed; RR of 16/24 analyses statistically significant (p=0.05) ***Dutch registry data*** *Mortality in <5 vs >25* 94-95: 16.1% vs 1.5% 96-98: 15.9% vs 0.6% 99-00 and 01-03: Comparative mortality rates unchanged, exact numbers not given.
Gooiker 2011 Systematic review and meta-analysis Surgical treatment of pancreatic cancer	All studies measuring association between hospital or surgeon volume and clinical outcomes, for surgical treatment of pancreatic cancer; excluded single-hospital or surgeon studies, and used primary data (no SR)	Medline, Embase, Cochrane Library, search done on Feb 1 2010, also reference lists of relevant articles, and "related articles" on PubMed. MA: OR for mortality or HR for survival reflects odds of mortality in highest-volume vs lowest-volume group	Hospital or surgeon volume	Postoperative mortality (30-day, 60-day, in- hospital or postoperative mortality), or survival	***Systematic review*** 14 included studies, 11 hospital volume, 2 surgeon volume, one study had both Cutoff values varied: low-volume ranged from 1-5 procedures/year, high volume ranged from min 7-36 procedures/year ***Meta-analysis*** *Hospital volume and postoperative mortality* OR: 0.32 (0.16-0.64), RR: 0.16 (0.02-1.36), HR: 0.44 (0.35-0.56) *Surgeon volume and postoperative mortality* OR: 0.46 (0.17-1.26), HR: 0.49 (0.29-0.84) *Hospital volume and 5-year survival* HR: 0.79 (0.70-0.89)
Garcea 2009 Systematic review Hepatic surgery	Comparative studies of pre-/ post-centralization data, Comparative studies of different volume surgeons	CINAHL, Clinical Trials Database, Current Contents Connect, Current Controlled Trials, EMBASE, medline, National Research Register, National health service centre research and Dissemination,	Centralization, hospital or surgeon volume	Mortality (hospital or 30-day), morbidity, duration of stay, resource utilization	10 studies included hepatic resection between 198 2003. N= 30,421 patients, between 293-16,582 per study Diagnoses: primary liver cancer, metastatic cancer, other diagnoses (trauma, benign, infectious) ***Hospital Volume*** Significant heterogeneity in high/low definitions. All studies showed improved outcomes for higher vs lower volume hospitals after adjustment for

	and/or hospitals as proxy	PubMed, Cochrane library 1997-June 2007 Also: grey lit			patient factors with logistic regression (numbers not given) ***Surgeon volume*** No studies reported on surgeon volume and outcome ***Overall survival*** One study showed overall survival advantage for high volume vs low volume after 3 years (P=0.02) ***Mortality*** 5/10 studies reported significantly lesser risk-adjusted mortality rate in higher vs lower volume hospitals, range 5.8-22.7% in low volume vs 1.5-9.4% in high volume ***Morbidity*** One study reported on this. Surgery at low-volume hospitals associated with increased risks of: reintubation RR, 2.5; 95% confidence inter9val [CI], 1.8--3.4), pulmonary failure (RR, 2.3; 95% CI, 1.6--3.5), pneumonia (RR, 0.35; 95% CI, 1.05-- 5.6), acute renal failure (RR, 2.0; 95% CI, 1.1-- 3.7), acute myocardial infarction (RR, 2.6; 95% CI 1.2--5.9), and aspiration pneumonitis (RR, 1.4; 95% CI, 0.9--2.0). ***Duration of stay*** 4/5 studies that reported this found significantly lesser postoperative hospital stay in high vs low volume hospitals ***Costs*** two studies reported; one found no difference between high and low volume hospitals, one study found that costs of resection in low-volume hospitals higher than in high volume

PR: pancreatic resection; RR: relative risk; MA: meta-analysis; OR: odds ratio; HR: hazard ratio;

See Appendix 1 for a list of identified studies that were included in at least one of the systematic reviews in Table 1. Please note that these studies were not included in Table 2.

Table 2. Pancreatic primary studies meeting inclusion criteria for EBS #17-2

Author, year, etc	Procedure and population	Methods	Intervention	Outcomes of interest	Brief results
Hospital volume					
Alsfasser 2012	Pancreatic surgery (for tumor or for chronic pancreatitis) Germany	Survey of German Society of General and GI surgery, info on pancreatic operations in 2006, 2008, 2009 Type of hospital, size/number of beds, number of PR	Hospital volume; university vs teaching vs other hospital *Volume cutoff** In 2006: 1-11, 12-17, 18-31, 32+ in 2008-9: 1-11, 12-18, 19-33, 34+	Mortality, reoperations,	Data received from 222 hospitals for 2006, 154 hospitals in 2008, 158 hospitals in 2009 Relative number of operations increased in university hospitals and decreased in teaching hospitals from 2006-2008 (p≤0.03) Chi-square values showed no difference between mortality rates for any of the volume categories, in any of the given years No difference between rates of reoperation for any volume category in any given year (p>0.08)
Allareddy 2007	Pancreatectomy (as one of several procedures studied)	Retrospective analysis of NIS 2000-2003 Multivariable logistic regression	Hospital volume *Volume cutoff:* Leapfrog threshold** *For ESO: cutoff is*	In-hospital mortality, spillover effect	Data on 4931 PAN available Overall in-hospital mortality for PD: 6.21% LV hospitals associated with higher odds for in-hospital mortality compared to HV: OR 2.09 (1.46-2.98) P<0.001 *Spillover effect* Mortality OR for PAN compared against hospital

			≥13		volume cutoffs for CABG, PCI, AAA and ESO All non-significant except for ESO OR of PAN mortality vs ESO HV criteria: Met ESO: ref Did not meet ESO: 2.64 (1.63-4.30) No ESO: 3.18 (1.77-5.74)
Anderson 2012 , **Abstract**	Pancreaticoduodenectomy, bile duct resection, and combine liver bile duct section	Retrospective analysis of the US Nationwide Inpatient Sample database, 1998-2009	Hospital volume (high vs low), teaching/non-teaching	Rates of surgical treatment over time	N = 32 561 HV or teaching hospital more likely to receive surgical treatment (OR 1.3, p>0.001; OR 1.4, p<0.0001) and more surgery (OR 2.0, p<0.001; OR 2.3, p<0.001) Patients at HV or teaching hospitals were more likely to receive combined BD and liver resection, liver resection, or bile duct resection, compared to each less aggressive procedure (OR 1.2-6.6, p < 0.05
Balzano 2008	PD, Patients with pancreatic or periampullary disease [cancer], chronic pancreatitis Pancreatic cancer: 66.2% Other periampullary cancer: 23.5%	Bureau of Statistics, Italian ministry of health Inpatient discharge in Italy Logistic regression (OR adjusted for sex, payer, age, co morbidities and primary diagnosis)	Hospital volume *Volume cutoff:* 1-5, 6-13, 14-51, 89-104	Operative (hospital) mortality, length of stay	#PDs per volume category, lowest to highest: 518, 410, 455, 193 **Adjusted OR** *Highest category vs lowest:* OR 0.208 (0.082-0.526) OR significant for each volume category relative to the lowest volume category ***Length of stay*** Mean (sd) postoperative stay decreased from low- to very high-volume hospitals: 22.5 (15.7), 22.0 (15.1), 20.7 (14.4) and 18.4 (14.2) days respectively LOS at highest-volume hospitals significantly shorter than all other hospitals (P<0.001)
Bilimoria 2008	Patients 1994-1999 for 7 malignancies, including pancreatic	ROADS, in NCDB Cox proportional hazards, adjusting for sex, age, race, SES, stage, Charlson score, resection type, chemotherapy administration, radiation, and year of diagnosis	Hospital Volume *Volume cutoff:* No explicit cutoffs are given.	5 year survival rate	N = 13, 107 # hospitals per volume category (lowest & highest): 764, 37 Adjusted for Perioperative Mortality: 2.26 (1.78-2.86) Adjusted 5-year Survival : 1.22 (1.14-1.31)
Birkmeyer 2007	All patients 65-99, PR for cancer, years 1992-99	1992-2002 SEER-Medicare database Cox proportional hazards, adjusting for patient characteristics, censoring at end of follow-up (Dec 31, 2002) Adjusted: age, sex, race, year of procedure, acuity of admission	Hospital volume *Volume cutoff:* 0.3-2.0, 2.0-7.3, 8.3-135.5	5-year survival (or through to Dec 31, 2002)	# patients per volume category (lowest to highest): 286, 287, 282, respectively # hospitals per volume category (lowest to highest): 143, 59, 25 *Hazard ratio of mortality, high volume vs low* Unadjusted All patients: 0.77 (0.63-0.95) Survived surgery: 0.87 (0.71-1.05) Adjusted for patient characteristics All patients: 0.71 (0.58-0.87) Survived surgery: 0.78 (0.64-0.95)
Cox 2010 **Abstract**	PD or total PAN for malignancy	Statewide Planning and Research Cooperative hospital data between 2002 and 2007 (after regionalization). Logistic regression analysis. Same dataset was used in a previous study from 1984-1991 (before regionalization).	Hospital volume, Surgeon volume	Perioperative mortality, LOS	3051 procedures in 121 hospitals by 392 surgeons Overall perioperative mortality was 4.7%, which was lower than 15 years earlier (12.9%) 58.6% of cases performed at HV centers and 47.3% of procedures performed by HV surgeons *Mortality and surgeon volume:* HV 2.6%, moderate 4.0%, LV 9.9% *LOS and surgeon volume* HV 14.6, moderate 17.6 and LV 24.1 Compared to hospitals and surgeons with high caseloads, odds of death are 3.8 times higher in a minimal volume hospital (p<0.001) and 3.6 times higher for low volume surgeons (p<0.001)

