

The volume of surgical interventions and its impact on the outcome: feasibility study based on Belgian data - Supplement

KCE reports 1135

The Belgian Health Care Knowledge Centre

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KCE reports I13S

Title : The volume of surgical interventions and its impact on the outcome: feasibility study based on Belgian data - Supplement

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Acknowledgements Stephan Devriese, Kris Henau (Belgian Cancer Registry), Stefaan Van de Sande, Martine Verstrecken (Belgian Cancer Registry)

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Conflict of interest : Dr. Lerut received fees for attending a symposium. Dr. Taeymans received grants from private firms for conducting research. Dr. Renson was remunerated to participate to symposia on total knee replacement. Dr. Scalliet is member of Board of Directors of IBA which is a private company situated at Louvain-la-Neuve which is active in the fields of cancer diagnosis and therapy.

Disclaimer: The external experts collaborated on the scientific report that was subsequently submitted to the validators. The validation of the report results from a consensus or a voting process between the validators. Only KCE is responsible for errors or omissions that could persist. The policy recommendations are also under the full responsibility of KCE.

Layout : Ine Verhulst

Brussels, 13th July 2009

Study nr 2007-02

Domain : Good Clinical Practice (GCP)

MeSH : Outcome Assessment (Health Care) ; Health Resources ; Neoplasms/surgery ; Cardiovascular Surgical Procedures ; Orthopedics/surgery

NLM classification : W84.4

Language :English

Format : Adobe® PDF™ (A4)

Legal depot : D/2009/10.273/36

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How to refer to this document?

Vrijens F, De Gauquier K, Camberlin C. The volume of surgical interventions and its impact on the outcome: feasibility study based on Belgian data. Good Clinical Practice (GCP). Brussels: Belgian Health Care Knowledge Centre (KCE). 2009. KCE Reports I13S. D/2009/10.273/36



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Supplement Chapter II – Literature search

APPENDIX I: SEARCH FOR SYSTEMATIC REVIEWS: SEARCH TERMS, THEIR COMBINATIONS AND THE RESTRICTIONS USED

Database	Medline	
Host	Pubmed	
Date of search	30/09/2008	
Years covered	No time limit	
Search Strategy	(volume[Title] OR frequency[Title] OR quantity[Title] OR case load[Title] NOT lung volume[Title] NOT "Respiratory Function Tests"[Mesh] NOT "Cardiac Volume"[Mesh] NOT "Blood Volume"[Mesh]) AND ("Outcome Assessment (Health Care)"[Mesh] OR outcome[Title] OR outcomes[Title] OR regionalization[Title] OR "Quality Indicators, Health Care/statistics and numerical data"[Mesh] OR "Quality Indicators, Health Care/utilization"[Mesh] OR "Health Care Quality, Access, and Evaluation"[Mesh] OR "Length of Stay/statistics and numerical data"[Mesh] OR "Recovery of Function"[Mesh] OR "Intraoperative Complications"[Mesh] OR "complications "[Subheading] OR "Hospital Mortality"[Mesh] OR "Fatal Outcome"[Mesh] OR "Survival Rate"[Mesh] OR "Utilization Review"[Mesh] OR "Health Resources"[Mesh]) AND "humans"[MeSH Terms] AND (Review[ptyp] OR Meta-Analysis[ptyp])	
Summary of search strategy	P	"humans"[MeSH Terms]
	I & C	(volume[Title] OR frequency[Title] OR quantity[Title] OR case load[Title] NOT lung volume[Title] NOT "Respiratory Function Tests"[Mesh] NOT "Cardiac Volume"[Mesh] NOT "Blood Volume"[Mesh])
	O	("Outcome Assessment (Health Care)"[Mesh] OR outcome[Title] OR outcomes[Title] OR regionalization[Title] OR "Quality Indicators, Health Care/statistics and numerical data"[Mesh] OR "Quality Indicators, Health Care/utilization"[Mesh] OR "Health Care Quality, Access, and Evaluation"[Mesh] OR "Length of Stay/statistics and numerical data"[Mesh] OR "Recovery of Function"[Mesh] OR "Intraoperative Complications"[Mesh] OR "complications "[Subheading] OR "Hospital Mortality"[Mesh] OR "Fatal Outcome"[Mesh] OR "Survival Rate"[Mesh] OR "Utilization Review"[Mesh] OR "Health Resources"[Mesh])
	design	(Review[ptyp] OR Meta-Analysis[ptyp])
Language restrictions	none	
Number of citations	726	

Database	Embase	
Host	Embase.com	
Date of search	30/09/2008	
Years covered	No time limit	
Search Strategy	(volume:ti OR frequency:ti OR quantity:ti OR 'case load':ti NOT ('lung volume'/exp OR 'lung volume') NOT ('heart volume'/exp OR 'heart volume') NOT ('blood volume'/exp OR 'blood volume')) AND (('treatment outcome'/exp OR 'treatment outcome') OR ('outcome assessment'/exp OR 'outcome assessment') OR outcome:ti OR outcomes:ti OR ('regionalization'/mj OR 'regionalization') OR ('performance measurement system'/exp OR 'performance measurement system') OR ('clinical indicator'/exp OR 'clinical indicator') OR ('length of stay'/exp OR 'length of stay') OR ('convalescence'/exp OR 'convalescence') OR ('complication'/exp OR 'complication') OR ('surgical mortality'/exp OR 'surgical mortality') OR ('cancer mortality'/exp OR 'cancer mortality') OR ('fatality'/exp OR 'fatality') OR ('survival rate'/exp OR 'survival rate') OR ('utilization review'/exp OR 'utilization review') OR ('health care utilization'/exp OR 'health care utilization')) AND ([cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim) AND [humans]/lim AND [embase]/lim	
Summary of search strategy	P	[humans]/lim
	I & C	(volume:ti OR frequency:ti OR quantity:ti OR 'case load':ti NOT ('lung volume'/exp OR 'lung volume') NOT ('heart volume'/exp OR 'heart volume') NOT ('blood volume'/exp OR 'blood volume'))
	O	((('treatment outcome'/exp OR 'treatment outcome') OR ('outcome assessment'/exp OR 'outcome assessment') OR outcome:ti OR outcomes:ti OR ('regionalization'/mj OR 'regionalization') OR ('performance measurement system'/exp OR 'performance measurement system') OR ('clinical indicator'/exp OR 'clinical indicator') OR ('length of stay'/exp OR 'length of stay') OR ('convalescence'/exp OR 'convalescence') OR ('complication'/exp OR 'complication') OR ('surgical mortality'/exp OR 'surgical mortality') OR ('cancer mortality'/exp OR 'cancer mortality') OR ('fatality'/exp OR 'fatality') OR ('survival rate'/exp OR 'survival rate') OR ('utilization review'/exp OR 'utilization review') OR ('health care utilization'/exp OR 'health care utilization'))
	design	([cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)
Language restrictions	none	
Number of citations	39 of which 27 did not overlap with articles from Medline	

Database	Cochrane Database of Systematic Review, Cochrane Database of Reviews of Effects, Health Technology Assessment Database, NHS Economic Evaluation Database	
Host	Wiley InterScience	
Date of search	30/09/2008	
Years covered	No time limit	
Search Strategy	((volume):ti OR (frequency):ti OR (quantity):ti OR (case load):ti NOT (lung volume):ti NOT MeSH descriptor Lung Volume Measurements explode all trees NOT MeSH descriptor Blood Volume, this term only NOT MeSH descriptor Cardiac Volume, this term only) AND (MeSH descriptor Outcome Assessment (Health Care) explode all trees OR (outcome):ti OR (outcomes):ti OR (regionalization):ti OR MeSH descriptor Quality Indicators, Health Care, this term only with qualifiers: SN,UT OR MeSH descriptor Health Care Quality, Access, and Evaluation explode all trees OR MeSH descriptor Length of Stay explode tree 2 with qualifier: SN OR MeSH descriptor Recovery of Function, this term only OR MeSH descriptor Intraoperative Complications, this term only OR MeSH descriptor Mortality, this term only OR MeSH descriptor Utilization Review, this term only OR MeSH descriptor Health Resources, this term only)) in Cochrane Reviews, Other Reviews, Technology Assessments and Economic Evaluations	
Summary of search strategy	P	
	I & C	(volume):ti OR (frequency):ti OR (quantity):ti OR (case load):ti NOT (lung volume):ti NOT MeSH descriptor Lung Volume Measurements explode all trees NOT MeSH descriptor Blood Volume, this term only NOT MeSH descriptor Cardiac Volume, this term only)
	O	(MeSH descriptor Outcome Assessment (Health Care) explode all trees OR (outcome):ti OR (outcomes):ti OR (regionalization):ti OR MeSH descriptor Quality Indicators, Health Care, this term only with qualifiers: SN,UT OR MeSH descriptor Health Care Quality, Access, and Evaluation explode all trees OR MeSH descriptor Length of Stay explode tree 2 with qualifier: SN OR MeSH descriptor Recovery of Function, this term only OR MeSH descriptor Intraoperative Complications, this term only OR MeSH descriptor Mortality, this term only OR MeSH descriptor Utilization Review, this term only OR MeSH descriptor Health Resources, this term only)
	design	Cochrane Reviews, Other Reviews, Technology Assessments and Economic Evaluations
Language restrictions	none	
Number of citations	158 of which 152 did not overlap with articles from Medline	

APPENDIX 2 : FIRST CRITICAL APPRAISAL - CHECKLIST FOR A SYSTEMATIC REVIEW OF OBSERVATIONAL STUDIES

1. Did the review address an appropriate and clearly focused search question?
 - Patient
 - Intervention
 - Outcome
 - Study design
2. Was the literature search sufficiently rigorous to identify all the relevant studies?
 - Data sources
 - Description of search strategy
 - Years considered
 - Language restriction
3. Was the process of study selection adequate enough?
 - By two reviewers, independently from each other
 - In- and exclusion criteria are explicitly described
4. Did the review's authors do enough to assess the quality of the included studies?
 - By two reviewers, independently from each other
 - Use of explicit quality criteria
5. Was risk-adjustment adequately assessed?
6. Did the authors adequately describe the data extraction?
 - Description of data extraction
 - By two reviewers, independently from each other
7. Were the main characteristics of the original studies described?
8. Was clinical and statistical heterogeneity correctly handled?
9. Was statistical pooling adequate?
10. Overall appraisal

Based on the checklist of the Dutch Cochrane Centre concerning systematic reviews of observational studies (www.cochrane.nl).

APPENDIX 3 : DATA EXTRACTION TEMPLATE

PROCEDURE OR CONDITION		
Totality of systematic reviews for this procedure or condition		
Total number of SRs Publication date all SRs Total number of studies included Study period all SRs Outcome variables		
Description of each systematic review		
Main findings	Threshold volume	Quality of evidence
For each outcome variable: Volume-outcome association: inverse, direct, none or conflicting results When inverse or direct VOA: indication of statistical significance of primary studies between brackets	Threshold (low and/or high volume) per surgeon or per hospital: number of procedures or conditions per year	1) Fitness to support evidence: +, ++ or +++ 2) Number of primary studies and country of origin 3) Study period of primary studies 4) Percentage of primary studies with a statistically significant inverse or direct VOA <input type="checkbox"/> Grade B or C evidence level
Conclusion on volume – outcome association		
Main findings	Threshold volume	Quality of evidence
For which outcome variables is there a VOA? Distinction between hospital volume and surgeon volume.	One single minimal hospital volume threshold and, if possible, one minimal surgeon volume threshold.	Number of SRs with a Grade B or Grade C evidence level.

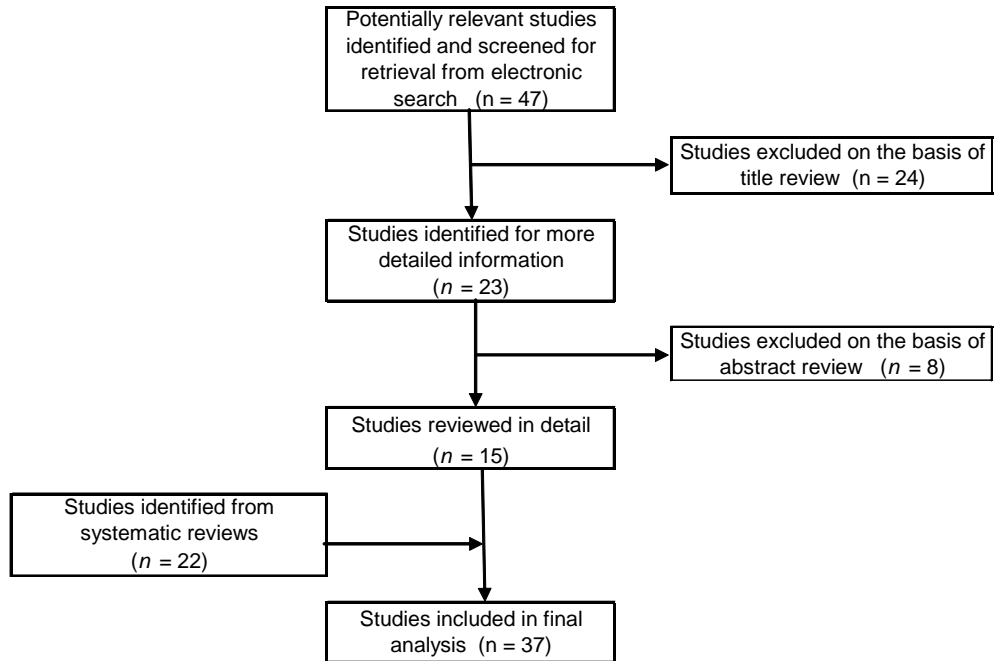
APPENDIX 4: SEARCH FOR PRIMARY STUDIES : SEARCH TERMS, THEIR COMBINATIONS AND THE RESTRICTIONS USED

OE SOPHAGEAL CANCER SURGERY

The systematic reviews identified 22 primary studies of which 18 were published between 2000 and 2004.¹⁻¹⁸ An attempt was made to complement these with an additional search for more recent studies which were published in the period 2004-2009.

Procedure	Oesophageal cancer surgery		
Date	13/03/2009		
Database	Medline Pubmed		
Years covered	2004 till 2009		
Search Strategy	#	Query	Results
	1	Search (volume[Title] OR frequency[Title] OR quantity[Title] OR "Workload"[Mesh] OR case load[Title] NOT lung volume[Title] NOT "Lung Volume Measurements"[Mesh] NOT "Cardiac Volume"[Mesh] NOT "Blood Volume"[Mesh]) AND ("Treatment Outcome"[Mesh] OR "Outcome Assessment (Health Care)"[Mesh] OR outcome[Title] OR outcomes[Title] OR regionalization[Title] OR "Quality Indicators, Health Care/statistics and numerical data"[Mesh] OR "Quality Indicators, Health Care/utilization"[Mesh] OR "Health Care Quality, Access, and Evaluation"[Mesh] OR "Length of Stay/statistics and numerical data"[Mesh] OR "Recovery of Function"[Mesh] OR "Intraoperative Complications"[Mesh] OR "complications "[Subheading] OR "Hospital Mortality"[Mesh] OR "Fatal Outcome"[Mesh] OR "Survival Rate"[Mesh] OR "Utilization Review"[Mesh] OR "Health Resources"[Mesh]) Limits: Publication Date from 2004/01/01 to 2009/03/13, Humans, English, French, German, Dutch	9996
	2	Search "Esophageal Neoplasms"[Mesh] Limits: Publication Date from 2004/01/01 to 2009/03/13, Humans, English, French, German, Dutch	5273
	3	Search #1 AND #2 Limits: Publication Date from 2004/01/01 to 2009/03/13, Humans, English, French, German, Dutch	47

Finally, this search resulted in 15 additional primary studies that analyzed the volume outcome association for oesophageal cancer surgery.¹⁹⁻³³ This brings us to a total of 37 primary studies. Figure 1 provides an overview of this literature search.

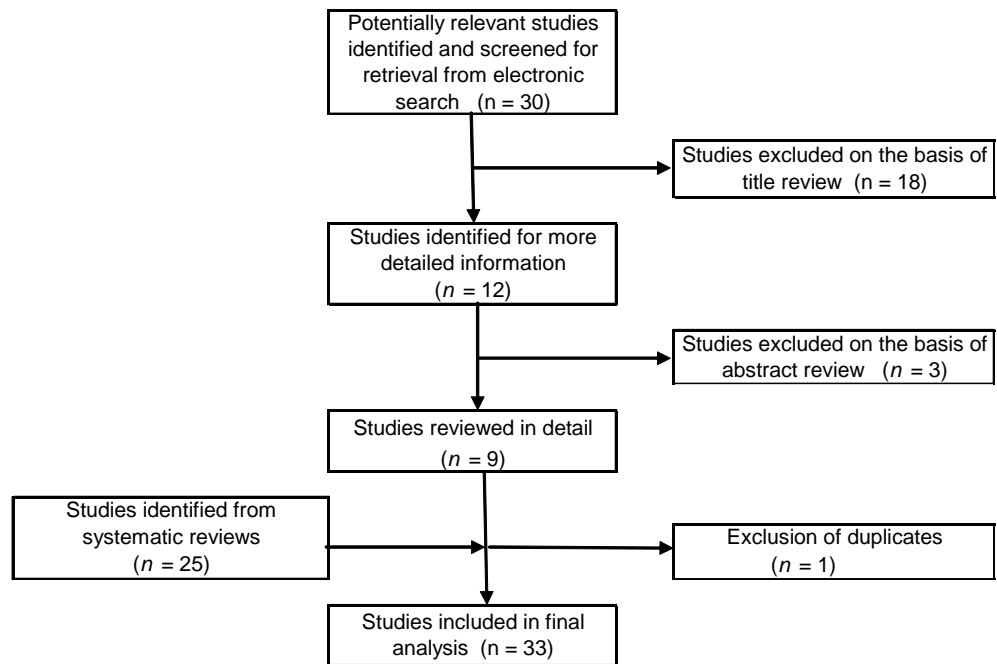
Figure 1 : Flow diagram of literature search for oesophageal cancer surgery

PANCREATIC CANCER SURGERY

The systematic reviews identified 25 primary studies of which 11 were published between 2000 and 2004.^{2, 3, 6, 9, 15, 16, 34-38} An attempt was made to complement these with an additional search for more recent studies which were published in the period 2004-2009.

Procedure	Pancreatic cancer surgery		
Date	13/03/2009		
Database	Medline Pubmed		
Years covered	2004 till 2009		
Search Strategy	#	Query	Results
	1	Search (volume[Title] OR frequency[Title] OR quantity[Title] OR "Workload"[Mesh] OR case load[Title] NOT lung volume[Title] NOT "Lung Volume Measurements"[Mesh] NOT "Cardiac Volume"[Mesh] NOT "Blood Volume"[Mesh]) AND ("Treatment Outcome"[Mesh] OR "Outcome Assessment (Health Care)"[Mesh] OR outcome[Title] OR outcomes[Title] OR regionalization[Title] OR "Quality Indicators, Health Care/statistics and numerical data"[Mesh] OR "Quality Indicators, Health Care/utilization"[Mesh] OR "Health Care Quality, Access, and Evaluation"[Mesh] OR "Length of Stay/statistics and numerical data"[Mesh] OR "Recovery of Function"[Mesh] OR "Intraoperative Complications"[Mesh] OR "complications "[Subheading] OR "Hospital Mortality"[Mesh] OR "Fatal Outcome"[Mesh] OR "Survival Rate"[Mesh] OR "Utilization Review"[Mesh] OR "Health Resources"[Mesh]) Limits: Publication Date from 2004/01/01 to 2009/03/13, Humans, English, French, German, Dutch	9996
	2	Search "Pancreatic Neoplasms"[Mesh] Limits: Publication Date from 2004/01/01 to 2009/03/13, Humans, English, French, German, Dutch	7985
	3	Search #1 AND #2 Limits: Publication Date from 2004/01/01 to 2009/03/13, Humans, English, French, German, Dutch	30

Finally, this search resulted in 8 additional primary studies that analyzed the volume outcome association for pancreatic cancer surgery.^{32, 33, 39-44} This brings us to a total of 33 primary studies. Figure 2 provides an overview of this literature search.

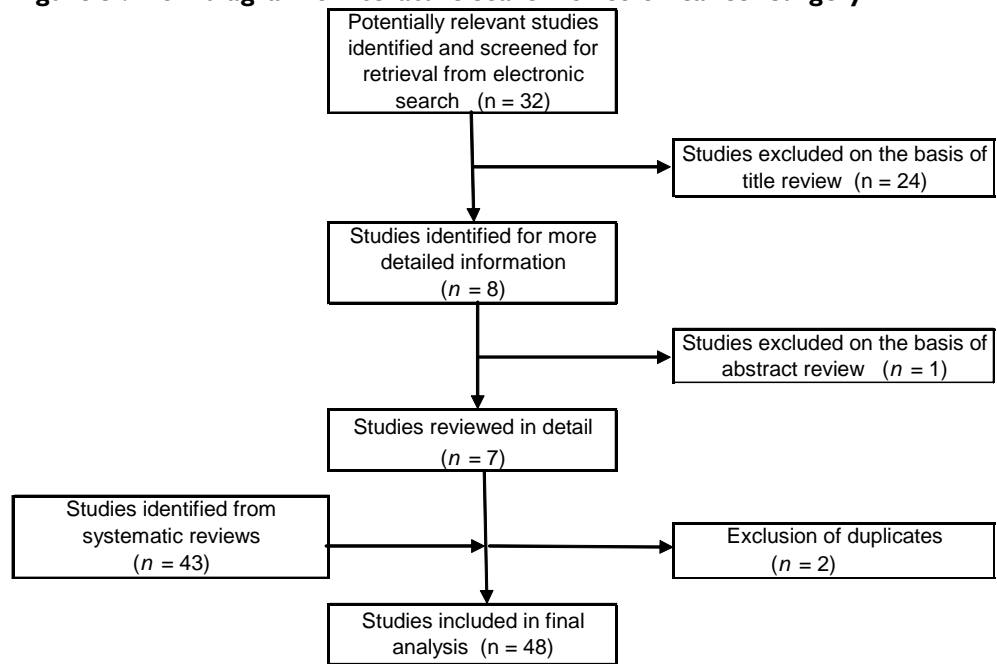
Figure 2 : Flow diagram of literature search for pancreatic cancer surgery

COLON CANCER SURGERY

The systematic reviews identified 43 primary studies that examined colon cancers or colorectal cancers. Of these, 22 were published between 2000 and 2004.^{2, 9, 10, 15, 16, 45-61} An attempt was made to complement these with an additional search for more recent studies which were published in the period 2004-2009.

Procedure	Colon cancer surgery		
Date	13/03/2009		
Database	Medline Pubmed		
Years covered	2004 till 2009		
Search Strategy	#	Query	Results
	1	Search (volume[Title] OR frequency[Title] OR quantity[Title] OR "Workload"[Mesh] OR case load[Title] NOT lung volume[Title] NOT "Lung Volume Measurements"[Mesh] NOT "Cardiac Volume"[Mesh] NOT "Blood Volume"[Mesh]) AND ("Treatment Outcome"[Mesh] OR "Outcome Assessment (Health Care)"[Mesh] OR outcome[Title] OR outcomes[Title] OR regionalization[Title] OR "Quality Indicators, Health Care/statistics and numerical data"[Mesh] OR "Quality Indicators, Health Care/utilization"[Mesh] OR "Health Care Quality, Access, and Evaluation"[Mesh] OR "Length of Stay/statistics and numerical data"[Mesh] OR "Recovery of Function"[Mesh] OR "Intraoperative Complications"[Mesh] OR "complications "[Subheading] OR "Hospital Mortality"[Mesh] OR "Fatal Outcome"[Mesh] OR "Survival Rate"[Mesh] OR "Utilization Review"[Mesh] OR "Health Resources"[Mesh]) Limits: Publication Date from 2004/01/01 to 2009/03/13, Humans, English, French, German, Dutch	9996
	2	Search ("Colonic Neoplasms"[Mesh] OR "Sigmoid Neoplasms"[Mesh]) Limits: Publication Date from 2004/01/01 to 2009/03/13, Humans, English, French, German, Dutch	7992
	3	Search #1 AND #2 Limits: Publication Date from 2004/01/01 to 2009/03/13, Humans, English, French, German, Dutch	32

Finally, this search resulted in 5 additional primary studies that analyzed the volume outcome association for colon cancer surgery.^{32, 62-65} This brings us to a total of 48 primary studies. Figure 3 provides an overview of this literature search.

Figure 3 : Flow diagram of literature search for colon cancer surgery

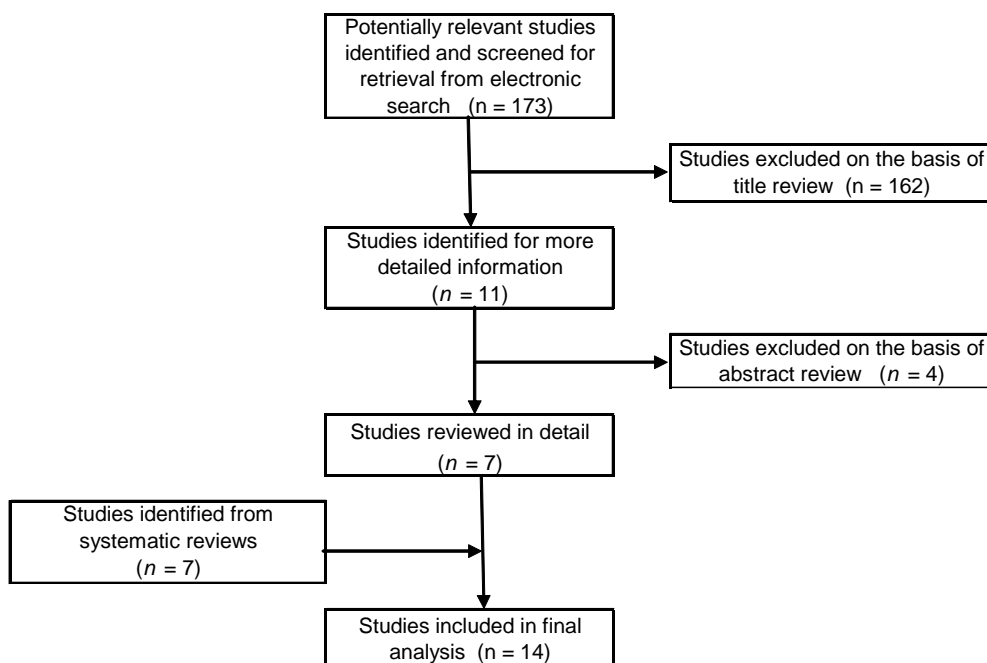
BREAST CANCER SURGERY

The systematic reviews identified 7 primary studies of which 2 were published in 2003,^{66, 67} and 4 between 1993 and 1999.⁶⁸⁻⁷¹ An attempt was made to complement these with an additional search for more recent studies which were published in the period 2004-2009.

Procedure	Breast cancer surgery		
Date	13/03/2009		
Database	Medline Pubmed		
Years covered	2004 till 2009		
Search Strategy	#	Query	Results
	1	Search (volume[Title] OR frequency[Title] OR quantity[Title] OR "Workload"[Mesh] OR case load[Title] NOT lung volume[Title] NOT "Lung Volume Measurements"[Mesh] NOT "Cardiac Volume"[Mesh] NOT "Blood Volume"[Mesh]) AND ("Treatment Outcome"[Mesh] OR "Outcome Assessment (Health Care)"[Mesh] OR outcome[Title] OR outcomes[Title] OR regionalization[Title] OR "Quality Indicators, Health Care/statistics and numerical data"[Mesh] OR "Quality Indicators, Health Care/utilization"[Mesh] OR "Health Care Quality, Access, and Evaluation"[Mesh] OR "Length of Stay/statistics and numerical data"[Mesh] OR "Recovery of Function"[Mesh] OR "Intraoperative Complications"[Mesh] OR "complications "[Subheading] OR "Hospital Mortality"[Mesh] OR "Fatal Outcome"[Mesh] OR "Survival Rate"[Mesh] OR "Utilization Review"[Mesh] OR "Health Resources"[Mesh]) Limits: Publication Date from 2004/01/01 to 2009/03/13, Humans, English, French, German, Dutch	9996
	2	Search "Breast Neoplasms"[Mesh] Limits: Publication Date from 2004/01/01 to 2009/03/13, Humans, English, French, German, Dutch	38507
	3	Search #1 AND #2 Limits: Publication Date from 2004/01/01 to 2009/03/13, Humans, English, French, German, Dutch	173

Finally, this search resulted in 7 additional primary studies that analyzed the volume outcome association for breast cancer surgery.⁷²⁻⁷⁸ This brings us to a total of 14 primary studies. Figure 4 provides an overview of this literature search.

Figure 4 : Flow diagram of literature search for breast cancer surgery



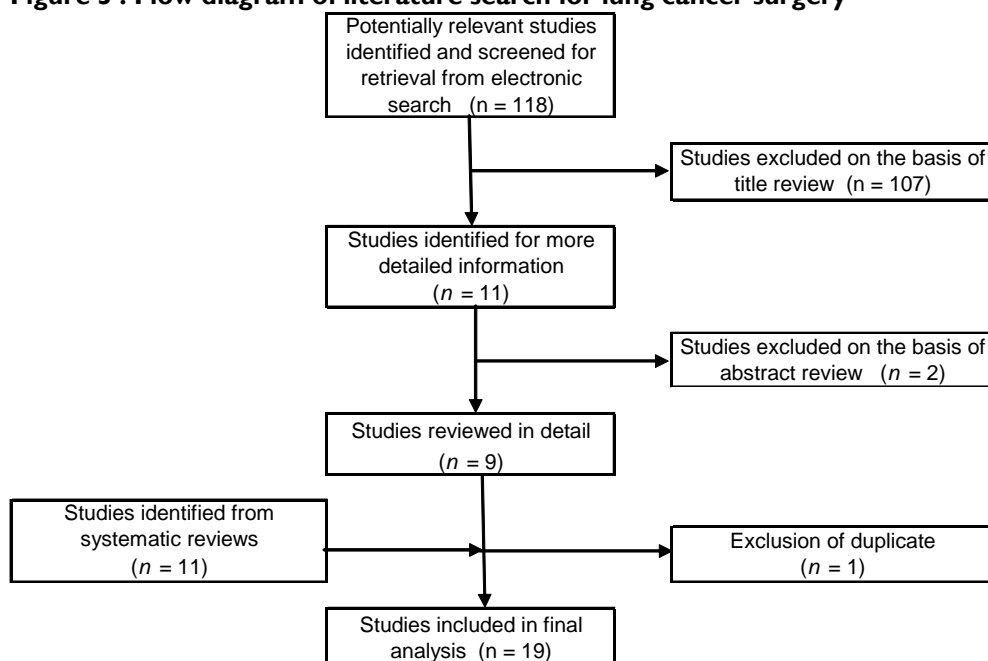
LUNG CANCER SURGERY

The systematic reviews identified 11 primary studies of which 7 were published in between 2001 and 2004,^{2, 3, 9, 15, 16, 49, 79} and 4 between 1992 and 1999.⁸⁰⁻⁸³ An attempt was made to complement these with an additional search for more recent studies which were published in the period 2004-2009.

Procedure	Lung cancer surgery		
Date	13/03/2009		
Database	Medline Pubmed		
Years covered	2004 till 2009		
Search Strategy	#	Query	Results
	1	Search (volume[Title] OR frequency[Title] OR quantity[Title] OR "Workload"[Mesh] OR case load[Title] NOT lung volume[Title] NOT "Lung Volume Measurements"[Mesh] NOT "Cardiac Volume"[Mesh] NOT "Blood Volume"[Mesh]) AND ("Treatment Outcome"[Mesh] OR "Outcome Assessment (Health Care)"[Mesh] OR outcome[Title] OR outcomes[Title] OR regionalization[Title] OR "Quality Indicators, Health Care/statistics and numerical data"[Mesh] OR "Quality Indicators, Health Care/utilization"[Mesh] OR "Health Care Quality, Access, and Evaluation"[Mesh] OR "Length of Stay/statistics and numerical data"[Mesh] OR "Recovery of Function"[Mesh] OR "Intraoperative Complications"[Mesh] OR "complications "[Subheading] OR "Hospital Mortality"[Mesh] OR "Fatal Outcome"[Mesh] OR "Survival Rate"[Mesh] OR "Utilization Review"[Mesh] OR "Health Resources"[Mesh]) Limits: Publication Date from 2004/01/01 to 2009/03/13, Humans, English, French, German, Dutch	9996
	2	Search "Lung Neoplasms"[Mesh] Limits: Publication Date from 2004/01/01 to 2009/03/13, Humans, English, French, German, Dutch	22072
	3	Search #1 AND #2 Limits: Publication Date from 2004/01/01 to 2009/03/13, Humans, English, French, German, Dutch	118

Finally, this search resulted in 8 additional primary studies that analyzed the volume outcome association for lung cancer surgery.^{21, 32, 84-89} This brings us to a total of 19 primary studies. Figure 5 provides an overview of this literature search.

Figure 5 : Flow diagram of literature search for lung cancer surgery



CAROTID ENDARTERECTOMY (CEA) + CAROTID STENTING (CAS)

The systematic reviews identified 40 primary studies of which 12 were published between 2000 and 2005.^{2-4, 90-98} This number was considered sufficient for the discussion.

CORONARY ARTERY BYPASS SURGERY (CABG)

The systematic reviews identified 33 primary studies of which 10 were published between 2000 and 2004.^{2-4, 99-105} This number was considered sufficient for the discussion.