de Wilde 2012	PD 100% cancer patients is implied, but not stated	Kiwa Prismant nationwide registry 2004-2009	Centralization, volume *Volume cutoff:* <5, 5-10, 11-19, ≥20 (but analyzed using Leapfrog cutoff)	In-hospital mortality	N=2156 patients ***Centralization*** Proportion of PD in centres ≥11 PD/y increased from 52.9% to 91.2% from 2004-2009 Mortality rate in <11 vs ≥11 hospitals was 11% vs 4.5% over 2004-2009 (p<0.001) *Volume vs Mortality, 2004-2009* OR , vs ≥20 category 11-19: 2.00 (1.23-3.25) 5-10: 3.22 (2.00-5.18) <5: 5.08 (2.84-9.07)
Ghaferi 2011	Pancreatectomy (cancer operation) – implied that all diagnosis codes were for cancer	Medicare Provider Analysis and Review files from 2005-2007 Risk-adjustment for age, sex, race, urgency, comorbidities Logistic regression	Hospital volume *Volume cutoff:* LV: <2 HV: >27	30-day or in-hospital mortality; Major complications; Failure to rescue (mortality following complication)	*Risk-adjusted mortality:* 3.1% vs 13.3% in HV vs LV hospitals ***Odds ratios*** Overall mortality: OR 4.85 (3.53-6.68) Major complications: OR 1.72 (1.39-2.13) Failure to Rescue: OR 3.21 (2.18-4.72)
Gasper et al. 2009	Pancreatic resection (as one of several procedures)	California Office of Statewide Health Planning and Development (OSHPD) patient discharge data	Hospital Volume *Volume cutoff:* No explicit cutoffs are given.	In hospital mortality	Of 8901 patients, 5294 patients had pancreatic cancer. Data split into 2- 5 year periods, 1995-1999 (period B) and 2000-2004 (period C) to compare to original data – 1990-1994 (period A). ***Risk Adjusted Mortality Rate*** HV: 3.5% (Period A), 1.8% (Period B), 1.5% (Period C) LV: 14.1% (Period A), 7.0 (Period B), 5.6% (Period C) ***Odds ratio*** Period A – N/A OR from low- to very high-volume hospitals (Period B): 7.60 (2.89 =20), 5.24 (2.05-13.40), 4.40 (1.73-11.2), 2.08 (0.70-6.22), 2.27 (0.83-6.25),1 OR from low- to very high-volume hospitals (Period C): 4.02 (2.42-6.66), 3.27 (1.86-5.77), 2.50 (1.50-4.15), 1.39 (0.80-2.42), 1.66 (0.94-2.91),1
Ho 2006	Whipple procedure (PD) for cancer	Statewide hospital discharge files for Florida, NJ, NY, 1988-2000. Three time periods: 88-91, 92-96, 97-00 Logistic regression, adjusting for clustering of patients within surgeons and surgeons in hospitals, as well as patient/hospital characteristics	Hospital procedure volume surgeon procedure volume *Volume cutoff:* No explicit cutoffs are given, volume may be treated as continuous	Inpatient mortality	8253 Whipple procedures performed ***Adjusted OR for inpatient mortality*** 1992-96: OR 0.97 (0.76-1.23) 1997-2000: OR 0.91 (0.71-1.17) Hospital volume (ln): OR 0.85 (0.74-0.97) Surgeon volume (ln): OR 0.80 (0.69-0.92)
Jensen 2007	Pancreaticoduod enectomy	National Patient Registry and	Hospital procedure	Length of stay,	# patients, 1996-2001 =363, 2002-2004 = 218 ***Length of stay (mean)***

<table>
<tr><td></td><td>(Whipple procedure)</td><td>discharge information 1996-2004</td><td>volume

Cut offs
<5, 5-20, >20</td><td>Hospital mortality</td><td>1996-2001= 24.5, 2002-2004 = 23.9
Hospital mortality<table><tr><td></td><td>1996-2001</td><td>2002-2004</td></tr><tr><td><5</td><td>10.0 (3.3-21.8)</td><td>6.3 (0.2-30.2)</td></tr><tr><td>5-20</td><td>10.2 (7.0-13.4)</td><td>7.6 (3.7-13.7)</td></tr><tr><td>>20</td><td>-</td><td>5.6 (1.6-13.8)</td></tr></table></td></tr>
<tr><td>Joseph 2009</td><td>Pancreatectomy</td><td>2005 Leapfrog Group database and Health Grades Website</td><td>Hospital Volume

Part 1: Hospital cutoffs (very low to very high), 1-5, 6-10, 11-30, >30

Part 2 LV (< 10 a year), HV (>11 per year)</td><td>Mortality, system clinical resources,</td><td>N=434 hospitals
Clinical support factor:<table><tr><td></td><td>Odds Ratio</td><td>P value</td></tr><tr><td>ICU staffing</td><td>1.76 (1-45-2.13)</td><td><.0001</td></tr><tr><td>Safe Practice Score</td><td>1.27 (1.05-1.52)</td><td>0.01</td></tr><tr><td>HeathGrades 5 start rating</td><td>1.48 (1.16-1.88)</td><td><0.001</td></tr><tr><td>General surgery residency</td><td>2.74 (2.21-3.40)</td><td><0.0001</td></tr><tr><td>Gastroenterology fellowship</td><td>3.85 (3.00-4.95)</td><td><0.0001</td></tr><tr><td>Interventional radiology</td><td>2.02 (1.64-2.47)</td><td><0.0001</td></tr></table>Mortality
N=28 hospitals, LV = 19, HV =9
Volume OR 0.86 (0.60-1.24), ns
Cumulative system clinical support OR = 0.78 (0.73-0.87), p <0.001*
*non-significant results when 6 support factors were analyzed separately.</td></tr>
<tr><td>Kim 2011</td><td>Pancreatic resection, including PAN, Whipple’s PD, and pylorus-preserving PD</td><td>HIRA claims database (2005-2006)
Logistic regression adjusted for age, sex, route of admission , type of health security , and comorbidity</td><td>Hospital Volume

Hospital cut offs not mentioned</td><td>mortality</td><td># patients 3,168
<u>Odds ratios associated with mortality</u>:
Very low =1
Low 0.58 (0.29-1.11), p=0.11
Medium 0.57 (0.29-1.08), p = 0.09
High 0.21 (0.08-0.49), p=0.0008
Very high, 0.24 (0.08-0.58), p <0.0037</td></tr>
<tr><td>LaPar 2012</td><td>Patients who underwent pancreatic resection in 2008.
This study also included esophagectomy, abdominal aortic aneurysm repair, and coronary artery bypass grafting.</td><td>Retrospective cohort from the HCUP-NIS (U.S.) comparing inpatient mortality by hospital volume.
Hierarchical generalized linear models, adjusted by patient age, gender, and comorbid disease: 3 models: 1) volume as linear effect; 2) volume using restricted cubic spline; 3) volume using quintiles.</td><td>Volume cutoffs:

NR</td><td>In-hospital mortality</td><td>Weighted total of 19,194 patients

In hospital mortality
Linear effect total:: LR = 3.24, p=0.0719
Quintile total: LR: 5.53, p=0.2371
Spline total: LR 4.59, p=0.2044</td></tr>
<tr><td>Learn, 2010</td><td>Patients aged 18 years or older who underwent pancreatectomy for pancreatic cancer in the US.</td><td>Retrospective cohort from the HCUP-NIS (U.S.) from 1997 to 2006 comparing inpatient mortality between time</td><td>Volume cutoff (annual)

High>9
Medium: 4-9
Low 1-3</td><td>Inpatient mortality</td><td>7542 patients
Inpatient mortality
Annual volume of procedures at treating hospitals: OR (per case): 0.97 95% CI 0.95-0.99, p =0.018
Teaching vs non-teaching: OR= 0.68 95% CI 0.53-0.87, p =0.002</td></tr>
</table>

	This study also included esophagectomy, gastrectomy, and major lung resection.	periods, by hospital volume, by hospital type (teaching vs. non-teaching). Logit-linked generalized estimating equations adjusted using Elixhauser comorbidity index			
Lemmens 2011	Patients diagnosed with primary cancer of the pancreatic head, extrahepatic bile ducts, ampulla of Vater or duodenum.	Retrospective cohort from the Eindhoven Cancer Registry (Netherlands) from 1995-2000 and 2005-2008 comparing hospital volume and surgical volume and in-hospital mortality between time periods using Kaplan-Meier time series analysis.	Hospital Volume, Surgical Volume	In-hospital mortality,	2129 patients (1139 patients between 1995-2000; 990 patients between 2005-2008) ***Number and Proportion of Resections (%)*** 1995-2000 vs 2005-2008: 19.0 vs 30.0, p<0.001 ***In-hospital mortality:*** The in-hospital mortality rate dropped from 24% in 1995-2000 to 3.6% in 2005-2008 (p<0.001). In 2008, the in-hospital mortality rate was zero. Adjusted HR associated with mortality between time periods: 0.70 (95% 0.51-0.97)
McDade 2012 **Abstract**	Patients undergoing PR	Retrospective analysis using the Massachusetts Division of Health Care Finance and Policy data between 2005-2009 comparing the number of PR performed yearly in hospital death and LOS	Hospital Volume Leapfrog criteria (>11 per year)	Hospital LOS, in hospital death	N = 704 Majority resected at HV hospital (76%) Median LOS 8/- days, with LOS >1 week associated with LV hospitals (p = 0.0002) In hospital deaths LV 7 pts, 4.14% of 169 pts vs HV 7 pts, 1.31% of 535 pts, p= 0.0214
Mukherjee 2008	Patients with pancreatic pathologies who underwent a surgical procedure	Retrospective cohort from January 1999 to December 2006 comparing the number PDs performed yearly as well as grouping pre-Cancer Outcome Guideline (COG) and post COG, hospital stay and 30 day mortality and mean survival	Hospital Volume	Hospital LOS, 30 day mortality and mean survival	N = 140 patients 30 day operative mortality was 2.86% Median hospital stay was 16 days (7-318 days) **Mean Survival** Pancreaticductal adenocarcinoma : 24.8 months (95% CI 19.6-30.0) Bile duct cancer: 26 months (95% CI .76-34.3) Duodenal cancer: 33.26 months (95% CI 18.73-47.78) Ampullary cancer: 45.1 months (95% CI 28.7-61.64) Mortality decreased from 9.7% (pre-COG) to 5.0% (post-COG) (Fisher's exact test, p= .448; OR = 2.74 (95% CI 0.58-12.88). Morbidity decreased from 41.6% (pre COG) to 35.3% (post COG) (Fisher's exact test, p = 0.565 OR = 1.29 (95% CI, 0.74-3.56)
Nathan 2009	Patient > 18 years who underwent pancreatic resection between 1999-2005 This study also included hepatic resection (please see Table 3 for details).	Retrospective analysis from the Sate Inpatient Database between 1999 and 2005 comparing hospital and surgical volume and in patient mortality. Three level mixed effects logistic regression models	Hospital Volume, Surgery Volume Surgery volume cut off: LV 1-24 MV 25-124 HV 125-358	In patient mortality	N = 10,694 Overall mortality = 3.3% ***Mortality*** High Vs Low Hospital volume: OR 0.32, p<0.001 The effect of hospital volume did not persist after adjusting for surgeon volume (p = 0.28) High Vs Low Surgery volume: Or 0.30, p< 0.001 The effect of surgeon volume remained significant after adjusting for hospital volume (p<0.001)
Rangelova	PR	Retrospective	Hospital Volume	Mortality,	N = 6101 pts