HEART VALVE REPLACEMENT OR REPAIR

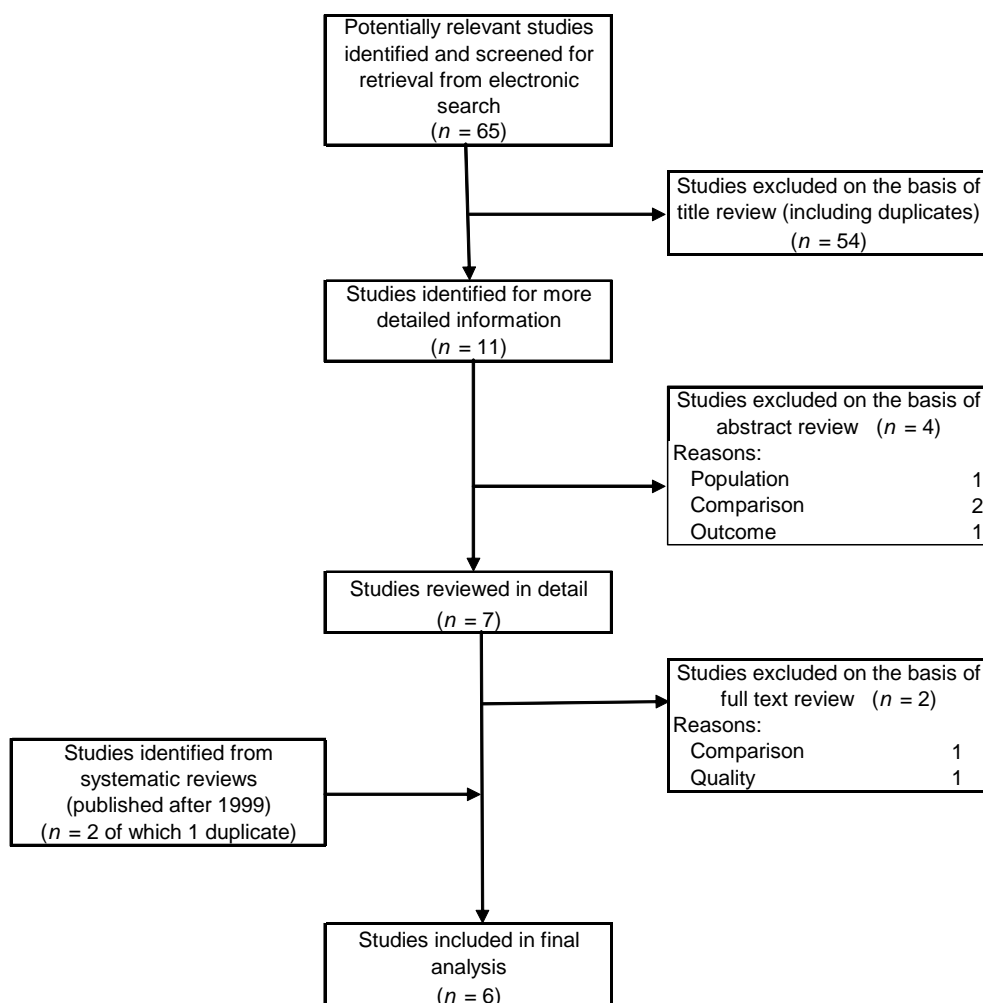
The systematic reviews identified 2 primary studies that were published in 2002 and 2003.^{2,3} These were complemented with an additional search for more recent studies which were published in the period 2000-2008.

Procedure	Heart valve replacement or repair (valvuloplasty)		
Date	02/10/2008		
Database	Medline Pubmed		
Years covered	2000 till 2008		
Search Strategy	#	Query	Results
	1	Search (volume[Title] OR frequency[Title] OR quantity[Title] OR "Workload"[Mesh] OR case load[Title] NOT lung volume[Title] NOT "Lung Volume Measurements"[Mesh] NOT "Cardiac Volume"[Mesh] NOT "Blood Volume"[Mesh]) AND ("Treatment Outcome"[Mesh] OR "Outcome Assessment (Health Care)"[Mesh] OR outcome[Title] OR outcomes[Title] OR regionalization[Title] OR "Quality Indicators, Health Care/statistics and numerical data"[Mesh] OR "Quality Indicators, Health Care/utilization"[Mesh] OR "Health Care Quality, Access, and Evaluation"[Mesh] OR "Length of Stay/statistics and numerical data"[Mesh] OR "Recovery of Function"[Mesh] OR "Intraoperative Complications"[Mesh] OR "complications "[Subheading] OR "Hospital Mortality"[Mesh] OR "Fatal Outcome"[Mesh] OR "Survival Rate"[Mesh] OR "Utilization Review"[Mesh] OR "Health Resources"[Mesh]) Limits: Publication Date from 2000/01/01 to 2008/10/02, Humans, English, French, German, Dutch	14657
	2	Search "Heart Valve Prosthesis Implantation"[Mesh] OR "Heart Valve Prosthesis"[Mesh] OR "Heart Valve Diseases/surgery"[Mesh] OR "Heart Valves/surgery"[Mesh] Limits: Publication Date from 2000/01/01 to 2008/10/02, Humans, English, French, German, Dutch	10744
	3	Search #1 AND #2 Limits: Publication Date from 2000/01/01 to 2008/10/02, Humans, English, French, German, Dutch	37

Procedure	Heart valve replacement or repair (valvuloplasty)		
Date	02/10/2008		
Database	Embase via Embase.com		
Years covered	2000 till 2008		
Search Strategy	#	Query	Results
	1	(volume:ti OR frequency:ti OR quantity:ti OR 'case load':ti NOT ('lung volume'/exp OR 'lung volume') NOT ('heart volume'/exp OR 'heart volume') NOT ('blood volume'/exp OR 'blood volume')) AND (('treatment outcome'/exp OR 'treatment outcome') OR ('outcome assessment'/exp OR 'outcome assessment') OR outcome:ti OR outcomes:ti OR ('regionalization'/mj OR 'regionalization') OR ('performance measurement system'/exp OR 'performance measurement system') OR ('clinical indicator'/exp OR 'clinical indicator') OR ('length of stay'/exp OR 'length of stay') OR ('convalescence'/exp OR 'convalescence') OR ('complication'/exp OR 'complication') OR ('surgical mortality'/exp OR 'surgical mortality') OR ('cancer mortality'/exp OR 'cancer mortality') OR ('fatality'/exp OR 'fatality') OR ('survival rate'/exp OR 'survival rate') OR ('utilization review'/exp OR 'utilization review') OR ('health care utilization'/exp OR 'health care utilization')) AND ([dutch]/lim OR [english]/lim OR [french]/lim OR [german]/lim) AND [humans]/lim AND [embase]/lim AND [2000-2008]/py	3364
	2	'heart valve surgery'/exp AND ([dutch]/lim OR [english]/lim OR [french]/lim OR [german]/lim) AND [humans]/lim AND [embase]/lim AND [2000-2008]/py	12209
	3	#1 AND #2	28

Finally, this search resulted in four additional primary studies that analyzed the volume outcome association for heart valve replacement or repair.^{34, 101, 106, 107} This brings us to a total of six primary studies. Figure 6 provides an overview of this literature search.

Figure 6 : Flow diagram of literature search for the procedure heart valve replacement or repair



PERCUTANEOUS CORONARY INTERVENTION (PCI)

The systematic reviews identified 40 primary studies of which 22 were published between 2000 and 2005.¹⁰⁸⁻¹²⁹ This number was considered sufficient for the discussion.

TOTAL HIP REPLACEMENT/ARTHROPLASTY (THR)

The systematic reviews identified 20 primary studies of which 4 were published between 2001 and 2004,¹³⁴⁻¹³⁷ and 7 between 1995 and 1999.^{81, 138-143} This number was considered sufficient for the discussion.

TOTAL KNEE REPLACEMENT/ARTHROPLASTY (TKR)

The systematic reviews identified 16 primary studies of which 5 were published between 2002 and 2004,¹⁴⁴⁻¹⁴⁸ and 10 between 1995 and 1999.^{138, 142, 143, 149-155} This number was considered sufficient for the discussion.

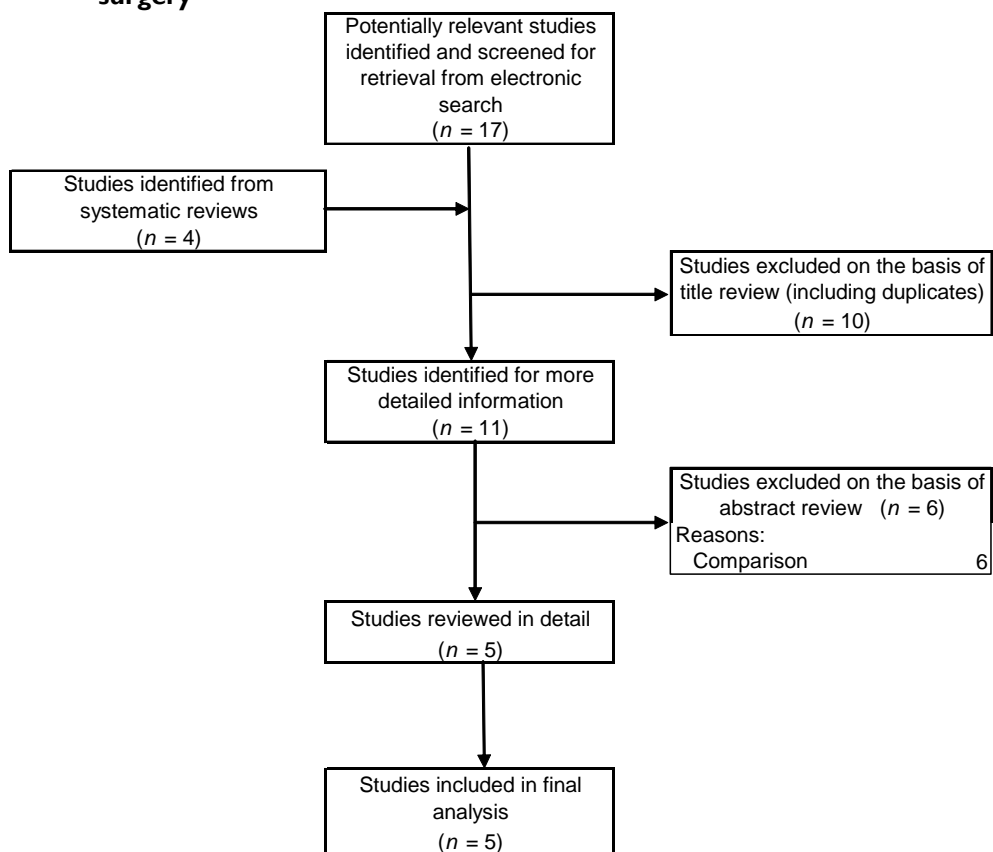
HIP FRACTURE SURGERY

The systematic reviews identified 8 primary studies of which 4 were published between 1988 and 2000.^{143, 156-158} An attempt was made to complement these with an additional search for more recent studies which were published in the period 2000-2008.

Procedure	Hip fracture surgery		
Date	22/12/2008		
Database	Medline Pubmed		
Years covered	2000 till 2008		
Search Strategy	#	Query	Results
	1	Search (volume[Title] OR frequency[Title] OR quantity[Title] OR "Workload"[Mesh] OR case load[Title] NOT lung volume[Title] NOT "Lung Volume Measurements"[Mesh] NOT "Cardiac Volume"[Mesh] NOT "Blood Volume"[Mesh]) AND ("Treatment Outcome"[Mesh] OR "Outcome Assessment (Health Care)"[Mesh] OR outcome[Title] OR outcomes[Title] OR regionalization[Title] OR "Quality Indicators, Health Care/statistics and numerical data"[Mesh] OR "Quality Indicators, Health Care/utilization"[Mesh] OR "Health Care Quality, Access, and Evaluation"[Mesh] OR "Length of Stay/statistics and numerical data"[Mesh] OR "Recovery of Function"[Mesh] OR "Intraoperative Complications"[Mesh] OR "complications"[Subheading] OR "Hospital Mortality"[Mesh] OR "Fatal Outcome"[Mesh] OR "Survival Rate"[Mesh] OR "Utilization Review"[Mesh] OR "Health Resources"[Mesh]) AND (("2000/01/01"[PDAT] : "2008/12/22"[PDAT]) AND "humans"[MeSH Terms] AND (English[lang] OR French[lang] OR German[lang] OR Dutch[lang]))	15110
	2	Search "Hip Fractures"[Mesh] AND (("2000/01/01"[PDAT] : "2008/12/22"[PDAT]) AND "humans"[MeSH Terms] AND (English[lang] OR French[lang] OR German[lang] OR Dutch[lang]))	4071
	3	Search #1 AND #2 AND (("2000/01/01"[PDAT] : "2008/12/22"[PDAT]) AND "humans"[MeSH Terms] AND (English[lang] OR French[lang] OR German[lang] OR Dutch[lang]))	17

Finally, this search resulted in one additional primary study that analyzed the volume outcome association for hip fracture.¹⁵⁹ This brings us to a total of five primary studies. Figure 7 provides an overview of this literature search.

Figure 7 : Flow diagram of literature search for the procedure hip fracture surgery



APPENDIX 5 : FIRST CRITICAL APPRAISAL OF THE SYSTEMATIC REVIEWS

Table I : Critical appraisal of systematic reviews of poor quality

Adapted Cochrane checklist	Battaglia 2006 ¹⁶⁰	Brisman 2005 ¹⁶¹	Hébert- Croteau 2007 ⁷²	Hillner 2000 ¹⁶²	Hölscher 2004 ³³	Le Pimpec- Barthes 2006 ¹⁶³	Meyer 2005 ¹⁶⁴	Obladen 2007 ¹⁶⁵	Slim 2002 ¹⁶⁶	Weitz 2004 ¹⁶⁷
1. Adequate research question?	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
2. Adequately performed search?	No	Partly	Partly	No	No	Partly	Yes	No	Yes	No
3. Adequate selection of articles?	No	Yes	No	Yes	No	No	No	Yes	No	No
4. Adequate quality appraisal of articles?	No	No	No	No	No	No	No	No	No	No
5. Adequate assessment of risk-adjustment?	No	No	No	Yes	No	No	No	No	Yes	Yes
6. Adequate description of data extraction procedure?	No	No	No	Yes	Yes	No	No	No	No	No
7. Description of main characteristics of included articles?	Yes	No	No	No	Yes	Yes	Partly	Yes	No	No
8. Adequate handling of clinical and statistical heterogeneity?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
9. Adequate statistic pooling?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
10. Overall appraisal	Poor	Poor	Poor	Poor	Poor	Poor	Poor	Poor	Poor	Poor

NA = Not Applicable because meta-analysis was not performed

Table 2 : Critical appraisal of systematic reviews of fair and good quality (part I)

Adapted Cochrane checklist	Chowdhury 2007 ¹⁶⁸	Dudley 2000 ¹⁶⁹	Gandjour 2003 ¹⁷⁰	Halm 2002 ¹⁷¹	Henebiens 2007 ¹⁷²	Hodgson 2001 ¹⁷³	Holt_AAA 2007 ¹⁷⁴	Holt_CEA 2007 ¹⁷⁵	IQWiG_AA 2006 ¹⁷⁶	IQWiG_P TCA 2006 ¹⁷⁷
1. Adequate research question?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Adequately performed search?	Yes	Yes	Yes	Yes	Yes	Partly	Yes	Yes	Yes	Yes
3. Adequate selection of articles?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Adequate quality appraisal of articles?	Yes	No	Yes	No	Yes	Yes	Partly	Partly	Yes	Yes
5. Adequate assessment of risk-adjustment?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Adequate description of data extraction procedure?	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
7. Description of main characteristics of included articles?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8. Adequate handling of clinical and statistical heterogeneity?	NA	NA	NA	NA	NA	NA	Yes	Partly	NA	NA
9. Adequate statistic pooling?	NA	NA	NA	NA	NA	NA	Partly	Partly	NA	NA
10. Overall appraisal	Good	Fair	Good	Fair	Good	Fair	Fair	Fair	Good	Good

NA = Not Applicable because meta-analysis was not performed

Table 3 : Critical appraisal of systematic reviews of fair and good quality (part 2)

Adapted Cochrane checklist	Iversen_Pa rt I 2007 ¹⁷⁸	Iversen_Pa rtII 2007 ¹⁷⁹	Kalant 2004 ¹⁸⁰	Khuri 2005 ¹⁸¹	Killeen 2007 ¹⁸²	Killeen 2005 ¹⁸³	Metzger 2004 ²³	NHS-CRD report 8 1997 ¹⁸⁴	Nuttall 2004 ¹⁸⁵	Shackley 2000 ¹⁸⁶
1. Adequate research question?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Adequately performed search?	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Partly	Yes
3. Adequate selection of articles?	Yes	Yes	Partly	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Adequate quality appraisal of articles?	Yes	Yes	No	No	No	No	No	Yes	No	No
5. Adequate assessment of risk-adjustment?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Adequate description of data extraction procedure?	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No
7. Description of main characteristics of included articles?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8. Adequate handling of clinical and statistical heterogeneity?	Yes	Yes	NA	NA	NA	NA	Yes	No	NA	NA
9. Adequate statistic pooling?	Yes	Yes	NA	NA	NA	NA	Partly	No	NA	NA
10. Overall appraisal	Good	Good	Fair	Fair	Fair	Fair	Fair	Fair	Fair	Fair

NA = Not Applicable because meta-analysis was not performed

Table 4 : Critical appraisal of systematic reviews of fair and good quality (part 3)

Adapted Cochrane checklist	Shervin 2007 ¹⁸⁷	Stengel 2004 ¹⁸⁸	Tjarda van Heek 2005 ¹⁸⁹	Van Geenen 2002 ¹⁹⁰	Wilt 2006 ¹⁹¹	Wilt 2008 ¹⁹²
1. Adequate research question?	Yes	Yes	Yes	Yes	Yes	Yes
2. Adequately performed search?	Partly	Yes	Yes	Partly	No	Yes
3. Adequate selection of articles?	Yes	Yes	Yes	No	Yes	Yes
4. Adequate quality appraisal of articles?	No	Yes	Partly	No	No	Yes
5. Adequate assessment of risk-adjustment?	Yes	Yes	Yes	Yes	Yes	Yes
6. Adequate description of data extraction procedure?	Yes	Yes	Partly	Yes	Yes	Yes
7. Description of main characteristics of included articles?	Yes	Yes	Yes	Yes	Yes	Yes
8. Adequate handling of clinical and statistical heterogeneity?	NA	Yes	NA	NA	NA	Yes
9. Adequate statistic pooling?	NA	Yes	NA	NA	NA	Yes
10. Overall appraisal	Fair	Good	Fair	Fair	Fair	Good

NA = Not Applicable because meta-analysis was not performed

APPENDIX 6 : SELECTION OF PROCEDURES IN BELGIAN DATA: SPECIFICATIONS ON EXCLUSION OR INCLUSION, ESTIMATED NUMBER OF PROCEDURE/CONDITIONS IN BELGIUM, SELECTED OUTCOME VARIABLES

The estimated number of procedures was added when this information was considered useful and available.