2012 **Abstract**		analysis using the Swedish Patient Register comparing hospital volume effects on long term mortality after PR in Sweden between 1987 and 2008. Multivariate Cox regression analyses adjusted for age, sex, Charlson index, type of procedure, tumour location.	Birkmeyer criteria : LV: 1-2 resections/yr; HV: >16 resections/year	long term survival	Mortality Overall : HR 0.76; CI 0.67-0.85 90 day: HR 0.57; CI 0.42-0.77 5 year: HR 0.82; 0.71-0.95 Mortality decreased in HV compared to LV hospitals (p<0.01) Mortality (resections due to malignant disease) 90 day: HR 0.65, CI 0.45-0.93 5 year: HR 0.61, CI 0.39-0.93 Mortality further decreased in HV compare to LV hospitals (p = 0.01)
Reames, 2013 **Abstract**	Patients who underwent a pancreatic resection. This study also included: abdominal aortic aneurysm repair; aortic valve surgery, mitral valve surgery, coronary artery bypass, carotid endarterectomy, colon resection, and esophageal resection.	Retrospective cohort study using National Medicare claims data from 1998 through 2008 to compare operative mortality by hospital volume. Multivariate logistic regression models adjusted by patient characteristics.	Hospital Volume cutoffs: Hospitals were grouped into quintiles of operative volume. Cutoffs were NR.	Operative mortality	Operative mortality: 1998-1999: Adjusted OR: 5.46 (95% CI : 2.97-10.01) 2007-2008: Adjusted OR: 3.27 (95% CI: 2.31-4.62)
Riall 2008	Patients who underwent a pancreatic resection between 1999 and 2005	Retrospective analysis from the Texas Hospital Inpatient Discharge Public Use Data between 1999 and 2005 investigating variability among high-volume hospitals in comparison to mortality and length of stay	High Volume Hospitals	LOS, mortality	N patients = 2481 N HV hospitals = 12 Overall mortality was 2.8% Number of resections ranged at each hospital from 78-608 cases for the 7 years Significant HV hospital variability in mortality (range, 0.7% - 7.7%, p<.0001) Significant HV hospital variability in LOS (range of medians 9-21 days, p<.0001
Schmidt 2010	Patients who underwent a PD between 1980 and 2007	Retrospective analysis from the Indiana University Hospital between 1980 and 2007 comparing surgical volume, hospital volume, mortality and morbidity.	Hospital Volume, Surgeon Experience, Surgical Volume There was a steady increase in hospital volume, but a dramatic difference in 2003. Due to this, outcomes were analyzed before and after rapid increase in 2003. (i.e. Periods 1 and 2).	Mortality, morbidity	***Hospital Volume:*** Period 1 (1980-2003) N = 563, Mean 24/yr Period 2 (2004-2007) N = 440, Mean 110/yr Mortality: Period 1 vs 2 = 4% vs 2%, p = 0.04 Morbidity: Remained the same in both periods ***Surgeon Experience*** Experience surgeon = >50 PD during the two periods Less experienced surgeon: < 50 PD during the two periods Less experienced surgeons performed PD with comparable mortality (4% vs 3%) Experience surgeons had proportionally less morbidity (39% vs 53%, p =.001) ***Surgeon Volume*** Low volume <20/yr High volume >20/yr Mortality 4% vs 2%, p = 0.09 Morbidity 44% vs 38% = p = 0.07
Schneider	Patients who	Retrospective cross-	Surgical Volume	LOS,	N = 25 464

2013	underwent PD	sectional analysis from the Agency for healthcare Research and Quality Healthcare Costs and Utilization Project NIS dataset between 2003 and 2009 comparing length of stay , hospital volume, surgical volume, hospital teaching status and complications	and Hospital Volume Surgery Volume: Low 1-4/yr Med: 5-15/yr High: >16/yr Hospital Volume Low 1-9 /yr Med: 10-31/yr High >32 /yr	Teaching Status, and medical complications	***Hospital Teaching Status*** Hospital Volume : p<.001 Teaching: LV 59% MV 87.1% HV 100% Non-teaching: LV 41.0% MV 12.9% HV 0% **Surgery Volume: P<.001** Teaching: LV 66.2% MV 88.6% HV 93.8% Non-teaching: LV 33.8%, MV 11.4%, HV 6.2% **Medical Complications (adjusted, controlling for age, gender, comorbidity, hospital factors)** Hospital Volume, p <.001: MV RR 0.88 (CI 95% 0.81-0.95) HV RR 0.74 (CI 95% 0.67-0.82) **Surgeon Volume, p<.001:** MV RR 0.56 (CI 95% 0.41-0.78) HV RR 0.46 (CI 95% 0.29-0.79) ***Length of stay*** Median 13, mean 16.7 days Teaching vs non-teaching (median) 12 vs 16 days p <.001 **Hospital volume, p<.001** MV RR 0.88 (CI 95% 0.81-0.95) HV RR 0.74 (CI 95% 0.66-0.91) **Surgeon Volume, p<.001** MV RR 0.67 (95% CI 0.62-0.73) HV 0.67 (CI 95% 0.60-0-74)
Schneider 2013 **Abstract**	Pancreatic Cancer patient's undergoing PD	Retrospective analysis using the NIS database to compare variation in LOS after PD for pancreatic cancer at the patient, surgeon and hospital levels between 2003-2009	Hospital Volume Surgeon Volume Surgeon terciles low 1-4; medium 5-15; high >16 Hospital terciles: low 1-9; medium 10-31; high >32	Morbidity, mortality, LOS,	N = 5,190 Median LOS: 13 days **Surgeon volume** Median annual surgeon volume= 8, range 1-54 procedures Associated with median LOS (low-16 days, med-11 days, high-12 days, p<0.001) **Hospital volume** Median annual hospital volume = 18 (range 1-129) Associated with median LOS (low-16 days, med-11 days, high-11 days, p<0.001) Patients operated on by HV surgeons (RR=0.67) or at HV hospitals (RR=0.75) had reduced risk of a LOS that exceeded the median (both P<0.001).
Skipworth, 2010	Patients' undergoing pancreatectomy (PAN) between 1982 and 2003 This study also included hepatic resection (details below).	Retrospective analysis of post-operative in-hospital records and mortality data between 1982 and 2013 from the Information Services Division (ISD) Scotland investigating hospital volume and in-hospital mortality.	Hospital volume In Scotland, few hospitals are likely to reach criteria for HV according to international standards. For this study, data from all hospitals across the 22 years were analyzed independently to derive "hospital-years", ie one hospital would have 22 associated hospital year mortality rates if it performed a resection every year for the entire study period.	In hospital mortality Death during the admission for which the patient underwent surgery and was not risk adjusted.	*N = 61 hospitals, 10,625 all patients, 1014 PAN* *In hospital mortality (1982-2003) = 8.1%* *Annual PAN (1982-2003) –from 0.31 per 100,000 to 1.60 (chi square p<0.001).* ***Hospital Volume:*** The number of centres performing PAN remained relatively static over the 22 year study period (Approx 11 hospitals per year). The percentage of PAN performed in the highest-volume centres increased significantly (1982 – 0.0% - 2003 – 88.9%, p <0.001) *Mortality Rates:* *Q1: Resection /yr = 1; Resection (N) = 97; Death (N / %) = 17/ 17.5%* *Q2: Resection /yr = 2; Resection (N) = 102; Death (N / %) = 11 /10.8%* *Q3: Resection /yr = 3-5; Resection (N) = 133; Death (N / %) = 7 / 5.3%* *Q4: Resection /yr = >6; Resection (N) = 682; Death (N / %) = 47 / 6.9%* Postoperative in hospital mortality decreased as quartiles of hospitals increased (chi square p = 0.002. OR of in hospital death was significantly reduced (OR