These numbers were derived from several data sources:

- 'RI' documents N, RIZIV-INAMI, year 2004;
- 'BCR' Belgian Cancer Registry, year 2003;
- 'MCD' Minimal Clinical Data, year 2004.

The '<' symbol in front of the number indicates that it concerns a maximum. The BCR data, for example, refer to the absolute number of cancers which are not all surgically treated.

65 procedures and conditions studied in systematic reviews (SRs in which studied)	32 procedures and conditions selected in Belgian data	12 procedures finally analysed in Belgian data	Comments on exclusion or inclusion	Estimated number of procedures (RI), hospital stays (MCD) or cancers (BCR)	Comments on outcome variables
Cardiovascular procedures and conditions					
Elective Abdominal Aortic Aneurysm repair (^{168-172, 174, 176, 181, 182, 184, 186, 191})	No	No	Diameter of the aneurysm, necessary for correct risk-adjustment, is not available in MCD. In KCE report 23 on the technology assessment of elective endovascular repair of AAA, the issue of volume outcome relationship was briefly studied. ¹⁹³		
Ruptured Abdominal Aortic Aneurysm repair (^{169-171, 174, 181, 182, 184, 186})	No	No	Which outcome? Mortality rate is in any case very high.		
Carotid Endarterectomy (CEA) (^{168-171, 175, 181, 182, 184, 186})	Yes	Yes	Although distinction between Carotid Endarterectomy (CEA) and Carotid stenting (CAS) is difficult because of lack of specific procedure codes (RIZIV-INAMI or ICD), it should be possible with codes for implants.	3507 (MCD)	
Lower extremity arterial bypass (^{169-171, 181, 182, 184, 186})	No	No	Best outcome measure is amputation rate after several years, but this is not available in the Belgian data.		
Coronary artery bypass graft (CABG) (^{168-171, 180, 181, 184})	Yes	Yes	Distinction must be made between conventional CABG and off pump coronary artery bypass (OPCAB) where the cardiopulmonary bypass pump is no longer employed.	6356 (RI)	EuroSCORE is used for risk stratification for coronary surgery Can the euroSCORE be calculated on basis of the MCD?
Percutaneous coronary intervention (PCI) (^{168-171, 177, 184})	Yes	Yes		23574 (RI)	How to perform a thorough cardiac risk-adjustment? Only age, sex and medication use are available in MCD-MFD.

65 procedures and conditions studied in systematic reviews (SRs in which studied)	32 procedures and conditions selected in Belgian data	12 procedures finally analysed in Belgian data	Comments on exclusion or inclusion	Estimated number of procedures (RI), hospital stays (MCD) or cancers (BCR)	Comments on outcome variables
Cardiac catheterization ⁽¹⁸⁴⁾	No	No	Often performed in day-care hospital. Mortality is not a good outcome measure.		
Acute myocardial infarction ^(169-171, 184)	No	No	In KCE report 14, a first attempt was made to study the volume outcome relationship in patients with AMI. The analysis of the variability in outcome (short term mortality) between hospitals is greatly complicated by the transfer policy i.e. patients being treated by more than 1 hospital. After adjustment for age, sex, cardiovascular history and diabetes, the Standardized Mortality Ratios range from 62% to 150%. Other important clinical factors that influence the outcome, but that are not available in the administrative database, are needed before any conclusions can be drawn on the differences in outcomes between the hospitals. ¹⁹⁴		
Pacemaker implantation ⁽¹⁸⁴⁾	No	No	Infection of the pouch or the electrodes as outcome measure can not be analysed because it is often treated in another hospital than the one where the primary implantation took place. Linkage of both hospital stays would require complicated data analysis.		
Pediatric heart surgery ^(168-171, 181, 184)	No	No	Is de facto regionalized.		
Heart transplantation and Heart/Lung transplantation ^(169, 170, 184)	Yes	No	Very few numbers of interventions per year. Data from several years are needed.	111 (RI)	
Heart valve replacement or repair (valvuloplasty) ⁽¹⁸¹⁾	Yes	Yes	Although RIZIV-INAMI code is identical for replacement or repair, distinction should be possible with codes for implants. How about percutaneous heart valve replacement? Probably not yet performed in 2004.	4009 (RI)	
Mechanical circulatory support ⁽¹⁸¹⁾	No	No	Overlap with other cardiac interventions. Different devices are used.		
Neurological procedures and conditions					
Elective cerebral aneurysm repair ^(169, 171, 181)	Yes	No	Distinction between elective and ruptured cerebral aneurysm can be made on basis of the ICD-9-CM diagnosis code. No RIZIV-INAMI codes available for surgical clipping and endovascular.	411 (RI)	
Ruptured cerebral aneurysm repair/Subarachnoid haemorrhage ^(169, 171, 181, 184)	Yes	No			
Cerebrovascular accident ⁽¹⁸⁴⁾	Yes	No	Often without surgery.	16688 (MCD)	
Ventriculo-peritoneal shunt in paediatric surgery ⁽¹⁸¹⁾	No	No	Is de facto regionalized.		
Craniotomy ⁽¹⁸¹⁾	No	No	Patient population is too heterogeneous.		

65 procedures and conditions studied in systematic reviews (SRs in which studied)	32 procedures and conditions selected in Belgian data	12 procedures finally analysed in Belgian data	Comments on exclusion or inclusion	Estimated number of procedures (RI), hospital stays (MCD) or cancers (BCR)	Comments on outcome variables
Orthopaedic surgery					
Shoulder arthroplasty ⁽¹⁸¹⁾	No	No	Outcome: re intervention, revision should be studied after several years but is not available in our data.	712 (RI)	Pain and mobility remain best outcome measures but are not available.
Total hip replacement ^(168-171, 181, 184)	Yes	Yes		16075 (MCD)	
Total knee replacement ^(168-171, 181, 184, 188)	Yes	Yes		12557 (MCD)	
Hip fracture surgery ^(170, 171, 184)	Yes	Yes	Limit to fracture proximal femur.	12959 (RI)	
Spine surgery ⁽¹⁸⁴⁾	Yes	No	Procedures are too heterogeneous.	22443 (RI)	
Trauma					
Trauma ^(168-170, 181, 184)	No	No	In most volume outcome studies that analyse severe trauma patients, hospital stays are identified through a severity of injury score which is not available in MCD/MFD. ¹⁹⁵		
Intensive care					
Neonatal intensive care ^(169, 170, 184)	No	No	The number of NIC centres is already regionalised and the patient population is too heterogeneous.		
Paediatric intensive care ⁽¹⁸⁴⁾	Yes	No	Patient population is too heterogeneous.		
Adult intensive care ^(169, 184)	No	No	Patient population is too heterogeneous.		
Oncologic procedures and conditions					
Oesophageal cancer surgery ^(23, 168-171, 181, 183, 184)	Yes	Yes	Inclusion of cardia tumours.	<737 (BCR)	General remarks for all cancers: 1) Since the selection is based on procedure codes and diagnostic codes, cancers without surgery will be included in the database. This allows an analysis of the ratio "surgery/only non surgical treatment" per cancer type and per hospital, which will possibly reveal a difference in therapeutical decision making between hospitals. 2) Adjuvant therapy should be used in the process of risk adjustment whenever there is evidence in the guidelines that a specific form of adjuvant therapy is indicated. 3) The experts emphasise that process measures (e.g. the number of axillary lymph
Gastric cancer surgery ^(168-170, 181, 183, 184)	Yes	No	Cardia tumours will be included with oesophageal cancer surgery.	<1200 (BCR)	
Pancreatic cancer surgery ^(168-171, 181, 183, 184, 189, 190)	Yes	Yes		<962 (BCR)	
Hepatic cancer surgery ^(168-170, 181, 183)	Yes	No	BCR data contain information on staging for only 44% of patients.	<349 (BCR)	
Colorectal cancer surgery ^(168-171, 173, 178, 179, 181, 183, 184)	Yes	Partly	Colon and sigmoid tumours will be analysed. Rectal tumours will not be analysed in Belgian data because of similarities with the Procare project. ¹⁹⁶	<6575 (BCR)	
Pelvic cancer surgery ⁽¹⁶⁹⁾	No	No	Overlap with other cancers and patient population too heterogeneous.		

65 procedures and conditions studied in systematic reviews (SRs in which studied)	32 procedures and conditions selected in Belgian data	12 procedures finally analysed in Belgian data	Comments on exclusion or inclusion	Estimated number of procedures (RI), hospital stays (MCD) or cancers (BCR)	Comments on outcome variables	
Breast cancer surgery (^{169-171, 181, 183, 184})	Yes	Yes	Long term mortality seems essential to measure a possible volume-outcome association.	<9134 (BCR)	nodes which is removed during an axillary lymph node dissection) are probably far better indicators of quality of care for cancers than outcome measures. The problem is, however, that such process measures are not available in the MCD. 4) For most cancers, mortality should be assessed after at least three years. The fact that we only dispose of two-year mortality for this study is a big handicap. 5) Most oncologic aftercare is multi-disciplinary of nature. Therefore the question arises whether the VOA should not be limited to hospital volume.	
Lung cancer surgery (^{168-171, 181, 183, 184})	Yes	Yes		<5781 (BCR)		
Prostate cancer surgery (^{169-171, 181, 183-185, 192})	Yes	No	Outcome is too difficult to study while incontinence and impotence are not traceable in MCD and, mortality is often low.	<7975 (BCR)		
Cystectomy for cancer (^{181, 183, 185})	Yes	No		<1720 (BCR)		
Nephrectomy for cancer (^{181, 183, 185})	Yes	No	Staging is indispensable since code for nephrectomy is used for cancers in different stages.	<1162 (BCR)		
Ovarectomy for cancer (¹⁸¹)	Yes	No	BCR data contain information on staging for only 54% of patients.	<899 (BCR) 511 (MCD)		
Intracranial cancer surgery (^{181, 183})	Yes	No	Patient population too heterogeneous.	<655 (BCR) 564 (RI)		
Acoustic neurinoma (¹⁸¹)	No	No	Condition is too rare. Prevalence of about 1 in 100000.			
Transsphenoidal surgery for pituitary tumours (¹⁸¹)	Yes	No	Condition is too rare.	222 (RI)		
Testicular cancer (¹⁶⁹)	Yes	No	Condition is too rare.	228 (BCR)		
Paediatric oncology (¹⁶⁹)	No	No	Is de facto regionalized and patient population is very heterogeneous.	350 (BCR)		
Bone marrow transplantation (¹⁶⁹)	No	No	Patient population too heterogeneous and outcome after several years and interference with stem cell transplantation.	622 (RI)		
Gastrointestinal procedures						
Appendicectomy (^{169, 184})	No	No	Mortality is very rare.	13124 (MCD)		
Cholecystectomy (^{169, 170, 184})	No	No	Patient population is too heterogeneous and different surgical procedures. Lack of clear outcome measure.			
Colectomy (not for cancer) (^{170, 184})	Yes	No				
Bariatric surgery (¹⁸¹)	Yes	No	RIZIV-INAMI codes are not unique for bariatric surgery. Risk-adjustment for BMI is not possible since this information is not available in MCD.			

65 procedures and conditions studied in systematic reviews (SRs in which studied)	32 procedures and conditions selected in Belgian data	12 procedures finally analysed in Belgian data	Comments on exclusion or inclusion	Estimated number of procedures (RI), hospital stays (MCD) or cancers (BCR)	Comments on outcome variables
Pancreatic transplantation ⁽¹⁸¹⁾	No	No	Procedure is too rare. Was performed only 6 times in 2004, in 3 hospitals (RIZIV-INAMI data). There were also 17 kidney/pancreas transplantations.	6 (RI)	
Liver transplantation ^(168, 170)	Yes	No	Procedure is performed not frequent enough. Mortality will be very high and problem of many confounding factors.	183 (RI)	
Surgery for gastric ulcer ⁽¹⁸⁴⁾	Yes	No	Surgery has become a rarity as treatment of a gastric ulcer.		
Medical diagnoses/procedures					
AIDS ^(169, 170, 184)	No	No	Is de facto regionalized, treatment has changed drastically since latest publication.		
Respiratory insufficiency ^(169, 184)	No	No	Vague definition, often ambulatory treatment.		
COPD ⁽¹⁸⁴⁾	No	No	Vague definition, often ambulatory treatment.		
Pneumonia ⁽¹⁸⁴⁾	Yes	No	Selection of community acquired pneumonia category 4 (with respiration and stay on intensive care) is difficult. How to distinct between CAP and nosocomial pneumonia?		
Kidney/urinary tract infection ⁽¹⁸⁴⁾	No	No	Vague definition, often ambulatory treatment.		
Cirrhosis ⁽¹⁸⁴⁾	No	No	Patient population is too heterogeneous.		
Miscellaneous procedures					
Cataract surgery ⁽¹⁸⁴⁾	No	No	Mostly performed in day-care hospital.		
Hernia repair ^(169, 184)	No	No	Often performed in day-care hospital.		
Cleft palate repair ⁽¹⁶⁸⁾	No	No	In 2004, procedure was performed in 13 hospitals. Problem: which outcome?	179 (RI)	
Parathyroid surgery ⁽¹⁶⁹⁾	No	No	In 2004, procedure was performed in 113 hospitals with number of procedures per hospital varying from a minimum of 1 to a maximum of 44, with 5 as an average. Problem: which outcome?	539 (RI)	
Caesarean section ⁽¹⁸⁴⁾	No	No	Outcome in mothers i.e. adhesions = long term = not available. Risk adjustment should be the indication which is not available in MCD.		
Hysterectomy (not for cancer) ^(169, 184)	No	No	Outcome is not measurable.		
Kidney transplantation ⁽¹⁶⁹⁾	No	No	Outcome (rejection, hypertension) is long term.		

APPENDIX 7 : SECOND QUALITY APPRAISAL - APPRAISAL OF THE METHOD OF DATA SYNTHESIS THAT WAS APPLIED IN THE SYSTEMATIC REVIEWS

Systematic review	Description of method of data synthesis that was applied in the systematic review	Is the SR suitable as supporting evidence in relation to the VOA?
Chowdhury 2007 ¹⁶⁸	Risk adjustment was assessed but not used as a selection criterion.	+
Dudley 2000 ¹⁶⁹	Studies were scored based on case-mix adjustment, range of predictor variable, number of hospitals in each volume category, age of the data used and country in which study was performed. For each condition, one study with the highest score was selected for study inclusion.	+++
Gandjour 2003 ¹⁷⁰	Studies were scored based on case-mix adjustment, range of predictor variable, number of hospitals or physicians in each volume category, age of the data used and type of hospital in which study was performed. For each diagnosis and intervention the study most likely to provide an unbiased estimate of the effect of volume on mortality rate was identified using the modified algorithm developed by Dudley et al. ¹⁶⁹	+++
Halm 2002 ¹⁷¹	Studies were scored based on case-mix adjustment, sample size, sample representation, number of hospitals or physicians studied, type of primary outcome, the number of volume strata examined, the unit of analysis, the measurement of appropriateness of patient selection, and measurement of clinical processes of care. But, this score is not used for study selection and all primary studies are included.	+
Hodgson 2001 ¹⁷³	Assessment of inclusiveness of important prognostic factors in multivariable analysis (age, sex, tumour stage, radiotherapy) but no selection of studies on the basis of the degree of risk-adjustment.	+
Holt 2007 ¹⁷⁵	The presence or absence of case-mix adjustment was recorded. For the meta-analysis, case-mix adjusted data were used where available.	+++
IQWiG 2006 ¹⁷⁷	Quality appraisal based on case-mix adjustment, quality of the statistical model and completeness leads to division into high ^{111, 124} , moderate ^{109, 110, 112-114, 116, 117, 119-122, 129} and low ^{108, 115, 118} quality studies.	+++
Iversen 2007 Part I ¹⁷⁸	Studies correcting their analyses for case-mix were considered to have higher impact in the forest plot. Finally, the greatest weight was given to studies with evidence on level 1 and on level 2.	+++
Iversen 2007 Part II ¹⁷⁹	Studies correcting their analyses for case-mix were considered to have higher impact in the forest plot. Finally, the greatest weight was given to studies with evidence on level 1 and on level 2.	+++
Kalant 2004 ¹⁸⁰	Risk adjustment was assessed but not used as a selection criterion.	+
Khuri 2005 ¹⁸¹	Risk adjustment was assessed but not used as a selection criterion.	+
Killeen 2007 ¹⁸²	Studies were scored based on case-mix adjustment, range of predictor variable, number of hospitals in each volume category, age of the data used and country in which study was performed (method developed by Dudley). ¹⁶⁹ Only high-quality studies (score >4) were selected for study inclusion.	+++
Killeen 2005 ¹⁸³	Studies were scored based on case-mix adjustment, range of predictor variable, number of hospitals in each volume category, age of the data used and country in which study was performed (method developed by Dudley). ¹⁶⁹	+++

	Only high-quality studies (score >4) were selected for study inclusion.	
Metzger 2004 ²³	Identification of the study most likely to yield an unbiased estimate of the effect of volume on mortality by considering study sample size, range of volume among the hospitals, risk-adjustment, location of the study and timeliness of data.	+++
NHS Centre for Reviews and Dissemination 1997 ¹⁸⁴	Studies were scored on a 4-point scale: 0 = no adjustment, 1 = adjustment for sex and age, 2 = adjustment for some clinical risk factors, 3 = extensive adjustment using validated clinical risk factors. The risk-adjustment score was, however, not used as selection criterion.	++
Shackley 2000 ¹⁸⁶	Studies were categorized into 3 groups according to whether they made full adjustment (demographic factors, co-morbidity and severity/stage of illness), partial adjustment (not for severity/stage of illness) or no adjustment for case mix. However, all studies were represented in the article.	++
Stengel 2004 ¹⁸⁸	Studies were scored on a 2-point scale: 1 = no adjustment, 2 = adjustment for sex, age, co-morbidity. Five primary studies were included in the meta-analysis; four of these were risk-adjusted for age, gender and co-morbidity.	++
Tjarda Van Heek 2005 ¹⁸⁹	Risk adjustment was assessed but not used as a selection criterion.	+
Van Geenen 2002 ¹⁹⁰	Risk adjustment was assessed but not used as a selection criterion.	+

APPENDIX 8 : EVIDENCE TABLES FOR ONCOLOGIC PROCEDURES

OESOPHAGEAL CANCER SURGERY		
Totality of systematic reviews		
Total number of SRs	8 ^{23, 168-171, 181, 183, 184}	
Publication date all SRs	1997-2007	
Total number of studies included	22 ^{1-18, 80, 197-199}	
Study period all SRs	1957-1999	
Outcome variables	In-hospital mortality ^{23, 168-171, 181, 183} ; 30-day mortality ^{23, 181, 183, 184} ; 5-year mortality ^{183, 184} ; Length of stay ^{168, 183} .	
Chowdury 2007¹⁶⁸		
Main findings	Threshold volume	Quality of evidence
<u>Outcome in general (In-hospital mortality or Length of stay):</u> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (mix SS & NS)	High volume hospital range 6 to 30, Low volume hospital range 1 to 6, High volume surgeon range 6 to 12, Low volume surgeon range 4 to 6.	1) Fitness to support evidence: + 2) 4 primary studies ^{11-13, 199} Origin: 3/4 USA, 1/4 Scotland 3) Study period: Not specified 4) Inverse VOA is mainly based on SS primary studies <input type="checkbox"/> GRADE C evidence level
Killeen 2005¹⁸³		
Main findings	Threshold volume	Quality of evidence
Killeen et al. explicitly mention that the cardia is included in the oesophageal cancer. <u>Mortality:</u> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (>75% SS) Number needed to treat (NNT) = 7 to 9 patients for a high-volume provider to prevent 1 death.	High volume hospital range 6 to 83, Low volume hospital range 2 to 13, High volume surgeon range 6 to 48, Low volume surgeon range 1 to 6.	1) Fitness to support evidence: +++ 2) 10 primary studies ^{1-3, 7-9, 15, 80, 199} Origin: 8/10 USA, 1/10 Canada, 1/10 UK 3) Study period: 1984-1999 4) Inverse VOA is mainly based on SS primary studies <input type="checkbox"/> GRADE B evidence level
Khuri 2005¹⁸¹		
Main findings	Threshold volume	Quality of evidence
<u>In-hospital mortality:</u> - inverse relation with hospital volume (>75% SS) <u>30-day mortality:</u> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (>75% SS)	High volume hospital range 6 to 200, Low volume hospital range 2 to 22, High volume surgeon range 19 to 40, Low volume surgeon range 1 to 2.	1) Fitness to support evidence: + 2) 12 primary studies ^{1-6, 8, 9, 16, 80, 197, 199} Origin: 10/12 USA, 1/12 Canada, 1/12 UK 3) Study period: 1984-1999

OESOPHAGEAL CANCER SURGERY		
4) Inverse VOA is mainly based on SS primary studies <input type="checkbox"/> GRADE C evidence level		
Metzger 2004 ²³		
Main findings <i>Mortality:</i> - inverse relation with hospital volume (>75% SS) Median mortality is 18% in low volume hospitals (<5 esophagec-tomies per year) versus 4.9% in high volume hospitals (>20 operations per year). Pooled effect shows OR = 0.43 (95% CI 0.31-0.58) favoring high volume hospitals.	Threshold volume High volume hospital >20. This cut-off level was calculated using the method of receiver-operator curve. Low volume hospital <5.	Quality of evidence 1) Fitness to support evidence: +++ 2) 13 ^{2, 5, 7, 10-12, 14, 15, 17, 18, 80, 197, 199} of which 8 were usable for meta-analysis ^{2, 7, 10-12, 15, 17, 80} Origin: 9/13 USA, 1/13 Sweden, 1/13 Canada, 1/13 Netherlands, 1/13 UK 3) Study period: 1984-1998 4) Inverse VOA is mainly based on SS primary studies <input type="checkbox"/> GRADE B evidence level
Gandjour 2003 ¹⁷⁰		
Main findings <i>Mortality:</i> - inverse relation with hospital volume (>75% SS)	Threshold volume High volume hospital >7.	Quality of evidence 1) Fitness to support evidence: +++ 2) 2 primary studies ^{80, 199} Origin: 2/2 USA 3) Study period: 1984-1994 4) Inverse VOA is based on SS primary studies <input type="checkbox"/> GRADE C evidence level
Halm 2002 ¹⁷¹		
Main findings <i>Mortality:</i> - inverse relation with hospital volume (>75% SS)	Threshold volume High volume hospital range 11 to 200, Low volume hospital range 5 to 10.	Quality of evidence 1) Fitness to support evidence: + 2) 3 primary studies ^{80, 197, 199} Origin: 3/3 USA 3) Study period: 1984-1997 4) Inverse VOA is based on SS primary studies <input type="checkbox"/> GRADE C evidence level
Dudley 2000 ¹⁶⁹		
Main findings <i>Mortality:</i> - inverse relation with hospital volume (>75% SS)	Threshold volume Low volume hospital range 1 to 6.	Quality of evidence 1) Fitness to support evidence: +++ 2) 2 primary studies ^{80, 199} Origin: 2/2 USA 3) Study period: 1984-1994 4) Inverse VOA is based on SS primary studies <input type="checkbox"/> GRADE C evidence level
NHS 1997 ¹⁸⁴		

OESOPHAGEAL CANCER SURGERY

Main findings

Mortality:

- inverse relation with surgeon volume (only 1 SS study)

Threshold volume

High volume surgeon range 3 to 6.

Quality of evidence

- 1) Fitness to support evidence: ++
 - 2) 1 primary study ¹⁹⁸
 - Origin: 1/1 UK
 - 3) Study period: 1957-1976
 - 4) Inverse VOA is based on SS primary studies
- GRADE C evidence level**

Conclusion on volume - outcome association for oesophageal cancer surgery

Main findings

INVERSE relation between:

- hospital volume – mortality
- surgeon volume - mortality

Threshold volume

Minimal hospital volume threshold:

- lower threshold: 6 oesophagectomies per annum

- upper threshold: 13 oesophagectomies per annum.

These thresholds correspond more or less with the thresholds in the SRs. More importantly, they correspond with the thresholds issued by the US Agency for Healthcare Research (i.e. 6 per annum) and Quality and the US Leapfrog Group (i.e. 13 per annum).^{200, 201}

Quality of evidence

- 2 out of 8 SRs have Grade B evidence level ^{23, 183}
- 6 out of 8 SRs have Grade C evidence level ^{168-171, 181, 184}

PANCREATIC CANCER SURGERY		
Totality of systematic reviews		
Total number of SRs	9 ^{168-171, 181, 183, 184, 189, 190}	
Publication date all SRs	1997-2007	
Total number of studies included	25 ^{2, 3, 6, 9, 15, 16, 34-38, 80, 197, 202-213}	
Study period all SRs	1984-1999	
Outcome variables	In-hospital ^{168-171, 181, 183, 184, 189, 190} ; 30-day mortality ^{181, 183, 189} ; 64-day mortality ^{181, 183} ; 3-year mortality ¹⁸¹ ; 30-day readmission ¹⁸¹ ; Pancreatic fistula rate ¹⁸⁴ ; Bleeding rate ^{181, 183} ; Infection rate ^{181, 183} ; Length of stay ^{168, 181} .	
Chowdury 2007¹⁶⁸		
Main findings	Threshold volume	Quality of evidence
<u>Outcome in general (In-hospital mortality or Length of stay):</u> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (>75% SS)	High volume hospital range 25 to 50, Low volume hospital range 1 to 5, High volume surgeon range 4 to 41, Low volume surgeon range 1 to 9.	1) Fitness to support evidence: + 2) 5 primary studies ^{35, 197, 204, 209} Origin: 4/5 USA, 1/5 UK 3) Study period: Not specified 4) Inverse VOA is mainly based on SS primary studies <input type="checkbox"/> GRADE C evidence level
Killeen 2005¹⁸³		
Main findings	Threshold volume	Quality of evidence
<u>Mortality:</u> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (mix SS & NS) Number needed to treat (NNT) = 10 to 15 patients for a high-volume provider to prevent 1 death.	High volume hospital range 13 to 81, Low volume hospital range 1 to 10, High volume surgeon range 4 to 41, Low volume surgeon range 2 to 9.	1) Fitness to support evidence: +++ 2) 11 primary studies ^{2, 3, 9, 15, 35, 37, 205, 207, 208, 210, 211} Origin: 9/11 USA, 2/11 Canada 3) Study period: 1984-1999 4) Inverse VOA is mainly based on SS primary studies <input type="checkbox"/> GRADE B evidence level
Khuri 2005¹⁸¹		
Main findings	Threshold volume	Quality of evidence
<u>In-hospital mortality:</u> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (>75% SS) <u>30-day mortality:</u> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (only 1 SS study)	High volume hospital range 2 to 50, Low volume hospital range 1 to 22, High volume surgeon range 4 to 50, Low volume surgeon range 2 to 9.	1) Fitness to support evidence: + 2) 18 primary studies ^{2, 3, 6, 9, 16, 34, 36, 80, 197, 202, 203, 205-207, 209-212} Origin: 15/18 USA, 2/18 Canada, 1/18 UK 3) Study period: 1984-1999 4) Inverse VOA is mainly based on SS primary studies

PANCREATIC CANCER SURGERY

3-year mortality:

- inverse relation with hospital volume (only 1 SS study)

30-day readmission:

- inverse relation with hospital volume (only 1 SS study)

Bleeding and reinfection:

- inverse relation with hospital volume (only 1 SS study)

Length of stay:

- inverse relation with hospital volume (only 1 SS study)

GRADE C evidence level

Tjarda Van Heek 2005 ¹⁸⁹

Main findings

Mortality:

- inverse relation with hospital volume (>75% SS)

Threshold volume

High volume hospital range 2 to 25.

Quality of evidence

1) Fitness to support evidence: +

2) 12 ^{9, 35, 38, 197, 202, 204, 205, 207-210, 212}

Origin: 8/12 USA, 1/12 Canada, 1/12 Netherlands, 1/12 UK, 1/12 Finland

3) Study period: 1984-1998

4) Inverse VOA is mainly based on SS primary studies

GRADE C evidence level

Gandjour 2003 ¹⁷⁰

Main findings

Mortality:

- inverse relation with hospital volume (>75% SS)

- inverse relation with surgeon volume (only 1 SS study)

Threshold volume

High volume hospital >10,
High volume surgeon >9.

Quality of evidence

1) Fitness to support evidence: +++

2) 7 primary studies ^{80, 202, 205, 207, 208, 210, 211}

Origin: 6/7 USA, 1/7 Canada

3) Study period: Not specified

4) Inverse VOA is mainly based on SS primary studies

GRADE B evidence level

Van Geenen 2002 ¹⁹⁰

Main findings

Mortality:

- inverse relation with hospital volume (>75% SS)

- inverse relation with surgeon volume (>75% NS)

Threshold volume

High volume hospital range 2 to 50,
Low volume hospital range 2 to 20.