					= 0.35; 95% CI 0.19, 0.64, p< 0.001)
Stitzenberg, 2010	Patients 18 years of age or older who underwent pancreatic procedures between 1999-2007 Also looked at esophagus, colon and rectum.	A retrospective observational study from NIS between 1999-2009 examining trends in hospital procedure volume for pancreatic cancer procedures.	Hospital volume Hospital volume cut points were created by dividing 1999 population cases into 3 equal-sized groups on the basis of procedure volume of the treating hospital in 1999. LV 1-6, MV 7-26, HV >26	Mortality. Teaching hospital, payer, admission type	*N = 17, 658* ***Hospital Volume :*** Decrease in total number of hospitals performing pancreas procedures from 1999-2007, but a significant increase in HV (1999 = 38 vs 2007 = 101, p = 0.003). Proportion of procedures in LV in 2007 was significantly less than in 1999 (OR = 0.40, 95% CI 0.35, 0.46). Hospitals that were HV for one disease site tended to be HV for other disease sites (i.e. high correlations = esophagus: pancreas 0.557; pancreas: colon 0.439; pancreas: rectum 0.545). HV centers were likely to be teaching hospitals (e.g pancreas 100%, p<0.001). ***Admittance:*** 16.9% of all patients were admitted through emergency room (8.3% pancreas). This was associated with higher likelihood of surgery at LV center
Swan 2011 **Abstract**	Patients undergoing PD for pancreatic cancer	A retrospective comparative study from the NC Hospital Based And Freestanding Ambulatory Surgery Facility Database between two time periods 2004-2006 and 2007-2009. Regionalization of center in late 2006. Chi Square and Fisher's Exact Test	Hospital Volume Low (1-9 PD/yr), Med (10-19 PD/yr), High (>20 PD/yr)	Mortality, Morbidity	2004-2006 N (LV-HV) = 62, 80, 129 2007-2009 N (LV-HV) = 58, 46, 246 % of PD at HV increased significantly (47.6% to 70.3%), while decreasing for MV and LV centers, p<0.001 Mortality was less at HV (2.8%) compared to LV (10.3%) for the 2007-2009 timeframe (p=0.038). Non-significant across periods for any group. Overall mortality decreased from 6.6% to 4.6% across time periods (p = 0.31) Major morbidity at LV centers increased (p = 0.018). Morbidity was not significantly different between volume groups within either time period.
Topal 2008	Patients undergoing PD in 126 hospitals between 2000-2004	Retrospective analysis from the Federal Ministry of Public Health of Belgian hospitals of in-hospital death (surgery related or not) and length of stay after PD from 2000-2004	Hospital Volume Cut off quintiles: 1-2. 3-5, 6-10, 11-20, >20	Hospital mortality; hospital stay	*126 hospitals, 1794 patients* *Mortality:* Cut offs / # PD / OR 1-2 / 352 / 1 3-5 / 480 / 0.883 (0.535, 1.469) 6-10 / 187 / 0.931 (0.488, 1.788) 11-20 / 358 / 0.487 (0.259, 0.911) >20 / 417 / 0.409 (0.221, 0.774) Difference between 5 volume categories (p = 0.011) Difference between <10 PD/yr (10.7%) vs >10 PD/yr (5.4%; p <0.001) Overall hospital mortality : 8.4% Overall hospital days was 21.6 (range 3-117)
Yun 2012	Patients 20 years or older with pancreatic cancer undergoing surgery. Also looked at stomach, colon, rectum, lung and breast cancers	Population-based retrospective cohort analysis from the Korean Central Cancer Registry of hospital volume, From 2001-2005	Hospital volume Tertiles: high, med, low. Based on mean number of procedures (NR) Recategorize for sensitivity analysis (binary): Leapfrog Group (11 cases/yr)	5 year survival, Patient wait times	Total N= 147, 662; Pancreatic pts = 2,309 ***5 year Survival and Hospital Volume*** Overall survival for pancreatic 16.2%, Unadjusted HR = 1.49 (95% CI 1.34-1.66), Adjusted* HR = 1.26 (95% CI 1.11-1.43) *adjusted for age, sex, Charlson scale, hospital type, insurance, radiotherapy, chemotherapy, type of medical care institution, year of diagnosis and treatment delay or hospital volume ***Overall survival, surgical treatment delay and hospital volume (sensitivity analysis)*** HV and >31 day: adjusted HR = 1.07 (0.84-1.36) LV and 31 day: adjusted HR = 1.21 (1.08-1.36)

<table>
<tr><td></td><td></td><td></td><td></td><td></td><td>LV and >31 day: adjusted HR = 1.60 (1.33-1.92)</td></tr>
<tr><td>Zarate, 2011
Abstract</td><td>Patients undergoing PAN</td><td>Retrospective analysis of 24 hospitals in Queensland from 2000-2007
Cox proportional hazards regression model adjusted for comorbidity and other characteristics</td><td>Hospital Volume
Cut offs:
Low <3
Medium 3-6
High >6</td><td>In patient mortality, 2 year survival rates</td><td>N = 410 patients
Mortality (low-high) = 8.1%, 3.1%, 1.4%
Relative to HV, inpatient death was 5.7 times higher (95% CI 1.3-26.2) in LV
LV were 1.5 times more likely (95% CI 1.1-2.0) to die within 2 years compared to HV</td></tr>
<tr><td colspan="6">Hospital Other</td></tr>
<tr><td>Bilimoria 2007</td><td>Patients 1985-2004, pancreatectomy and other pancreatic surgeries</td><td>ROADS and FORDS, in NCDB
Cox proportional hazards, adjusting for sex, age, race, SES, stage, grade, resection type</td><td>Veterans Affairs hospitals versus non-VA hospitals (academic, community)</td><td>60 day mortality, 3 year survival</td><td>60-day mortality
<u>Adjusted HR, versus VA hospital</u>
Academic: 0.71 (0.41-1.24), p=0.23
Community: 0.80 (0.45-1.40), p=0.43
3 year survival
<u>Adjusted HR, versus VA hospital</u>
Academic: 1.63 (0.42-6.24), p=0.48
Community: 2.34 (0.6-9.2), p=0.22</td></tr>
<tr><td>Gooiker 2011</td><td>Patients with pancreatic surgery for malignancy of pancreas, duodenum, ampulla of Vater, hepatic bile duct</td><td>Comprehensive Cancer Centre West (western part of Netherlands), patients from Jan 1 1996 to Dec 31 2008
Three time periods:
1996-2000
2001-2005
2006-2008

Quality standards implemented in 2001, centralization in 2006
Crude outcomes only</td><td>Year of surgery</td><td>30 day mortality
90 day survival
1 year survival
2 year survival</td><td>Crude mortality outcomes (%)
<table>
<tr><td colspan="5">All pancreatic malignancies</td></tr>
<tr><td></td><td>1996-2000</td><td>2001-2005</td><td>2006-2008</td><td>p</td></tr>
<tr><td></td><td>N=85</td><td>N=89</td><td>N= 110</td><td></td></tr>
<tr><td>30-d</td><td>8</td><td>0</td><td>2</td><td>n/a</td></tr>
<tr><td>90-d</td><td>88</td><td>97</td><td>96</td><td>0.03</td></tr>
<tr><td>1-y</td><td>65</td><td>65</td><td>74</td><td>0.31</td></tr>
<tr><td>2-y</td><td>39</td><td>40</td><td>55</td><td>0.09</td></tr>
<tr><td colspan="5">Pancreatic adecnocarcinoma only</td></tr>
<tr><td></td><td>N=72</td><td>N=71</td><td>N=98</td><td>p</td></tr>
<tr><td>30-d</td><td>7</td><td>0</td><td>2</td><td>n/a</td></tr>
<tr><td>90-d</td><td>89</td><td>96</td><td>96</td><td>.12</td></tr>
<tr><td>1-y</td><td>64</td><td>56</td><td>71</td><td>.13</td></tr>
<tr><td>2-y</td><td>38</td><td>28</td><td>49</td><td>.04</td></tr>
</table></td></tr>
<tr><td>Merkow 2013</td><td>Patients who underwent a pancreatic resection with oncologic intent</td><td>Retrospective analysis from the American College of Surgeons National Surgical Quality Improvements Program between January 1, 2007 and December 31, 2011, comparing National Cancer Institute Cancer Centers (NCI-CC) and Non NCI CC and 30 days morbidity, mortality and prolonged LOS

Colorectal and Esophagogastric Surgery were also investigated.
Logistic Regression Model</td><td>NCI-CC vs Non NCI-CC</td><td>30 day morbidity, 30 day mortality, prolonged LOS</td><td>259 centers and 1,838 patients
NCI-CC Versus Non-NCI
Unadjusted OR (95% CI)
Mortality OR 0.74 (0.58-0.94), p<0.05
Serious morbidity OR 0.87 (0.80 -0.94), p <0.05
Prolonged LOS OR 0.66 (0.61-0.71), p<0.05
Risk-adjusted OR (95% CI)
Mortality OR 0.79 (0.60-1.05), p = ns
Serious morbidity OR 0.85 (0.73-1.00), p = ns
Prolonged LOS OR 0.54 (0.40-0.74), p < 0.05</td></tr>
<tr><td colspan="6">Surgeon volume</td></tr>
</table>