Quality of evidence

1) Fitness to support evidence: +

2) 10 ^{35, 80, 197, 202, 204-206, 208, 209, 212}

Origin: 8/10 USA, 1/10 Netherlands, 1/10 UK

3) Study period: Not specified

4) Inverse VOA is mainly based on SS primary studies

GRADE C evidence level

Halm 2002 ¹⁷¹

Main findings

Mortality:

- inverse relation with hospital volume (>75% SS)

- inverse relation with surgeon volume (mix SS & NS)

Threshold volume

High volume hospital range 3 to 200,
Low volume hospital range 1 to 22,
High volume surgeon range 10 to 42,

Quality of evidence

1) Fitness to support evidence: +

2) 10 primary studies ^{80, 202, 203, 205-208, 210-212}

Origin: 9/10 USA, 1/10 Canada

PANCREATIC CANCER SURGERY		
	Low volume surgeon range 1 to 9.	3) Study period: 1984-1997 4) Inverse VOA is mainly based on SS primary studies <input type="checkbox"/> GRADE C evidence level
Dudley 2000 ¹⁶⁹		
Main findings <i>Mortality:</i> - inverse relation with hospital volume (>75% SS)	Threshold volume Low volume hospital range 1 to 6.	Quality of evidence 1) Fitness to support evidence: +++ 2) 8 primary studies ^{80, 197, 205-209, 211} Origin: 7/8 USA, 1/8 UK 3) Study period: Not specified 4) Inverse VOA is based on SS primary studies <input type="checkbox"/> GRADE B evidence level
NHS 1997 ¹⁸⁴		
Main findings <i>Pancreatic fistula rate:</i> - inverse relation with surgeon volume (only 1 SS study)	Threshold volume High volume surgeon = 76, Low volume surgeon = 9.	Quality of evidence 1) Fitness to support evidence: ++ 2) 2 primary studies ^{208, 213} Origin: 2/2 USA 3) Study period: 1984-1995 4) Inverse VOA is based on 1 SS primary study <input type="checkbox"/> GRADE C evidence level
Conclusion on volume - outcome association for pancreatic cancer surgery		
Main findings INVERSE relation between: - hospital volume – mortality - surgeon volume - mortality	Threshold volume Minimal hospital volume threshold: 11 pancreatic resections per annum. This threshold corresponds more or less with the thresholds in the SRs. More importantly, it corresponds with the threshold issued by the US Agency for Healthcare Research and Quality and the US Leapfrog Group. ^{200, 201}	Quality of evidence - 3 out of 9 SRs have Grade B evidence level ^{169, 170, 183} - 6 out of 9 SRs have Grade C evidence level ^{168, 171, 181, 184, 189, 190}

COLON CANCER SURGERY		
Totality of systematic reviews		
Total number of SRs	9 ^{168-171, 173, 178, 179, 181, 183, 184}	
Publication date all SRs	1997-2007	
Total number of studies included	43 ^{2, 9, 10, 15, 16, 45-61, 80, 81, 197, 214-230, 231} It concerns studies that examined colon cancers or colorectal cancers (i.e. tumors of the colon or the rectum or both). Studies that investigated rectal cancer only, are excluded from this total number (which was not always possible for the individual SRs).	
Study period all SRs	1972-2000	
Outcome variables	In-hospital mortality ^{168-171, 173, 178, 181, 183, 184} ; 30-day mortality ^{173, 178, 179, 181, 183} ; 2-year survival ^{173, 181, 183} ; 3-year survival ^{173, 181, 183} ; 5-year survival ^{173, 181, 183, 184} ; 10-year survival ¹⁸⁴ ; Disease-specific survival ¹⁸¹ ; Overall survival ¹⁷⁹ ; Stoma rate / Abdominoperineal resection / Sphincter-sparing procedure ^{173, 179, 183} ; Postoperative morbidity ¹⁷⁸ ; Infection rate ¹⁸⁴ ; Anastomotic leakage rate ^{173, 178, 184} ; Locoregional or Cancer recurrence / Cancer free survival ^{173, 179, 181, 183, 184} ; Length of stay ^{168, 184} .	
Chowdury 2007 ¹⁶⁸		
Main findings	Threshold volume	Quality of evidence
<u>Outcome in general (In-hospital mortality or Length of stay):</u> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (>75% SS)	High volume hospital range 33 to 70, Low volume hospital range 23 to 40, High volume surgeon range 13 to 33, Low volume surgeon range 1 to 23.	1) Fitness to support evidence: + 2) 3 primary studies on colorectal cancer ^{49, 218, 222} Origin: 2/3 USA, 1/3 UK 3) Study period: Not specified 4) Inverse VOA is mainly based on SS primary studies <input type="checkbox"/> GRADE C evidence level
Iversen 2007 ^{178, 179}		
Main findings	Threshold volume	Quality of evidence
COLON CANCER <u>In-hospital mortality:</u> - inverse relation with hospital volume (>75% SS; forest plot shows OR 0.64 (95% CI 0.55-0.73)) - inverse relation with surgeon volume (>75% SS; forest plot shows OR 0.50 (95% CI 0.39-0.64)) <u>Overall survival:</u> - inverse relation with hospital volume (>75% SS; forest plot shows OR 1.22 (95% CI 1.16-1.28)) - inverse relation with surgeon volume (only one SS study; forest plot shows OR 1.25 (95% CI 1.16-1.34)) COLORECTAL CANCER <u>In-hospital mortality:</u> - inverse relation with hospital volume (mix SS & NS; forest plot shows	High volume hospital range 19 to 201, Low volume hospital range 10 to 61, High volume surgeon range 25 to 60, Low volume surgeon range 9 to 30.	1) Fitness to support evidence: +++ 2) 27 primary studies: 12 on colon cancer ^{2, 9, 10, 46, 52, 53, 55, 56, 58, 59, 81, 197} and 15 on colorectal cancer. ^{15, 45, 47-49, 51, 54, 57, 60, 61, 80, 218, 222, 227, 228} Origin: Countries of origin not specified in SR 3) Study period: Not specified 4) Inverse VOA is based on a mix of NS and SS primary studies <input type="checkbox"/> GRADE B evidence level

COLON CANCER SURGERY

a not statistically significant OR 0.74 (95% CI 0.47-1.16))
 - inverse relation with surgeon volume (>75% NS; forest plot shows a not statistically significant OR 0.82 (95% CI 0.54-1.24))

Overall survival:

- inverse relation with hospital volume (mix SS & NS; forest plot shows OR 1.17 (95% CI 1.11-1.23))
 - inverse relation with surgeon volume (mix SS & NS; forest plot shows a not statistically significant OR 1.37 (95% CI 0.94-1.99))

Killeen 2005 ¹⁸³

Main findings

Mortality:

- inverse relation with hospital volume (>75% SS)
 - inverse relation with surgeon volume (mix SS & NS)
 Number needed to treat (NNT) = 50 to 100 patients for a high-volume provider to prevent 1 death. The authors conclude there is a significant VOA, but the magnitude of the volume effect on mortality is variable and small (1-2%).
 Cave! These conclusions are also based on studies on rectal cancer.

Threshold volume

High volume hospital range 14 to 253,
 Low volume hospital range 1 to 84,
 High volume surgeon range 28 to 34,
 Low volume surgeon range 1 to 12.

Quality of evidence

- 1) Fitness to support evidence: +++
- 2) 16 primary studies: 12 on colon and colorectal cancer ^{2, 15, 49, 52, 54, 55, 57-59, 218, 222, 228} and 4 studies on rectal cancer ²³²⁻²³⁵
 Origin: 13/16 USA, 2/16 UK, 1/16 Canada
- 3) Study period: 1988-2000
- 4) Inverse VOA is based on a mix of NS and SS primary studies
 GRADE B evidence level

Khuri 2005 ¹⁸¹

Main findings

In-hospital mortality:

- inverse relation with hospital volume (>75% SS)
 - inverse relation with surgeon volume (mix NS & SS)

30-day mortality:

- inverse relation with hospital volume (mix NS & SS)
 - inverse relation with surgeon volume (>75% NS)

Threshold volume

High volume hospital range 25 to 380,
 Low volume hospital range 5 to 84,
 High volume surgeon range 7 to 34,
 Low volume surgeon range 1 to 21.

Quality of evidence

- 1) Fitness to support evidence: +
- 2) 13 primary studies ^{2, 9, 16, 47, 49, 55, 58, 59, 197, 218, 222, 227, 228}
 Origin: 9/13 USA, 1/13 Canada, 3/13 UK
- 3) Study period: 1989-1999
- 4) Inverse VOA is based on a mix of NS and SS primary studies
 GRADE C evidence level

Gandjour 2003 ¹⁷⁰

Main findings

Mortality:

- inverse relation with hospital volume (mix NS & SS)
 - inverse relation with surgeon volume (mix NS & SS)

Threshold volume

High volume hospital >40,
 High volume surgeon >10.

Quality of evidence

- 1) Fitness to support evidence: +++
- 2) 4 primary studies ^{58, 218, 222, 228}
 Origin: 3/4 USA, 1/4 UK
- 3) Study period: Not specified
- 4) Inverse VOA is based on a mix of NS and SS primary studies
 GRADE C evidence level

Halm 2002 ¹⁷¹

Main findings

Threshold volume

Quality of evidence

COLON CANCER SURGERY

<p><u>Mortality:</u> - inverse relation with hospital volume (mix SS & NS) - inverse relation with surgeon volume (>75% SS)</p>	<p>High volume hospital range 18 to 253, Low volume hospital range 10 to 84, High volume surgeon range 9 to 40, Low volume surgeon range 5 to 21.</p>	<p>1) Fitness to support evidence: + 2) 11 primary studies: 8 on colon and colorectal cancer.^{49, 58, 81, 197, 217, 218, 228, 229} and 3 on rectal cancer²³⁵⁻²³⁷ Origin: 10/11 USA, 1/11 UK 3) Study period: 1983-1997 4) Inverse VOA is mainly based on a mix of NS and SS primary studies <input type="checkbox"/> GRADE C evidence level</p>
<p>Hodgson 2001¹⁷³</p>		
<p>Main findings <u>Mortality:</u> - inverse relation with hospital volume (>75% NS) - inverse relation with surgeon volume (>75% NS)</p>	<p>Threshold volume High volume hospital range 25 to 1000, Low volume hospital range 25 to 150, High volume surgeon range 10 to 25, Low volume surgeon range 5 to 10.</p>	<p>Quality of evidence 1) Fitness to support evidence: + 2) 10 primary studies^{50, 58, 214, 218, 221-223, 227, 228, 231} Origin: 5/10 USA, 4/10 UK, 1/10 Germany 3) Study period: 1977-1996 4) Inverse VOA is based on NS primary studies <input type="checkbox"/> GRADE C evidence level</p>
<p>Dudley 2000¹⁶⁹</p>		
<p>Main findings <u>Mortality:</u> - inverse relation with hospital volume (>75% SS)</p>	<p>Threshold volume No threshold available.</p>	<p>Quality of evidence 1) Fitness to support evidence: +++ 2) 6 primary studies^{217, 220, 223-225, 229} Origin: 6/6 USA 3) Study period: All studies were published before 1990 4) Inverse VOA is based on SS primary studies <input type="checkbox"/> GRADE C evidence level</p>
<p>NHS 1997¹⁸⁴</p>		
<p>Main findings <u>In-hospital mortality:</u> - inverse relation with hospital volume (mix SS & NS)</p>	<p>Threshold volume Average number of treatments in hospital = 17.</p>	<p>Quality of evidence 1) Fitness to support evidence: ++ 2) 7 primary studies^{214-216, 219, 223, 226, 230} Origin: 4/7 USA, 2/7 UK, 1/7 Germany 3) Study period: 1972-1995 4) Inverse VOA is based on 1 SS primary study <input type="checkbox"/> GRADE C evidence level</p>
<p>Conclusion on volume - outcome association for colon cancer surgery</p>		
<p>Main findings INVERSE relation between: - hospital volume – mortality - surgeon volume - mortality</p>	<p>Threshold volume Studies differ widely in relation to the cut-off points used to define low and high volume.</p>	<p>Quality of evidence - 2 out of 9 SRs have Grade B evidence level^{178, 179, 183} - 7 out of 9 SRs have Grade C evidence level^{168-171, 173, 181, 184}</p>

BREAST CANCER SURGERY

Totality of systematic reviews

Total number of SRs	6 ^{169-171, 181, 183, 184}
Publication date all SRs	1997-2005
Total number of studies included	7 ^{66-71, 238}
Study period all SRs	1972-1995
Outcome variables	In-hospital mortality ^{170, 184} ; 1-year survival ¹⁸⁴ ; 3-year survival ¹⁸⁴ ; 5-year survival ^{169, 171, 181, 183, 184}

Killeen 2005¹⁸³

Main findings

5-year mortality:

- inverse relation with hospital volume (mix SS & NS)
- inverse relation with surgeon volume (>75% SS)

Threshold volume

High volume hospital >149,
Low volume hospital range 10 to 25,
High volume surgeon >50,
Low volume surgeon <10.

Quality of evidence

- 1) Fitness to support evidence: +++
 - 2) 4 primary studies^{66, 67, 70, 71}
Origin: 2/4 USA, 2/4 UK
 - 3) Study period: 1979-1995
 - 4) Inverse VOA is based on a mix of SS & NS primary studies
- GRADE C evidence level**

Khuri 2005¹⁸¹

Main findings

5-year mortality:

- inverse relation with hospital volume (only 1 SS study)
- inverse relation with surgeon volume (only 1 SS study)

Threshold volume

High volume hospital >149,
Low volume hospital <10,
High volume surgeon >29,
Low volume surgeon <10.

Quality of evidence

- 1) Fitness to support evidence: +
 - 2) 2 primary studies^{70, 71}
Origin: 1/2 USA, 1/2 UK
 - 3) Study period: 1979-1989
 - 4) Inverse VOA is based on SS primary studies
- GRADE C evidence level**

Gandjour 2003¹⁷⁰

Main findings

Mortality:

- inverse relation with hospital volume (only 1 NS study)

Threshold volume

High volume hospital >150.

Quality of evidence

- 1) Fitness to support evidence: +++
 - 2) 1 primary study⁶⁹
Origin: 1/1 USA
 - 3) Study period: Not specified
 - 4) Inverse VOA is based on NS primary studies
- GRADE C evidence level**

Halm 2002¹⁷¹

BREAST CANCER SURGERY

<p>Main findings</p> <p><u>5-year mortality:</u></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (only 1 SS study) - inverse relation with surgeon volume (only 1 SS study) 	<p>Threshold volume</p> <p>High volume hospital >149, Low volume hospital <10, High volume surgeon >29, Low volume surgeon <10.</p>	<p>Quality of evidence</p> <p>1) Fitness to support evidence: + 2) 2 primary studies ^{70, 71} Origin: 1/2 USA, 1/2 UK 3) Study period: 1979-1989 4) Inverse VOA is based on SS primary studies <input type="checkbox"/> GRADE C evidence level</p>
<p>Dudley 2000 ¹⁶⁹</p>		
<p>Main findings</p> <p><u>5-year mortality:</u></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (only 1 SS study) 	<p>Threshold volume</p> <p>No threshold available.</p>	<p>Quality of evidence</p> <p>1) Fitness to support evidence: +++ 2) 1 primary study ⁷⁰ Origin: 1/1 USA 3) Study period: Not specified 4) Inverse VOA is based on one SS primary studies <input type="checkbox"/> GRADE C evidence level</p>
<p>NHS 1997 ¹⁸⁴</p>		
<p>Main findings</p> <p><u>5-year mortality:</u></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (only 1 SS study) 	<p>Threshold volume</p> <p>High volume surgeon >50, Low volume surgeon <10.</p>	<p>Quality of evidence</p> <p>1) Fitness to support evidence: ++ 2) 3 primary studies ^{68, 71, 238} Origin: 1/3 USA, 1/3 Italy, 1/3 UK 3) Study period: 1972-1992 4) Inverse VOA is based on one SS primary studies <input type="checkbox"/> GRADE C evidence level</p>
<p>Conclusion on volume - outcome association for breast cancer surgery</p>		
<p>Main findings</p> <p>Limited evidence does not allow a conclusion on the volume-outcome association for breast cancer surgery.</p>	<p>Threshold volume</p> <p>Minimal hospital volume threshold: - lower threshold: 10 breast cancer surgery procedures per annum - upper threshold: 150 breast cancer surgery procedures per annum. These thresholds correspond with the thresholds in the SRs and with the threshold for breast clinics in Belgium i.e. 150 breast cancer cases per year.²³⁹</p>	<p>Quality of evidence</p> <p>Six out of six SRs have Grade C evidence level ^{169-171, 181, 183, 184} Cave! Very few primary studies for each SR.</p>

LUNG CANCER SURGERY

Totality of systematic reviews

Total number of SRs	7 ^{168-171, 181, 183, 184}
Publication date all SRs	1997-2007
Total number of studies included	11 ^{2, 3, 9, 15, 16, 49, 79-83}
Study period all SRs	1983-1999
Outcome variables	In-hospital mortality ^{168-171, 181, 183, 184} ; 30-day mortality ^{181, 183} ; 2-year mortality ¹⁸¹ ; 5-year mortality ¹⁸³ ; Length of stay ¹⁶⁸ .

Chowdury 2007¹⁶⁸

Main findings	Threshold volume	Quality of evidence
<u>Outcome in general (In-hospital mortality or Length of stay):</u> - inverse relation with hospital volume (only 1 SS study) - inverse relation with surgeon volume (only 1 SS study)	High volume hospital range 20 to 100, Low volume hospital <9, High volume surgeon >50, Low volume surgeon range 1 to 5.	1) Fitness to support evidence: + 2) 2 primary studies ^{49, 79} Origin: 2/2 USA 3) Study period: Not specified 4) Inverse VOA is based on SS primary studies <input type="checkbox"/> GRADE C evidence level

Killeen 2005¹⁸³

Main findings	Threshold volume	Quality of evidence
<u>Mortality:</u> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (>75% NS) Number needed to treat (NNT) = 20 to 50 patients for a high-volume provider to prevent 1 death.	High volume hospital range 35 to 66, Low volume hospital range 6 to 23, High volume surgeon >17, Low volume surgeon range 7 to 23.	1) Fitness to support evidence: +++ 2) 9 primary studies ^{2, 3, 9, 15, 49, 79, 80, 82, 83} Origin: 8/9 USA, 1/9 Canada 3) Study period: 1983-1999 4) Inverse VOA is mainly based on a mix of NS and SS primary studies <input type="checkbox"/> GRADE B evidence level

Khuri 2005¹⁸¹

Main findings	Threshold volume	Quality of evidence
<u>Mortality:</u> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (only 1 SS study)	High volume hospital range 35 to 169, Low volume hospital range 1 to 45, High volume surgeon range 17 to 131, Low volume surgeon range 1 to 7.	1) Fitness to support evidence: + 2) 8 primary studies ^{2, 3, 9, 16, 49, 79, 80, 82} Origin: 7/8 USA, 1/8 Canada 3) Study period: 1983-1999 4) Inverse VOA is mainly based on SS primary studies <input type="checkbox"/> GRADE C evidence level

Gandjour 2003¹⁷⁰

LUNG CANCER SURGERY

Main findings

Mortality:

- inverse relation with hospital volume (>75% NS)
- inverse relation with surgeon volume (only 1 NS study)

Threshold volume

- High volume hospital >1,
- High volume surgeon >3.

Quality of evidence

- 1) Fitness to support evidence: +++
 - 2) 3 primary studies^{80, 81, 83}
 - Origin: 3/3 USA
 - 3) Study period: Not specified
 - 4) Inverse VOA is mainly based on NS primary studies
- GRADE C evidence level**

Halm 2002¹⁷¹

Main findings

Mortality:

- inverse relation with hospital volume (mix SS & NS)

Threshold volume

- High volume hospital range 11 to 170,
- Low volume hospital range 5 to 37.

Quality of evidence

- 1) Fitness to support evidence: +
 - 2) 4 primary studies^{49, 80-82}
 - Origin: 4/4 USA
 - 3) Study period: 1983-1997
 - 4) Inverse VOA is mainly based on a mix of NS and SS primary studies
- GRADE C evidence level**

Dudley 2000¹⁶⁹

Main findings

Mortality:

- inverse relation with hospital volume (mix NS & SS)

Threshold volume

- No threshold available.

Quality of evidence

- 1) Fitness to support evidence: +++
 - 2) 2 primary studies^{80, 82}
 - Origin: 2/2 USA
 - 3) Study period: Not specified
 - 4) Inverse VOA is based on a mix of NS and SS primary studies
- GRADE C evidence level**

NHS 1997¹⁸⁴

Main findings

- No high-quality primary studies available.

Threshold volume

- No threshold available.

Quality of evidence

- 1) Fitness to support evidence: ++
- 2) 1 primary studies⁸²
- Origin: 1/1 USA
- 3) Study period: 1983-1986

Conclusion on volume - outcome association for lung cancer surgery

Main findings

- INVERSE relation between:
- hospital volume - mortality

Threshold volume

- Studies differ widely according to the cut-off points used to define low and high volume.

Quality of evidence

- 1 out of 7 SRs has Grade B evidence level¹⁸³
- 5 out of 7 SRs have Grade C evidence level^{168-171, 181}

APPENDIX 9 : EVIDENCE TABLES FOR CARDIOVASCULAR PROCEDURES

CAROTID ENDARTERECTOMY (CEA) AND CAROTID STENTING (CAS)		
Totally of systematic reviews		
Total number of SRs	9 ^{168-171, 175, 181, 182, 184, 186}	
Publication date all SRs	1997-2007	
Total number of studies included	40 ^{2-4, 81, 90-98, 169, 240-265}	
Study period all SRs	1976-2000	
Outcome variables	In-hospital mortality ^{168-170, 175, 181, 182, 184, 186} ; 30-day mortality ^{171, 181, 182} ; Stroke rate ^{175, 181, 182, 186} ; AML rate ¹⁸¹ ; Length of stay ^{168, 181, 182} .	
Killeen 2007 ¹⁸²		
Main findings	Threshold volume	Quality of evidence
<u>In-hospital mortality:</u> - inverse relation with hospital volume (mix SS & NS) - inverse relation with surgeon volume (mix SS & NS) <u>30-day mortality:</u> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (>75% SS) <u>Stroke rate:</u> - inverse relation with hospital volume (mix SS & NS) - inverse relation with surgeon volume (mix SS & NS) <u>Length of stay:</u> - inverse relation with hospital volume (>75% NS) - inverse relation with hospital volume (>75% NS)	High volume hospital range >20 to >164, Low volume hospital range <6 to <100, High volume surgeon range >10 to >50, Low volume surgeon range <1 to <18.	1) Fitness to support evidence: +++ 2) 24 primary studies ^{2, 91, 92, 95, 98, 240, 242, 244-247, 250-253, 255, 257-263, 265} Origin: 22/24 USA, 1/24 Canada, 1/24 Finland 3) Study period: 1976-1999 4) Inverse VOA is mainly based on a mix of SS & NS primary studies <input type="checkbox"/> GRADE B evidence level
Holt 2007 ¹⁷⁵		
Main findings	Threshold volume	Quality of evidence
<u>In-hospital mortality:</u> - inverse relation with hospital volume (mix SS & NS, but pooled effect shows a SS better outcome in high volume hospitals) <u>Stroke rate:</u> - inverse relation with hospital volume (mix SS & NS, but pooled effect shows a SS better outcome in high volume hospitals)	Weighted mean threshold between high volume and low volume hospital of 79 CEA per annum.	1) Fitness to support evidence: +++ 2) 22 primary studies ^{2, 81, 90, 91, 93, 94, 96-98, 169, 244-247, 251-253, 256, 258-260, 263, 265} Origin: Mostly USA 3) Study period: Not specified 4) Inverse VOA is based on a mix of SS & NS primary studies <input type="checkbox"/> GRADE B evidence level
Chowdury 2007 ¹⁶⁸		

CAROTID ENDARTERECTOMY (CEA) AND CAROTID STENTING (CAS)

Main findings	Threshold volume	Quality of evidence
<p><i>Outcome in general (In-hospital mortality or Length of stay):</i></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (mix SS & NS) - inverse relation with surgeon volume (>75% SS) 	<p>High volume hospital range 50 to 100 Low volume hospital range 20 to 44, High volume surgeon range >3 to 175, Low volume surgeon range 1 to 75.</p>	<p>1) Fitness to support evidence: + 2) 6 primary studies ^{91, 92, 242, 251, 256, 262} Origin: 5/6 USA, 1/6 Finland 3) Study period: Not specified 4) Inverse VOA is mainly based on SS primary studies <input type="checkbox"/> GRADE C evidence level</p>
Khuri 2005 ¹⁸¹		
<p>Main findings</p> <p><i>In-hospital mortality:</i></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (mix SS & NS) - inverse relation with surgeon volume (>75% SS) <p><i>30-day mortality:</i></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (>75% SS) <p><i>Stroke rate:</i></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (mix SS & NS) - inverse relation with surgeon volume (mix SS & NS) <p><i>AMI rate:</i></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (mix SS & NS) - inverse relation with surgeon volume (mix SS & NS) <p><i>Length of stay:</i></p> <ul style="list-style-type: none"> - inverse relation (i.e. shorter LOS) with hospital volume (>75% SS) - inverse relation with hospital volume (>75% NS) 	<p>Threshold volume</p> <p>High volume hospital range >50 to >164, Low volume hospital range <5 to <100, High volume surgeon range >=10 to =50, Low volume surgeon range 1 to <18.</p>	<p>Quality of evidence</p> <p>1) Fitness to support evidence: + 2) 23 primary studies ^{2-4, 81, 96, 98, 242-247, 249, 251-254, 256, 260-263, 265} Origin: 20/23 USA, 2/23 Canada, 1/23 Finland 3) Study period: 1979-2000 4) Inverse VOA is based on a mix of SS & NS primary studies <input type="checkbox"/> GRADE C evidence level</p>
Gandjour 2003 ¹⁷⁰		
<p>Main findings</p> <p><i>Mortality:</i></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (>75% SS) 	<p>Threshold volume</p> <p>High volume hospital = 101, High volume surgeon range = 5.</p>	<p>Quality of evidence</p> <p>1) Fitness to support evidence: +++ 2) 8 primary studies ^{97, 244, 247, 251, 252, 256, 259, 265} Origin: 7/8 USA, 1/8 Finland 3) Study period: Not specified 4) Inverse VOA is based on SS primary studies <input type="checkbox"/> GRADE B evidence level</p>
Halm 2002 ¹⁷¹		
<p>Main findings</p> <p><i>Mortality:</i></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (mix SS & NS) - inverse relation with surgeon volume (mix SS & NS) 	<p>Threshold volume</p> <p>High volume hospital median 50 (range 21 to 100), Low volume hospital median 10 (range 5 to 50), High volume surgeon median 30 (range 5 to 50), Low volume surgeon median 8 (range 1 to 30).</p>	<p>Quality of evidence</p> <p>1) Fitness to support evidence: + 2) 19 primary studies ^{81, 92, 242-247, 249, 251-254, 256, 260-263, 265} Origin: 17/19 USA, 1/19 Canada, 1/19 Finland 3) Study period: 1980-1997 4) Inverse VOA is based on a mix of SS & NS primary studies</p>

CAROTID ENDARTERECTOMY (CEA) AND CAROTID STENTING (CAS)

 GRADE C evidence level

Shackley 2000 ¹⁸⁶

Main findings

Mortality:
 - inverse relation with hospital volume (mix SS & NS)
 - inverse relation with surgeon volume (>75% SS)

Stroke rate:
 - inverse relation with hospital volume (mix SS & NS)
 - inverse relation with surgeon volume (>75% SS)

Threshold volume

High volume hospital range >15 to >100,
 Low volume hospital range 1 to <100,
 High volume surgeon range >10 to >50,
 Low volume surgeon range <1 to <21.

Quality of evidence

1) Fitness to support evidence: ++
 2) 17 primary studies ^{240, 244-247, 251-253, 255-258, 260-263, 265}
 Origin: 16/17 USA, 1/17 Finland
 3) Study period: Not specified
 4) Inverse VOA is mainly based on SS primary studies
 GRADE B evidence level

Dudley 2000 ¹⁶⁹

Main findings

Mortality:
 - inverse relation with hospital volume (mix SS & NS)

Threshold volume

Low volume hospital <101.

Quality of evidence

1) Fitness to support evidence: +++
 2) 9 primary studies ^{244-247, 251, 252, 256, 260, 265}
 Origin: 7/9 USA, 1/9 Canada, 1/9 Finland
 3) Study period: Not specified
 4) Inverse VOA is mainly based on a mix of SS and NS primary studies
 GRADE B evidence level

NHS 1997 ¹⁸⁴

Main findings

No high-quality studies available.

Threshold volume

No thresholds for high-quality studies available.

Quality of evidence

1) Fitness to support evidence: ++
 2) 8 primary studies ^{241, 245, 248, 253, 261-264}
 Origin: 8/8 USA
 3) Study period: 1977-1992
 4) Not applicable
 no evidence level

Conclusion on volume - outcome association for CEA and CAS

Main findings

INVERSE relation between:
 - hospital volume - mortality
 - hospital volume - stroke rate
 - surgeon volume - mortality
 - surgeon volume - stroke rate

Threshold volume

Minimal hospital volume threshold = 79 CEA per annum, as calculated by Holt. ¹⁷⁵

Quality of evidence

- 5 out of 8 SRs have Grade B evidence level ^{168-171, 175, 177, 181, 182, 184, 186}
 - 3 out of 8 SRs have Grade C evidence level ^{168-171, 175, 177, 181, 182, 184, 186}

CORONARY ARTERY BYPASS GRAFT (CABG)

Totality of systematic reviews

Total number of SRs	7 ^{168-171, 180, 181, 184}
Publication date all SRs	1997-2007
Total number of studies included	33 ^{2-4, 99-105, 215, 217, 220, 224, 225, 229, 266-282}
Study period all SRs	1972-2001
Outcome variables	In-hospital mortality ^{168-171, 180, 181, 184} ; 30-day mortality ¹⁸¹ ; Length of stay ¹⁶⁸ .

Chowdury 2007¹⁶⁸

Main findings	Threshold volume	Quality of evidence
<p><u>Outcome in general (In-hospital mortality or Length of stay):</u></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (>75% SS) 	<p>High volume hospital range 66 to 600, Low volume hospital range 6 to <200, High volume surgeon = 150, Low volume surgeon = 50.</p>	<p>1) Fitness to support evidence: + 2) 5 primary studies^{99, 100, 266, 271, 279} Origin: 5/5 USA 3) Study period: Not specified 4) Inverse VOA is based on SS primary studies <input type="checkbox"/> GRADE C evidence level</p>

Khuri 2005¹⁸¹

Main findings	Threshold volume	Quality of evidence
<p><u>In-hospital mortality:</u></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (mix SS & NS) - inverse relation with surgeon volume (>75% SS) <p><u>30-day mortality:</u></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (mix SS & NS) - inverse relation with surgeon volume (>75% SS) 	<p>High volume hospital range >350 to >849, Low volume hospital range <100 to =<500, High volume surgeon range >116 to >259, Low volume surgeon range <25 to <116.</p>	<p>1) Fitness to support evidence: + 2) 17 primary studies^{2-4, 101-105, 217, 229, 267, 269-271, 278-280} Origin: 17/17 USA, 1/17 Canada 3) Study period: 1979-2001 4) Inverse VOA is based on a mix of SS & NS primary studies <input type="checkbox"/> GRADE C evidence level</p>

Kalant 2004¹⁸⁰

Main findings	Threshold volume	Quality of evidence
<p><u>Peri-operative mortality:</u></p> <ul style="list-style-type: none"> - the OR values in high volume hospitals relative to low volume hospitals show a continuous increase with time and, for the past 10 years, a clustering about a value of 1.0; - inconclusive results for surgeon volume. <p>The authors conclude that these results indicate that though a VOA was evident during the early years of CABG surgery, its magnitude diminished over time, virtually to zero.</p>	<p>Low volume hospital range 150 to >658, but majority of authors have set the level at or near 200 cases per year. Low volume surgeon cutoff at 200.</p>	<p>1) Fitness to support evidence: + 2) 16 primary studies^{2, 99, 217, 220, 229, 266-269, 271, 272, 274, 276-278, 280} Origin: 15/16 USA, 2/16 Canada 3) Study period: 1972-1999 4) Inverse VOA is based on NS primary studies <input type="checkbox"/> GRADE C evidence level</p>

CORONARY ARTERY BYPASS GRAFT (CABG)

Gandjour 2003 ¹⁷⁰

Main findings

Mortality:

- inverse relation with hospital volume (>75% NS)
- inverse relation with surgeon volume (>75% NS)

Threshold volume

High volume hospital: variable ,
High volume surgeon range = 101.

Quality of evidence

- 1) Fitness to support evidence: +++
 - 2) 3 primary studies ^{271, 279, 280}
 - Origin: 3/3 USA
 - 3) Study period: Not specified
 - 4) Inverse VOA is based on NS primary studies
- GRADE C evidence level**

Halm 2002 ¹⁷¹

Main findings

Mortality:

- inverse relation with hospital volume (>75% SS)
- inverse relation with surgeon volume (>75% SS)

Threshold volume

High volume hospital median 500 (range 96 to 1421),
Low volume hospital median 100 (range 35 to 224),
High volume surgeon median 150 (range 116 to 259),
Low volume surgeon median 55 (range 51 to 116).

Quality of evidence

- 1) Fitness to support evidence: +
 - 2) 9 primary studies ^{217, 229, 267, 269-271, 278-280}
 - Origin: 9/9 USA, 1/9 Canada
 - 3) Study period: 1980-1995
 - 4) Inverse VOA is based on a mix of SS & NS primary studies
- GRADE C evidence level**

Dudley 2000 ¹⁶⁹

Main findings

Mortality:

- inverse relation with hospital volume (>75% SS)

Threshold volume

Low volume hospital <500.

Quality of evidence

- 1) Fitness to support evidence: +++
 - 2) 11 primary studies ^{217, 220, 224, 229, 267, 269, 270, 274, 278, 279, 282}
 - Origin: 11/11 USA, 1/11 Canada
 - 3) Study period: before 1990
 - 4) Inverse VOA is based on SS primary studies
- GRADE B evidence level**

NHS 1997 ¹⁸⁴

Main findings

Mortality:

- inverse relation with hospital volume (mix SS & NS)
- inverse relation with surgeon volume (mix SS & NS)

Threshold volume

Low volume hospital <200.

Quality of evidence

- 1) Fitness to support evidence: ++
 - 2) 18 primary studies ^{215, 217, 220, 225, 229, 266, 267, 269, 271-279, 281}
 - Origin: 18/18 USA
 - 3) Study period: 1972-1993
 - 4) Not applicable
- GRADE C evidence level**

Conclusion on volume - outcome association for CABG

Main findings

Threshold volume

Quality of evidence

CORONARY ARTERY BYPASS GRAFT (CABG)

INVERSE relation between: - hospital volume - mortality - surgeon volume – mortality	Minimal hospital volume threshold = 200 CABG per annum, as found by Kalant. ¹⁸⁰	- 1 out of 7 SRs has Grade B evidence level ¹⁶⁹ - 6 out of 7 SRs have Grade C evidence level ^{168-171, 180, 181, 184}
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HEART VALVE REPLACEMENT OR REPAIR (VALVULOPLASTY)

Totality of systematic reviews

Total number of SRs	1 ¹⁸¹
Publication date all SRs	2005
Total number of studies included	2 ^{2,3}
Study period all SRs	1994-1999
Outcome variables	30-day mortality ¹⁸¹ .