Balzano 2010; **abstract**	Patients undergoing PD from August 2001 to August 2009	Retrospective analysis of surgeon volume in a single high-volume institution	Surgeon volume *Volume cutoff (median):* Low ≤18 High ≥18	Operative mortality (30 day post discharge), morbidity, postoperative stay	# patients: 610 *Mortality:* HVS 3.9% vs LVS 4.3%, ns *Morbidity:* HVS 56.6% vs LVS 67.7%, p= .03 Severe complications (grade 3b-5): HVS 9.8% vs LVS 10.4%, ns Mild complications (1-3a): HVS 46.8% vs LVS 57.4%, p = 0.01 Median postoperative stay: HVS 13 days vs LVS 14 days (p = 0.04)
Boudourakis 2009	Patients ≥18, pancreatectomy with primary diagnosis of cancer	Cross-sectional analysis, comparing 1999 and 2005 discharge information from HCUP-NIS administrative database	Surgeon volume *Volume cutoff:* Low: ≤1 High: ≥5	Inpatient mortality, LOS	#patients: 1999: 306, 2005: 275 Unadjusted outcomes *Mortality (%)* 1999: HV: 2.5, LV: 10.3, p<0.05 2005: HV: 2.5, LV: 9.0, p=ns *LOS (mean d)* 1999: HV 13.3, LV: 20.6, p<0.001 2005: HV 13.6, LV: 24.1, p<0.001
Eppsteiner 2009	PR (distal pancreatectomy and PD) Any cause, malignancy =68% patients	Retrospective analysis using NIS discharge records, 1998-2005 Logistic regression (adjusted, propensity matching)	Surgeon volume; hospital volume *Volume cutoffs:* Surgeon: ≥5 HV Hospital: Leapfrog (≥11)	In-hospital Mortality	N= 3581 PR *Adjusted Mortality* LV vs HV surgeon: 6.4% vs 2.4%, p<0.001 Hazard ratios associated with mortality: HV hospital: HR 0.55 (0.32-0.97), p=0.04 HV surgeon: HR 0.49 (0.28-0.83), p=0.009 Malignant diagnosis: 1.19 (0.68-2.10), p=0.54 Teaching hospital: 0.93 (0.59-1.48), p=0.77
Hyder 2013	Pancreatectomy patients with available physician and hospital specific data	Retrospective analysis using SEER Medicare-linked database, 1998-2005 Logistic regression	Surgeon volume; hospital volume; *Volume cutoff:* Surgeon quartiles: very-low (1-2/yr); low (3-6/yr), medium (7-20/yr) and high (21-84/yr) Hospital quartiles: very low (1-4/yr), low (5-12/yr), medium (13-24/yr), and high (25-53/yr).	In-hospital morbidity, mortality, length of stay	# patients 1488 *Length of stay (median)* Very LV hospital vs HV hospital 17 days vs 13 days (p<0.001). Very LV surgeon vs HV surgeon 18 days vs 12.5 days (p<0.01). *90 day mortality (%)* Very LV hospital vs HV hospital: 17.2% vs 8.0% Very LV surgeon vs HV surgeon: 16.7% vs 7.7%
Kennedy 2010	PD	Providence Portland Healthy System electronic hospital record system and pancreatic database, Jan 2005- June 2008 T test(two tailed), Chi square, Logistic and linear regression	Surgical volume *Cut offs* HV ≥ 10 PD per year, LV < 9 PD per year	Mortality, Major Complications, Length of Stay, Total Cost	# patients: 94 Unadjusted outcomes *Mortality (%)* HV: 2.2, LV: 16, p=0.024 *LOS (median/mean)* HV 10/112.6/1, LV: 13/15.4, p=0.008 *Major Complications (%)* HV: 18, LV 44, p = 0.003 *Median total cost ($)* HV: $27,185, LV $33,007, ns
Kim 2012,	PD	Health Insurance Review and Assessment Service (2005-2008) T-test, Chi square, logistic regression	Surgical volume Quintiles, very-low, low, medium, high and very high	Hospital mortality (adjusted for risk factors: sex, age, admission route, general condition, SES	# patients: 4975 Unadjusted outcomes *Hospital volume (%) Very low-very high:* <10, 10-18, 19-35, 54-111, 215, p =ns Odds ratios associated with mortality: *HV, OR= 0.13 (0.05-0.32), <0.001* *Very HV OR = 0.16 (0.06-0.41), p<0.001*
Nienhuijs 2010	PR	Prospective cohort study comparing operative mortality,	Surgical volume	Mortality, morbidity	*Period A N = 82 Period B N = 76* *Morbidity* *Post-operative complications*

		morbidity and surgical volume before regionalization (Jan 1995- April 2000) and after (July 2005- July 2009) Fisher's exact test			A Vs B: 59 (71.9%) vs 26 (34.2%), p<0.001 *Re-operations* A Vs B: 31 (37.8%) vs 14 (18.4%), p = 0.008 *Intra-operative complications* A Vs B: 8 (9.8%) vs 3 (3.9%), p = 0.214 *Mortality* A Vs B: 20 (24.4%) vs 2 (2.6%), p< .0001
Pal 2008	Patients who underwent PD This study also included liver resection (details below)	Retrospective analysis from the Hospital Episode Statistic data between 1999-2005 comparing surgical volume and mortality. Data was divided into two cohorts (1999-2002, 2002-2005) in relation with the release of COG guideline.	Surgical Volume Quartiles: Very Low 1-43, Low 46-77, Medium 81-144, High 173-317	30 day mortality	*N = 3,378 pts, N= 159 centers* *% Mortality* 1999-2002: 6.2% 2002-2005: 5.7 % % Mortality in Quartiles (very low-high) 6.5, 8.0, 5.4, 3.8 % Mortality by volume (low vs high) 7.2% vs 4.5% OR = 1.60 (1.10 to 2.41) p = 0.016
Pecorelli 2012	Patients who underwent PD in a single high volume institution	Retrospective analysis from a electronic pancreatic surgery database between August 2001 and August 2009 comparing surgical volume, operative mortality and length of stay	Surgical volume The cutoff value to categorize high-volume surgeons and low volume surgeons was defined as 12 procedures per year	Operative mortality, LOS	*N = 610 patients* No difference between HVS and LVS groups was found in operative mortality (HV 14 vs LV 11, p = 0.84) and LOS (HV 13(7-102) vs LV 14 (7-73), p = 0.11)
Rosemurgy 2008	Patients who underwent a PD	Retrospective analysis from the State of Florida Agency for Health Care comparing PD undertaken over a 33 month period between January 1 2003 and September 30 2005 comparing surgical volume, average LOS, and in hospital mortality. Also compared with a previous report dataset conducted over 33 month period from January 1 1995 through September 30 1997	Surgical Volume Surgeons were grouped by the number of PD performed over 33 months. 1-3 PD (1 or fewer a year), 4-9 PD (1-3 per year), 10-16 PD (4-6 per year) or 17 or more PD (i.e. more than one every other month).	In hospital mortality, Average LOS	*# Surgeons, #PD over 33 months* 1995-1997 = 282, 698 2003-2005 = 266, 1314 88% increase in the number of PD with 6% fewer surgeons in 2003-2005 *Average LOS* 1995-1997= 21 days, 2003-2005= 16 days Average LOS was inversely related to the frequency with which surgeons undertook PD in 1995-1997 (p=0.03) and in 2003-2005 (p=0.001, Spearman regression). *In hospital mortality* 1995-1997 5.1%, 2003-2005 = 5.9%, p= 0.45 In both 1995-1997 and 2003-2005, in hospital mortality inversely related to frequency with which surgeons carried out PD (p=0.001)
Waljee, 2006	Patients aged 65- 99 who underwent PAN Study also invested coronary artery bypass grafting, elective abdominal	Center for Medicare and Medicaid Services, 1998-1999	Surgeon's age Surgeon volume, hospital volume Cutoffs: NR	Operative mortality	Total N 460,738 *Operative death & Surgeon Age* *Adjusted for Patient Characteristics (severity, race, gender, age):* <40 years vs >61 Years = OR 0.91 (95% CI 0.63-1.31) vs OR 1.39 (95% CI 0.85-2.27) *Adjusted for Patient and Provider Characteristics (surgeon volume, hospital volume, and hospital teaching status):* <40 years vs >61 Years =OR 0.88 (95% CI 0.62-1.24) vs 1.67 (95% CI 1.12-2.49) Practice setting according to surgeon age

	aortic aneurysm repair, aortic valve replaced, carotid endarterectomy, esophagectomy, lung resection, cystectomy.				<table><tr><td></td><td></td><td><40</td><td>41-50</td><td>51-60</td><td>>60</td></tr><tr><td>Surgeon volume</td><td>Low</td><td>36.3</td><td>33.6</td><td>36.8</td><td>38.5</td></tr><tr><td></td><td>Med</td><td>34.9</td><td>31.7</td><td>26.7</td><td>21.1</td></tr><tr><td></td><td>High</td><td>28.8</td><td>34.7</td><td>36.6</td><td>40.5</td></tr><tr><td>Hospital volume</td><td>Low</td><td>31.4</td><td>30.7</td><td>35.0</td><td>31.3</td></tr><tr><td></td><td>Med</td><td>37.4</td><td>41.0</td><td>29.8</td><td>22.2</td></tr><tr><td></td><td>High</td><td>31.2</td><td>28.3</td><td>35.2</td><td>46.4</td></tr><tr><td>Teaching hospital</td><td>Yes</td><td>48.0</td><td>50.0</td><td>47.9</td><td>60.4</td></tr></table>
Surgeon other					
Clark 2010	PD, % cancer diagnosis not specified	Florida Agency for Healthcare Admin Database, Jan 2002-Dec 2007 Chi-square and Mann-Whitney U tests	Surgical residency training programs	In-hospital mortality, LOS	#patients: 2345 <u>Training vs Non-Training</u> *Mortality* 2.7% vs 11%, p<0.001 *Median Length of stay (range)* 12 days (1-197) vs 17 days (1-85), P<0.001
Dai 2011, **Abstract**	Patients undergoing PD for periampullary cancer	Prospective analysis between pancreatic specialty group and non-pancreatic group in a tertiary teaching hospital between January 1986 to August 2010	Pancreatic Specialty vs non-pancreatic	Mortality	Total N 790 , specialty group N = 610, non-specialty group N = 180 *Mortality* Specialty (1.1%) vs non-specialty (2.8%), p=0.221
Minami 2011 **Abstract**	Patients undergoing PD in a medium-scale hospital	Prospective analysis of a medium scale hospital (10 PD/yr) comparing young trainees and skilled surgeons between 2006 and Jul 2010.	Surgeons skill level (<6 after medical school vs >6 years medical school)	Hospital stay	Trainee N = 17, skilled N = 35 Hospital stay 29.2 + 13.5 (range 12-60) vs 23.8 +12.1 (range 11-54), ns NS difference in operation complications and operation time
Wellner, 2011 **Abstract**	Patients undergoing pancreatic surgery	Over the period of ten years, outcome of pancreatic operations performed by two "senior" pancreatic surgeons (SPS) and one specializing junior pancreatic surgeon (JPS) were evaluated relative to increasing experience. The study was held in a high volume center	Surgeon experience	Mortality, morbidity	Total surgery N 583 (N = 245 for 2 SPS, N = 212 JPS) JPS Significant postoperative morbidity rate decreased significantly (from 25% to 9%, p = 0.022) with increasing case load to reach a level at the average SPS level (15%) after around 70 pancreatic surgeries Mortality rate – 4% to 0%, p=ns

*Volume cutoffs: all studies defined different cutoffs for volume levels (usually data-driven to create quartiles or quintiles). Numbers given represent the numbers of resections/operations used to define the study's volume categories.

**Leapfrog thresholds: ≥11 for pancreatic resection

PR: pancreatic resection; GI: gastrointestinal; PAN: pancreatectomy; PD: pancreaticoduodenectomy; NIS: Nationwide Inpatient Sample of the Healthcare Cost and Utilization Project; LV: low volume; HV: high volume; LOS: length of stay; HR: hazard ratio; ROADS: Commission on Cancer's Registry Operations and Data Standards; FORDS: Commission on Cancer's Facility Oncology Registry Data Standards; NCDB: National Cancer Database; SES: socioeconomic status; HCUP-NIS: Health care utilization project national inpatient sample; ESO: esophagi ectomy; CABG: coronary artery bypass graft; PCI: percutaneous coronary interventions; AAA: elective abdominal aortic aneurysm repair; ln: natural log;

Table 3. Hepatic primary studies meeting inclusion criteria for EBS #17-2

	Procedure and population	Methods	Intervention	Outcomes of interest	Brief results
Hospital volume					
Dixon 2009	Hepatic resections, any cause (51.9%	Calgary Health region administrative data, from 1991/92 to	Regional volume of LR	Operative mortality (death before	From 1991-2004, 424 LR Over time (from 1991-2004) steady decrease in

	cancer-related, primary or metastatic)	2003/04 Crude mortality rates using chi-squared, ANOVA, or Kruskal-Wallis		discharge);	annual mortality rate (prior to 2000, mortality rate 9.7%, afterward, dropped to 4.1%, p=0.020), corresponding to increase in overall volume of LR in CHR (figure 5)
Gasper et al. 2009	Hepatic resection (as one of several procedures)	California Office of Statewide Health Planning and Development (OSHPD) patient discharge data	Hospital Volume *Volume cutoff:* No explicit cutoffs are given.	In hospital mortality	Of 8901 patients, 1203 patients had pancreatic cancer. Data split into 2- 5 year periods, 1995-1999 (period B) and 2000-2004 (period C) to compare to original data – 1990-1994 (period A). *Risk Adjusted Mortality Rate* HV: 9.4% (Period A), 4.4%% (Period B), 2.8% (Period C) LV: 22.7% (Period A), 8.6%(Period B), 5.6% (Period C) Period A – N/A OR from low- to very high-volume hospitals (Period B): 4.32 (2.10-8.86), 3.53 (1.64-7.60), 0.47 (0.12-1.86), 1 OR from low- to very high-volume hospitals (Period C): 2.26 (0.94-5.41), 2.87 (1.24-6.61), 0.60 (0.22-1.62)
Lin, 2009	Patients with primary liver malignancy and underwent hepatectomies	Retrospective study from the Taiwan National Health Insurance Research Database and the Cause of Death Data File (Taiwan Department of Health), comparing hospital and surgical volume on 5 year survival.	Hospital volume, Surgeon volume Surgeon volume: low ≤ 19, medium 20-95, ≥ 96 cases Hospital Volume: low ≤ 87 cases, medium 88-298, ≥ 299 cases	5 year survival	N = 2799 patients <u>Hazard ratios associated with 5 year survival</u>: ***Unadjusted surgical volume:*** Low HR 1.516 (1.349-1.704), p<0.001 Med: HR 1.203 (1.066-1.357), p<0.01 ***Adjusted surgical volume:*** Low HR 1.411 (1.232-1.617), p<0.001 Med HR 1.189 (0.871-1.620), p ns ***Unadjusted hospital volume:*** Low: HR 1.335 (1.191-1.496), p<0.001 Med HR 0.925 (0.819-1.045), p ns ***Adjusted hospital volume*** Low: HR 1.211 (0.832-1.751), p ns Med: HR 1.110 (0.834-1.452), p ns
McKay 2008,	Patients 18 years or older who underwent hepatic resection	Retrospective study from Calgary and Capital health regions records from the years 1991-1992 to 2003-2004, comparing hospital and surgical volume, and surgical training on mortality Hierarchical Multilevel Regression	Hospital Volume, Surgeon volume, Surgeon Training Surgeon volume cutoff: HV >5, LV <5 Hospital volume cutoff (median): HV >24, LV <24	Operative mortality	# Patients = 1107 Average LOS – 13.5 (median 9 days, range 1-154 days), no different by either surgeon training or volume In-hospital mortality rate of 6.0% *Percentage of mortality rate in* Hospital HV vs LV 5.6% vs 13.6%, p =.0334 Surgeon HV vs LV 4.8% vs 10.9%, p=.0009 Surgeon training, p = .0032 Hepatopancreaticobiliary 4.6% Surgical oncology 6.3% Other subspecialty 7.2% General surgeons 15.3%
Nathan 2009	Patients who underwent hepatic resection between 1999-2005 This study also include pancreatic resection (please see Table 2).	Retrospective analysis from the Sate Inpatient Database between 1999 and 2005 comparing hospital and surgical volume and in patient mortality. Three level mixed effects logistic regression models	Hospital Volume, Surgery Volume	In patient mortality	N = 6,871 Overall mortality = 3.1% *Mortality* High Vs Low Hospital volume: OR 0.48, p = 0.04 High Vs Low Surgery volume: OR = 0.74, p = 0.42

Scarborough 2008	Patients 18 years or older who underwent a hepatic resection between 1988 and 2003	Retrospective analysis from the Nationwide Inpatient Sample database between 1988 and 2003 comparing 4 time periods, hospital volume, annual surgeon volume, and postoperative mortality. 4 time periods: 1) 1988-1991 1992-1995 1996-1999 2000-2003	Year of Study	Hospital Volume, Annual Surgeon Volume, Postoperative mortality *Surgical Volume* Low 1/yr Low-int 2/yr Int 3-5/yr High int 6-16 /yr High >17/yr *Hospital Volume* Low <2/yr Low-int 3-7/yr Inter 8-17/yr High-int 18-44/yr High > 45/yr	*Surgical Volume* Shift of patients from lower-volume surgeons to higher volume surgeons from 1988-2003. Low Volume – Period 1 vs 4: 53.9% vs 29.5%, p< .0001 High Volume – Period 1 vs 4: 10.4% vs 25.8%, p<.0001 *Hospital Volume* Increasing percentage of patients had their hepatic resections performed in higher volume hospitals during 15 year study period. High volume- Period 1 vs 4: 2.7% vs 29.9%, p<0.0001 Low volume- Period 1 vs 4: 61.6% vs 30.7%, p<.0001 Postoperative mortality have decreased significantly with time, from 10.0% in period ! to 4.7% in period 4 (p<0.001 after adjusting for patient age, gender, race, income, and co morbidity.)
Simunovic 2006	Patients who underwent livery procedure related to cancer diagnosis between 1990-1995 Study also looked at breast, colon, lung, esophagus	Retrospective analysis from the Ontario Cancer Registry between 1990-2000 comparing hospital volume, in hospital operative mortality, and hospital teaching status	Hospital volume HV- greater or equal to 23 LV less than 23	Hospital Teaching Status, in hospital operative mortality	N = 362 *In hospital operative mortality* Hospital Volume: LV= HR 6.7% vs HV 0.5%, p <.01 OR 7.1 (95% CI 0.5-99.7), p =0.15 Non-Teaching Status- HR 0.4 (95% CI 0.1-1.9), p = 0.22 *Long term survival* Hospital Volume : HR = 1.7 (95% CI 1.0-2.7), p =0.04 Teaching Status: HR = 1.0 (95% CI 0.6-1.5) p = 0.97
Simunovic 2010	Patients 20 years and older who underwent pancreatic resection between 1994 and 2004 in Ontario and Quebec, Canada.	Retrospective analysis from the Canadian Institute of Health Information database from 1994 -2004 comparing hospital volume and operative mortality	Hospital Volume HV greater or equal to 10 procedures in a given calendar year	Operative Mortality adjusted for increases in provincials case numbers over the 11 year study period, expected due to an aging population and potentially improved access to surgery	N = 1895 Ontario (ON) , 1396 Quebec (QC) *Provincial Rates* *Cases performed HV (1994 vs 2004)* ON: 33% vs 71% QC: 36% vs7.6% *Operative mortality-* ON: 10.4% vs 2.2% QC: 7.2% vs 9.8% Over the years 1994-2004, the slope of the log rate for regionalization of surgery to HV hospital increased significantly for ON (.08, p<.001) and QC (.07, p<.001). For periods 1994-1999 versus 2000-2004 and for regionalization to HV hospital, in the second period the mean log rate was significantly higher in ON and QC (0.41, p<.001 and .38, p<.001. **HV vs LV Hospital** ON= OR = .46 (95% CI 0.29-0.72), p<.001 QC= OR = .63 (95% CI 0.35-1.13, p =.12)
Skipworth, 2010	Patients' undergoing hepatectomy between 1982 and 2003 This study also included pancreatectomy (details above).	Retrospective analysis of post-operative in-hospital records and mortality data between 1982 and 2013 from the Information Services Division (ISD) Scotland investigating hospital volume and in-hospital mortality.	Hospital volume In Scotland, few hospitals are likely to reach criteria for HV according to international standards. For this study, data from all hospitals across the 22	In hospital mortality Death during the admission for which the patient underwent surgery and was not risk adjusted.	*N = 61 hospitals, 10,625 all patients, 757 Hepatectomy* *In hospital mortality (1982-2003) = 3.2%* *Annual hepatectomy (1982-2003) –from 0.02 per 100,000 to 1.56 (chi square p<0.001).* *Hospital Volume:* The number of centres performing PAN remained relatively static over the 22 year study period (Approx 6 hospitals per year). The percentage of PAN performed in the highest-volume centres increased significantly (1982 – 0.0% - 2003 – 98.7%, p <0.001) *Mortality Rates:* *Resection /yr* | *Resection (N)* | *Death (N / %)*

			years were analyzed independently to derive "hospital-years", ie one hospital would have 22 associated hospital year mortality rates if it performed a resection every year for the entire study period.		<table><tr><td>*Q1*</td><td>*1*</td><td>*66*</td><td>*4/ 6.1%*</td></tr><tr><td>*Q2*</td><td>*2*</td><td>*34*</td><td>*4 /11.8%*</td></tr><tr><td>*Q3*</td><td>*3-6*</td><td>*78*</td><td>*4 / 5.1%*</td></tr><tr><td>*Q4*</td><td>*>7*</td><td>*579*</td><td>*12 / 2.1%*</td></tr></table> Postoperative in hospital mortality decreased as quartiles of hospitals increased (chi square p = 0.004. OR of in hospital death was reduced in highest volume hospital but it was not significant (OR = 0.33; 95% CI 0.10, 1.05, p ns)
Yasunaga 2012	Patients undergoing liver resections	Japanese Diagnosis Procedure Combination Database, July and December 2007-2009	Hospital Volume Quartiles: very low (<18/year), low (18-35/year), high (36-70/year), very high (>70/year)	LOS, post-operative mortality	*# pts = 18 046, # hospitals 855* ***Length of stay rates for volume (mean, SD)*** very low to very high = 24.0 (20.5), 21.6 (19.2), 20.5 (17.2), 21.5 (16.5) ***In hospital mortality rates for volume (%)*** Very low to very high = 1.6%, 1.3%, 1.1%, 0.4% ***In hospital mortality rates for volume (OR)*** *Low OR 0.70 (95% CI 0.48-1.02) p = 0.060* *High OR 0.52 (95% CI 0.34-0.81), p = 0.004* *Very high Or 0.16 (95% CI 0.09-0.30), p<0.001*
Young 2010 **Abstract**	Patients older than 18 years of age undergoing hepatic resection	NIS, 1998-2007 Chi-square, multivariate logistic regression	Hospital Volume LV < 20 HV > 20	Mortality	*N = 9 289* LV patients 1.4 times (CI = 1.02-1.93) as likely to die as patients at HV
\Hospital other					
Dixon 2007	Patients w/ partial hepatectomy or lobectomy	Medicare Provider Analysis and review files from CMS, 1999-2000 Regression modeling, and binary logistic to account for clustering	Presence or absence of a liver transplant program, Also hospital volume *Volume cutoff:* LV 1-9 HV ≥10	30-day operative mortality (w/I 30 days of index procedure) LOS	N=4661 patients, 1235 hospitals, of which 79 had a transplant program ***Unadjusted mortality rates for volume:*** HV: 4.41% LV: 7.64% ***Length of Stay (OR)*** LV hospital: OR 0.958 (0.918-0.999), p = 0.0472 Transplant program: OR 0.975 (0.932-1.018), p = 0.2482 ***Mortality (OR)*** LV: 1.705 (1.221-2.381), p =0.0017 No transplant program: 0.987 (0.724-1.346), p = ns
Lancaster 2007	Hepatic Resection	Veterans Affairs NSQIP October 2001-September 2004 Logistic Regression and T-test	Type of Hospital (Veteran Affair vs Private Sector)	30 day Mortality, 30 day Morbidity, Length of Stay	N = 1,020 hepatic resections ***Unadjusted Outcomes*** ***30-d Mortality (%)*** *Private Sector(PS) Veteran Affair (VA) = 2.55% vs 6.75%, p= 0.0022* ***30-d Morbidity (%)*** *PS vs VA = 22.61% vs 27.85%, p = 0.0969* ***Total LOS (mean, SD)*** *PS vs VA = 9.78 (9.02) vs 11.65 (9.79), p = 0.0062* **Adjusted Outcomes** *After risk adjustment and potential confounds, the morbidity rate was found to be equivalent at the two types of hospitals (OR = 0.94; 95% CI, 0.62-1.42, p =0.77).* *After risk adjustment and potential confounds, there was no significant difference in mortality between the two type of hospitals (OR = 1.62, 95% CI, 0.61-4-32, p =0.33).*
Lordon 2008,	Patients with colorectal liver	Retrospective analysis, hospital records from	Referral to single centre	Hospital Stay, Overall Survival	N = 331 patients

	metastases referred to the hepatobiliary unit between September 1996 and November 2006	September 1996-November 2006 Chi Square, t test, log ranking and Cox regression	with multidisciplinary team and liver surgeon (MDT) vs other hospitals		*Hospital stay (days)* MDT vs other: 11.4 vs 11.4, p> ns *Overall survival (years)* MDT vs other: 3.6 (0.08-7.8) vs 2.61 (0-9.6), p< 0.0001
Surgeon Volume					
Eppsteiner 2008	Liver resection (wedge res or lobectomy), any cause % malignant diagnosis: ~76.7%	Retrospective analysis, discharge records of NIS 1998-2005 Propensity scores, logistic regression Case-controlled cohort comparison for adjusted models	Surgeon volume, hospital volume, *Volume cutoff*: HV surgeons: ≥10 LR/y HV hospital: ≥ LR/y	Mortality: death to any cause prior to discharge	2949 LR in time period Separately, neither treatment at HV center (HR 0.81, 0.48-1.38) or by HV surgeon (HR 0.68, 0.39-1.19) protective for mortality Malignant diagnosis: HR 0.73 (1.46-1.16) p=0.42 Teaching hospital: HR 1.06 (0.66-1.68), p=0.91 *Adjusted mortality models* N=1678 patients Patients at HV hospitals had lower adjusted mortality rate (2.6% vs 4.8% at LV, p=0.02) HV surgeon at HV hospital beneficial (HR 0.40, 0.21-0.80) (no other combination significant);
Kohn 2010	Hepatectomy	NIS: 1998-2006 Logistic Regression controlling for annual improvement in outcomes and Charlson comorbidity index score	Surgeon volume	Mortality, morbidity, Surgical Residency, fellowship program	# patients: 5298 ***Unadjusted outcomes*** Mortality : 6.44% ***Adjusted outcomes*** ***Effects of volume on*** Morbidity: OR 0.992 (0.987-0.996), p= .0006 Mortality: OR 0.975 (0.967-0.983), p <0.0001 ***Relation to Surgical Residency*** Morbidity: OR 0.851 (0.757-0.957), p= 0.0072 Mortality: OR 0.815 (0.706-0.941), p= 0.0052 ***Relations to Fellowship Program*** Morbidity: OR 0.931 (0.786-1.103), p = ns Mortality:: OR 0.855 (0.712-1.027), p =ns
McColl, 2013	Patients 18 years of age and older who underwent hepatic resections	Patient health records between 1995-2004 in either the Calgary or Capital (Edmonton) health regions. Chi square, Mann-WhitneyU tests, logistic regression, multiple linear regression models	Surgeon volume, training in hospital	In hospital mortality	# patients = 676 **Predictors of in-hospital mortality** *Unadjusted OR* HV Surgeon OR = 0.54 (0.31-0.93), p =05 Surgical oncology training OR = 1.52 (0.73-3.16), p = .05 Other surgical training OR = 1.95 (1.08-3.52), p = .05 *Adjusted OR* HV Surgeon OR = 0.42 (0.17-1.05), p = .05 Surgical oncology training OR = 0.51 (0.19-1.40), p = .05 Other surgical training OR = 0.59- (0.23-1.53), p = .05
Pal 2008 *(J Gastrointest Surg)*	Patients who underwent liver resection This study also included PD(details above)	Retrospective analysis from the Hospital Episode Statistic data between 1999-2005 comparing surgical volume and mortality. Data was divided into two cohorts (1999-2002, 2002-2005) in relation with the release of COG guideline.	Surgical Volume Quartiles: Very Low 1-43, Low 46-77, Medium 81-144, High 173-317	30 day mortality	*N = 5,672* *% Mortality* 1999-2002: 2.2% 2002-2005: 2.6 % %Mortality in Quartiles (very low-high) 3.1, 1.2,3.3,2.0 % Mortality by volume (low vs high) 2.2 vs 2.7 OR = 0.82 (0.50 – 1.67), p = 0.51
Surgeon other					
Bhayani 2013	Patients with partial, left or right hepatectomy, trisectionectomy	Retrospective analysis of NSQIP data, 2005-2011	Presence of fellows during hepatectomy (Attending vs Fellow)	Mortality; morbidity; Length of stay	#patients: 2877, 46.1% attending, 54% fellow <u>Attending vs Fellow</u> *Mortality* 2.7% vs 3.2%, p=0.5, *Morbidity*

					26.2 % vs 30.7%, p=0.008 *Median Length of Stay* 6 d vs 6 d, p=0.8 *Odds of morbidity associated with fellow involvement* Mortality: OR 1.1 (0.7-2.6), p =0.08 Morbidity: OR 1.21 (1.02-1.4), p = 0.03
Shaw, 2012 **Abstract**	Patients undergoing hepatectomy	Retrospective analysis of the University Health Consortium from 2008-2011	Surgeon specialty (general surgeon, surgical oncologist, transplant surgeon)	Mortality, LOS, 30 day re-admission	General Surgeon N= 643, 19% Surgical oncologist N= 1538, 44% Transplant surgeon N= 1283, 37% No difference between general and specialist surgeons for in hospital mortality (1.9% vs 2.4%), total LOS (7 days vs 7 days) and 30 day re-admission (12% vs 8%).

*Volume cutoffs: all studies defined different cutoffs for volume levels (usually data-driven to create quartiles or quintiles). Numbers given represent the numbers of resections/operations used to define the study's volume categories.

NIS: Nationwide Inpatient Sample of the Healthcare Cost and Utilization Project; LV: low volume; HV: high volume; LOS: length of stay; HR: hazard ratio; ROADS: Commission on Cancer's Registry Operations and Data Standards; FORDS: Commission on Cancer's Facility Oncology Registry Data Standards; NCDB: National Cancer Database; SES: socioeconomic status; HCUP-NIS: Health care utilization project national inpatient sample; ESO: esophagi ectomy; CABG: coronary artery bypass graft; PCI: percutaneous coronary interventions; AAA: elective abdominal aortic aneurysm repair; ln: natural log

Table 4. Hepatio-Pancreatico-Bilary primary studies meeting inclusion criteria for EBS #17-2

	Procedure and population	Methods	Intervention	Outcomes of interest	Brief results
Hospital volume					
Schneider, 2014 **Abstract**	Patients undergoing complex hepato pancreato biliary surgery	Retrospective analysis using the Surveillance, Epidemiology and End Results (SEER)-Medicare linked data from 1998-2007 examining hospital-volume related differences, LOS and mortality	Hospital Volume Tertiles: LV <4 cases/year Intermediate (IV) 4-10 cases/yr HV >11 cases/yr	LOS Mortality	N = 12, 209 Patients treated at HV centers (75.8%) were more likely to have >3 comorbidities vs IV (71.5%) or LV (67.3%) centers (p<0.001) Mortality (LV-HV)= 10.7%, 8.4%, 5.6%, p<0.001 LOS (LV-HV)= 12 days, 11 days, 10 days, P<0.001
Surgeon other					
Csikesz 2008 *(J Gastrointes Surg)*	12,004 Hepato-Pancreatico-Biliary surgeries between 1998-2005	Retrospective analysis using NIS discharge records, 1998-2005	hospital volume, surgeon volume, surgeon specialty *Volume cutoff*: HV surgeons: ≥15 cases/yr MV surgeons: 3-14 cases/yr	In-hospital mortality	12,004 HPB surgeries by 4,355 surgeons Surgeon volume per HPB surgery, LV, MV, HV, 10%, 30% 60% *Mortality* No difference in mortality after HPB surgery depending on surgeon specialty (p = 0.59). Surgery performed at transplant center had lower odds of perioperative mortality (OR= 0.79 (0.63-0.98), p= 0.04)

See Appendix 1 for a list of identified studies that were included in at least one of the systematic reviews in Table 1. Please note that these studies were not included in Table 2.

Because the initial search was conducted in February 2014, an updated search was run from January 2014 to May 2015. A total of 2,344 citations were identified via OVID. Of those, 25 were selected for full text review. Two studies that reported different results from those reported above were included in Table 7. Studies that confirmed the results and were not extracted are listed in Appendix 2.

Table 5. Updated literature search January 2014 to May 2015.

	Procedure and population	Methods	Intervention	Outcomes of interest	Brief results
Hospital other					
Kanhere 2014	53 patients undergoing PD between 1998-2003	Retrospective analysis of database for periampullary carcinoma, 1998-2003. Study was performed at a low volume university teaching hospital in Australia equipped with all the expertise and infrastructure to provide a health care delivery system that is equivalent to high-volume centres.	Age (<74, >74)	Postoperative morbidity, in-hospital mortality, operating time, LOS	N = 53 patients Group A (<74) = 34; Group B (>74) =19 Operating Time : Group A = 399 (253-960), Group B 395 (254-1,104, p = ns Median LOS = 14 (8-180) days Morbidity rate was 41% (22/53 patients) Mortality 3.8% * If the system processes at high volume centres can be replicated in low-volume centres with good surgical expertise, equivalent outcomes can be achieved. * Whilst centralization for complex surgery is logical to obtain the best outcome, study shows that replicating the system processes at high-volume centres makes it possible to achieve good outcomes in low-volume centres with adequate expertise. This is good alternative when centralization is not feasible due to geographic and logistic reasons.
Hospital Volume					
Ravaioli 2014	Patients undergoing curative HPB resection)	Patients were evaluated at an LV hospital before (2006-2008) and during the collaboration between HV and LV centres (2009-2012) and at 2 hospitals with HV for either liver of pancreatic resection (2009-2012)	Hospital Volume	LOS, Hospital mortality	LV : N liver: 2006-08 = 29, 2009-12= 85 LV: N pancreas: 2006- 08 = 17, 2009-12 = 63 *Hospital Mortality:* Liver: 2006-2008 3.5%; 2009-2010 2.9%; 2011-2012 - Pancreas: 2006-2008 17.6%; 2009-2010 11.1%; 2011-2012 2.8% *Overall mortality at 6 months:* 2006-2008 17.8%, 2009-2012 6%, p<0.05 *LOS (median)* Liver: Before : 10 days During : 7 days, p =ns Pancreas: Before: 14 days, During: 11 days, p=ns The reoperation rate was higher at the LV center (14% vs 5% at the HV center, p<0.05), although rates at the LV hospital decreased year on year and were similar to those at the HV center by the last study year (27% in 2009, 17% in 2010, 13% in 2011, and 5% in 2012). *Collaborative efforts between centers with low and high HPB surgical volume resulted in significant improvement in outcomes at the LV hospital, which achieve results similar to those at the HV centers *objective of the collaboration was not to transform an LV center into an HV center, but to pragmatically improve HPB results in the LV center in accordance with health organization, costs, and patient features.

Instructions. Instructions. For each document, please respond YES or NO to all the questions below. Provide an explanation of each answer as necessary.

1. Does any of the newly identified evidence, on initial review, contradict the current recommendations, such that the current recommendations may cause harm or lead to unnecessary or improper treatment if followed?	No
2. On initial review, a. Does the newly identified evidence support the existing recommendations? b. Do the current recommendations cover all relevant subjects addressed by the evidence, such that no new recommendations are necessary?	Yes Yes
3. Is there a good reason (e.g., new stronger evidence will be published soon, changes to current recommendations are trivial or address very limited situations) to postpone updating the guideline? Answer Yes or No, and explain if necessary:	No
4. Do the PEBC and the DSG/GDG responsible for this document have the resources available to write a full update of this document within the next year?	N/A

Review Outcome	ENDORSED
DSG/GDG Approval Date	December 1st, 2015
DSG/GDG Commentary	

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APPENDIX 1. List of Identified Studies Included in at Least One of the Systematic Reviews in Table 1.

1. Balzano G, Zerbi A, Capretti G, Rocchetti S, Capitanio V, Di Carlo V. Effect of hospital volume on outcome of pancreaticoduodenectomy in Italy. British Journal of Surgery. 2008;95(3):357-62.
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APPRENDIX 2. List of identified studies that confirmed the results and were not extracted in updated search (January 2014-May 2015).

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APPRENDIX 3. Members of the Expert Panel in December 2015

The 2015 Expert Panel was convened to include representation from across Ontario and across professional disciplines (surgery, pathology, radiology, medical oncology and radiation oncology).

Dr. Michael Marcaccio, Surgeon (Co-Chair) Juravinski Hospital and Cancer Center	Dr. Alice Wei (Co-Chair) University Health Network Quality Lead, Cancer Care Ontario Surgical Oncology Program
Dr. Jason Pantarotto, Radiation Oncologist The Ottawa Hospital	Dr. Douglas Quan, Surgeon London Health Sciences Centre
Dr. Paul Karanicolas, Surgeon Sunnybrook Health Sciences Centre	Dr. Natalie Coburn, Surgeon Sunnybrook Health Sciences Centre
Dr. Shiva Jayaraman, Surgeon St. Joseph's Health Centre Toronto	Dr. Fady Balaa, Surgeon The Ottawa Hospital
Dr. Jeff Shum, Surgeon Health Sciences North	Dr. Jeff Kolbasnik, Surgeon Milton District Hospital
Dr. Diederick Jalink, Surgeon Kingston General Hospital	Dr. Mohamed Husien, Surgeon Grand River Hospital
Dr. Korosh Khalili, Radiologist University Health Network	Dr. Peter Dauphinee, Surgeon Royal Victoria Regional Health Centre
Dr. Steve Gallinger University Health Network	Dr. Mark Hartmann Health Sciences North, Northeast Cancer Centre

Appendix 4- Document Assessment and Review Outcome Definitions

1. **EDUCATION AND INFORMATION** – An education and information document is a document that will no longer be tracked or updated but may still be useful for academic or other informational purposes. The document is moved to a separate section of our website, each page is watermarked with the word “EDUCATION AND INFORMATION”.

2. **ENDORSED** – An endorsed document is a document that the DSG/GDG has reviewed for currency and relevance and determined to be still useful as guidance for clinical decision making. A document may be endorsed because the DSG/GDG feels the current recommendations and evidence are sufficient, or it may be endorsed after a literature search uncovers no evidence that would alter the recommendations in any important way.

3. **DELAY** – A delay means that there is reason to believe new, important evidence will be released within the next year that should be considered before taking further action.

4. **UPDATE** – An Update means that the DSG/GDG recognizes that there is new evidence that makes changes to the existing recommendations in the guideline necessary but these changes are more involved and significant than can be accomplished through the Document Assessment and Review process. The DSG/GDG will rewrite the guideline at the earliest opportunity to reflect this new evidence. Until that time, the document will still be available as its existing recommendations are still of some use in clinical decision making.

Literature Search Strategy:

Medline

1. exp liver neoplasms/su
2. exp hepatectomy/
3. hepatic surgery.mp.
4. exp liver/su
5. exp pancreas/su
6. exp pancreatic neoplasms/su
7. pancrea$ surgery.mp.
8. exp pancreatectomy/
9. exp biliary tract diseases/su
10. biliary surgery.mp.
11. exp cholecystectomy/
12. exp biliary tract surgical procedures/
13. pancrea$ resection.mp.
14. liver resection.mp.
15. hepatic resection.mp.
16. exp pancreaticoduodenectomy/
17. bile duct surgery.mp.
18. biliary tract surgery.mp.
19. or/1-18
20. exp patient admission/
21. exp health manpower/
22. hospital volume$.mp.
23. exp hospital mortality/
24. surgeon volume$.mp.
25. surgical volume$.mp.
26. exp hospitals/
27. Or/20-26
28. 19 and 27
29. (2006: or 2007: or 2008: or 2009: or 201:).ed

Embase

1. exp liver tumor/su
2. exp liver resection/
3. exp liver/su
4. exp pancreas/su
5. exp pancreas tumor/su
6. exp pancreas resection/
7. exp biliary tract disease/su
8. exp biliary tract surgery/
9. exp pancreaticoduodenectomy/
10. or/1-9
11. hepatic surgery.mp.
12. pancrea$ surgery.mp.
13. biliary surgery.mp.
14. pancrea$ resection.mp.
15. liver resection.mp.
16. hepatic resection.mp.
17. bile duct surgery.mp.
18. biliary tract surgery.mp.
19. or/11-18
20. 10 or 19
21. exp hospital admission/
22. exp health care manpower/
23. exp mortality/
24. exp hospital/
25. hospital volume$.tw.
26. surgeon volume$.mp.
27. surgical volume$.mp.
28. or/21-27
29. 20 and 28
30. exp cancer mortality/
31. exp surgical mortality/
32. 21 or 22 or 24 or 25 or 26 or 27 or 30 or 31
33. 20 and 32
34. (2006: or 2007: or 2008: or 2009: or 201:).dd