Khuri 2005¹⁸¹

Main findings	Threshold volume	Quality of evidence
<u>30-day mortality:</u> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (>75% SS)	High volume hospital range 163 to 199, Low volume hospital range 43 to 68, High volume surgeon range >42, Low volume surgeon range <22.	1) Fitness to support evidence: + 2) 2 primary studies ^{2,3} Origin: 2/2 USA 3) Study period: 1994-1999 4) Inverse VOA is based on SS primary studies <input type="checkbox"/> GRADE C evidence level

Conclusion on volume - outcome association for heart valve replacement or repair

Main findings	Threshold volume	Quality of evidence
Limited evidence does not allow a conclusion on the VOA for heart valve replacement or repair.	Studies differ widely according to the cut-off points used to define low and high volume.	Only 1 SR with Grade C evidence level. ¹⁸¹

PERCUTANEOUS CORONARY INTERVENTION (PCI)		
Totality of systematic reviews		
Total number of SRs	6 ^{168-171, 177, 184}	
Publication date all SRs	1997-2007	
Total number of studies included	40 ^{108-129, 283-300}	
Study period all SRs	1977-2002	
Outcome variables	In-hospital mortality ^{168-171, 177, 184} ; 30-day mortality ¹⁷⁷ ; AMI rate ^{177, 184} ; Stroke rate ¹⁷⁷ ; CABG rate ^{177, 184} ; Complication rate ¹⁸⁴ ; Length of stay ^{168, 184} .	
Chowdury 2007¹⁶⁸		
Main findings	Threshold volume	Quality of evidence
<u>Outcome in general (In-hospital mortality or Length of stay):</u> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (>75% SS)	High volume hospital range >33 to 600 Low volume hospital range 1 to 200, High volume surgeon range >11 to >50, Low volume surgeon range 1 to <30.	1) Fitness to support evidence: + 2) 10 primary studies ^{122, 124, 128, 283, 286, 290, 291, 294, 295, 298} Origin: 10/10 USA, 1/10 Canada 3) Study period: Not specified 4) Inverse VOA is based on SS primary studies <input type="checkbox"/> GRADE C evidence level
IQWiG 2006¹⁷⁷		
Main findings	Threshold volume	Quality of evidence
<u>Mortality:</u> distinction between: * <u>PCI for mixed indications</u> (i.e. primary and elective) - Conflicting results for hospital volume which means that there are primary studies that indicate an inverse relation with hospital volume and other studies that indicate a direct relation with hospital volume - Conflicting results for surgeon volume * <u>Primary PCI</u> (i.e. immediately after the onset of AMI) - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (mix SS & NS) <u>AMI rate:</u> - Direct relation with hospital volume (>75% NS). <u>Emergency CABG rate:</u> - Conflicting results for hospital volume - Inverse relation with surgeon volume (>75% SS)	High volume hospital range 160 to 1000, Low volume hospital range 1 to 600, High volume surgeon range 10 to 140, Low volume surgeon range 1 to 125.	1) Fitness to support evidence: +++ 2) 17 primary studies ^{108-122, 124, 129} Origin: 14/17 USA, 1/17 Italy, 1/17 Japan, 1/17 Germany 3) Study period: 1994-2002 4) Conflicting results on VOA <input type="checkbox"/> GRADE B evidence level
Gandjour 2003¹⁷⁰		

PERCUTANEOUS CORONARY INTERVENTION (PCI)

Main findings	Threshold volume	Quality of evidence
<p><u>Mortality:</u></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (>75% SS) - conflicting results for surgeon volume 	<p>High volume hospital range 200 to 400, High volume surgeon range 10 to 163.</p>	<p>1) Fitness to support evidence: +++ 2) 17 primary studies ^{123-127, 129, 283-288, 290, 291, 296, 298, 300} Origin: 16/17 USA, 1/17 Canada, 1/17 Germany 3) Study period: Not specified 4) Inverse relation with hospital volume is based on SS primary studies; conflicting results for surgeon volume <input type="checkbox"/> GRADE B evidence level</p>
Halm 2002 ¹⁷¹		
Main findings	Threshold volume	Quality of evidence
<p><u>Mortality:</u></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (mix SS & NS) - inverse relation with surgeon volume (mix SS & NS) 	<p>High volume hospital median 400 (range 160 to 1000), Low volume hospital median 200 (range 46 to 200), High volume surgeon median 138 (range 50 to 250), Low volume surgeon median 75 (range 25 to 85).</p>	<p>1) Fitness to support evidence: + 2) 11 primary studies ^{126, 129, 285-287, 291-294, 296, 297} Origin: 11/11 USA 3) Study period: 1989-1997 4) Inverse VOA is based on a mix of SS & NS primary studies <input type="checkbox"/> GRADE C evidence level</p>
Dudley 2000 ¹⁶⁹		
Main findings	Threshold volume	Quality of evidence
<p><u>Mortality:</u></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (>75% SS) 	<p>Low volume hospital <400.</p>	<p>1) Fitness to support evidence: +++ 2) 7 primary studies ^{121, 284-287, 294, 297} Origin: 7/7 USA, 1/7 Canada 3) Study period: Not specified 4) Inverse VOA is based on SS primary studies <input type="checkbox"/> GRADE B evidence level</p>
NHS 1997 ¹⁸⁴		
Main findings	Threshold volume	Quality of evidence
<p><u>Mortality:</u></p> <ul style="list-style-type: none"> - no relation with hospital volume - no relation with surgeon volume <p><u>AMI rate:</u></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (>75% SS) <p><u>Emergency CABG rate:</u></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (>75% SS) <p><u>Complication rate:</u></p> <ul style="list-style-type: none"> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (>75% SS) <p><u>Length of stay:</u></p> <ul style="list-style-type: none"> - inverse relation (i.e. shorter LOS) with surgeon volume (>75% SS) 	<p>High volume hospital >400, Low volume hospital <200, High volume surgeon <50, Low volume surgeon <50.</p>	<p>1) Fitness to support evidence: ++ 2) 6 primary studies ^{286, 289, 290, 294, 298, 299} Origin: 6/6 USA, 1/6 Canada 3) Study period: 1977-1994 4) Mainly inverse relation with outcome, based on SS studies <input type="checkbox"/> GRADE C evidence level</p>

PERCUTANEOUS CORONARY INTERVENTION (PCI)

Conclusion on volume - outcome association for PCI

Main findings

CONFLICTING results (i.e. mix of inverse and direct relation) for:

- hospital volume - mortality for PCI for mixed indications
- surgeon volume – mortality for PCI for mixed indications
- hospital volume – emergency CABG rate

INVERSE relation between:

- hospital volume – mortality for primary PCI
- surgeon volume – mortality for primary PCI
- surgeon volume - emergency CABG rate

Threshold volume

Minimal hospital volume threshold:

- lower threshold: 200 PCI per annum
- upper threshold: 400 PCI per annum.

These thresholds correspond with the majority of the thresholds in the SRs, and with those issued by the US Agency for Healthcare Research and Quality, the US Leapfrog Group and the American College of Cardiology/American Heart Association.^{200, 201, 301}

Quality of evidence

- 3 out of 6 SRs have Grade B evidence level^{168-171, 177, 184}
- 3 out of 6 SRs have Grade C evidence level^{168-171, 177, 184}

APPENDIX 10 : EVIDENCE TABLES FOR ORTHOPAEDIC PROCEDURES

TOTAL HIP REPLACEMENT/ARTHROPLASTY (THR)		
Totally of systematic reviews		
Total number of SRs	6 ^{168-171, 181, 184}	
Publication date all SRs	1997-2007	
Total number of studies included	20 ^{81, 134-143, 215, 220, 224, 225, 229, 241, 267, 276, 302}	
Study period all SRs	1972-1997	
Outcome variables	In-hospital mortality ^{168-171, 180, 181, 184} ; In-hospital complications ^{168-171, 180, 181, 184} ; Mortality at 60 days, 90 days, 1 year or 3 years ^{181, 184} ; THR failure/revision rate at 18 or 48 months ¹⁸¹ ; Dislocation rate at 90 days ¹⁸¹ ; Deep wound infection rate at 90 days, 1 year or 3 years ¹⁸¹ ; Pulmonary embolism rate at 90 days ¹⁸¹ ; In-hospital complication rate ¹⁸¹ ; Length of stay ^{168, 184} .	
Chowdury 2007¹⁶⁸		
Main findings	Threshold volume	Quality of evidence
<u>Outcome in general (In-hospital mortality or Length of stay):</u> - inverse relation with surgeon volume (mix SS & NS)	High volume surgeon >32, Low volume surgeon <10.	1) Fitness to support evidence: + 2) 2 primary studies ^{137, 142} Origin: 2/2 USA 3) Study period: Not specified 4) Inverse VOA is based on mix of SS & NS primary studies <input type="checkbox"/> GRADE C evidence level
Khuri 2005¹⁸¹		
Main findings	Threshold volume	Quality of evidence
<u>In-hospital mortality:</u> - no relation with hospital volume - no relation with surgeon volume <u>In-hospital complications</u> (without specification on which complications): - no relation with hospital volume - no relation with surgeon volume <u>90-day mortality:</u> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (>75% NS) <u>THR failure rate:</u> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (>75% SS) <u>90-day dislocation rate:</u> - inverse relation with hospital volume (>75% SS)	High volume hospital range 10 to 100, Low volume hospital range 10 to 25, High volume surgeon range 12 to 50, Low volume surgeon range 5 to 9.	1) Fitness to support evidence: + 2) 4 primary studies ^{134-136, 141} Origin: 3/4 USA, 1/4 Canada 3) Study period: 1992-1996 4) Inverse VOA is mainly based on SS primary studies <input type="checkbox"/> GRADE C evidence level

TOTAL HIP REPLACEMENT/ARTHROPLASTY (THR)

- inverse relation with surgeon volume (>75% SS)
- 90-day deep wound infection rate
- inverse relation with hospital volume (mix SS & NS)
- inverse relation with surgeon volume (mix SS & NS)

Gandjour 2003 ¹⁷⁰

Main findings

Mortality:

- Conflicting results for hospital volume which means that there are primary studies that indicate an inverse relation with hospital volume (NS) and other studies that indicate a direct relation with hospital volume (NS)
- inverse relation with surgeon volume (mix SS & NS)

Threshold volume

High volume hospital range 10 to 108 ,
High volume surgeon range 28 to 100.

Quality of evidence

- 1) Fitness to support evidence: +++
 - 2) 4 primary studies ^{81, 140-142}
 - Origin: 3/4 USA, 1/4 Canada
 - 3) Study period: Not specified
 - 4) Inverse VOA is based on a mix of SS & NS primary studies
- GRADE C evidence level**

Halm 2002 ¹⁷¹

Main findings

Mortality:

- inverse relation with hospital volume (mix SS & NS)
- inverse relation with surgeon volume (mix SS & NS)

Threshold volume

High volume hospital median 100 (range 15 to 213),
Low volume hospital median 16 (range 6 to 42),
High volume surgeon median 27 (range 10 to 100),
Low volume surgeon median 9 (range 2 to 10).

Quality of evidence

- 1) Fitness to support evidence: +
 - 2) 8 primary studies ^{81, 139-143, 229, 267}
 - Origin: 6/8 USA, 1/8 Canada, 1/8 Norway
 - 3) Study period: 1980-1997
 - 4) Inverse VOA is based on a mix of SS & NS primary studies
- GRADE C evidence level**

Dudley 2000 ¹⁶⁹

Main findings

Mortality:

- inverse relation with hospital volume (mix SS & NS)

Threshold volume

No threshold available.

Quality of evidence

- 1) Fitness to support evidence: +++
 - 2) 8 primary studies ^{138, 140, 142, 143, 220, 224, 225, 267}
 - Origin: 8/8 USA
 - 3) Study period: Not specified
 - 4) Inverse VOA is based on a mix of SS & NS primary studies
- GRADE B evidence level**

NHS 1997 ¹⁸⁴

Main findings

No high-quality study available.

Threshold volume

No threshold available.

Quality of evidence

- 1) Fitness to support evidence: ++
 - 2) 9 primary studies ^{142, 215, 220, 225, 229, 241, 267, 276, 302}
 - Origin: 9/9 USA
 - 3) Study period: 1972-1992
 - 4) Not applicable
- no GRADE evidence level**

TOTAL HIP REPLACEMENT/ARTHROPLASTY (THR)

Conclusion on volume - outcome association for total hip replacement (THR)

Main findings	Threshold volume	Quality of evidence
CONFLICTING results (i.e. mix of inverse, direct and no relation) for: - hospital volume – in-hospital mortality	Minimal hospital volume threshold: - lower threshold: 10 THR per annum - upper threshold: 100 THR per annum. These thresholds correspond with the majority of the thresholds in the SRs.	- 1 out of 5 SRs has Grade B evidence level ¹⁶⁹ - 4 out of 5 SRs have Grade C evidence level ^{168-171, 180, 181, 184} Cave! Very few primary studies for each SR. Only 1 SR analyzed outcome measures other than mortality. ¹⁸¹

TOTAL KNEE REPLACEMENT/ARTHROPLASTY (TKR)

Totality of systematic reviews

Total number of SRs	7 ^{168-171, 181, 184, 188}
Publication date all SRs	1997-2007
Total number of studies included	16 ^{138, 142-155, 215}
Study period all SRs	1984-2000
Outcome variables	In-hospital mortality ^{168-171, 181, 184, 188} ; Mortality at 90 days ^{181, 188} ; Revision rate at 1 or 3 years ¹⁸¹ ; Deep wound infection rate in-hospital or at 90 days ^{181, 188} ; Pulmonary embolism rate in-hospital or at 90 days ¹⁸¹ ; AMI rate at 90 days ¹⁸¹ ; Pneumonia with hospitalization at 90 days ¹⁸¹ ; Deep venous thrombosis rate in-hospital ^{181, 188} ; In-hospital complication rate ^{181, 184, 188} ; Length of stay ^{168, 181, 184, 188} .

Chowdury 2007 ¹⁶⁸

Main findings	Threshold volume	Quality of evidence
<u>Outcome in general (In-hospital mortality or Length of stay):</u> - inverse relation with surgeon volume (>75% SS)	Low volume surgeon <10.	1) Fitness to support evidence: + 2) 1 primary study ¹⁴² Origin: USA 3) Study period: 1992 4) Inverse VOA is based on SS primary study <input type="checkbox"/> GRADE C evidence level

Khuri 2005 ¹⁸¹

Main findings	Threshold volume	Quality of evidence
<u>In-hospital mortality:</u> - inverse relation with hospital volume (>75% SS) - inverse relation with surgeon volume (>75% SS) <u>90-day mortality:</u>	High volume hospital range 113 to 250, Low volume hospital range 25 to 85, High volume surgeon range 42 to 60, Low volume surgeon range 12 to 14.	1) Fitness to support evidence: + 2) 3 primary studies ¹⁴⁶⁻¹⁴⁸ Origin: 2/3 USA, 1/3 Canada 3) Study period: 1993-2000

TOTAL KNEE REPLACEMENT/ARTHROPLASTY (TKR)

- inverse relation with hospital volume (mix SS & NS)

Revision rate:

- inverse relation with hospital volume (>75% SS)

Complication rate:

- inverse relation with hospital volume (>75% SS)

- inverse relation with surgeon volume (>75% SS)

Length of stay:

- inverse relation with hospital volume (>75% SS)

- inverse relation with surgeon volume (>75% SS)

4) Inverse VOA is mainly based on SS primary studies

GRADE C evidence level

Stengel 2004 ¹⁸⁸

Main findings

In-hospital mortality:

- inverse relation with hospital volume (>75% SS)

90-days mortality:

- inverse relation with hospital volume (>75% NS)

Complication rate:

- direct relation with hospital volume i.e. less complications in low volume hospitals (>75% NS)

Infection rate:

- inverse relation with hospital volume (>75% NS)

Deep venous thrombosis rate:

- inverse relation with hospital volume (>75% SS)

Threshold volume

High volume hospital range 42 to 180 ,
High volume surgeon range 14 to 50.

Quality of evidence

1) Fitness to support evidence: ++

2) 13 primary studies of which 5 were suitable for meta-analysis ^{138, 142-146, 148, 150-155}

Origin: 11/13USA, 2/13 Canada

3) Study period: 1984-1999

4) Inverse VOA is based on a mix of SS & NS primary studies

GRADE B evidence level

Gandjour 2003 ¹⁷⁰

Main findings

Mortality:

- inverse relation with hospital volume (mix SS & NS)

Threshold volume

High volume hospital range 10 to 107.

Quality of evidence

1) Fitness to support evidence: +++

2) 2 primary studies ^{142, 155}

Origin: 2/2 USA

3) Study period: 1985-1992

4) Inverse VOA is based on a mix of SS & NS primary studies

GRADE C evidence level

Halm 2002 ¹⁷¹

Main findings

Mortality:

- inverse relation with hospital volume (>75% SS)

Threshold volume

High volume hospital = 200,
Low volume hospital = 25.

Quality of evidence

1) Fitness to support evidence: +

2) 1 primary study ¹⁶⁰

Origin: USA

3) Study period: 1993-1994

4) Inverse VOA is based on SS primary studies

GRADE C evidence level

Dudley 2000 ¹⁶⁹

TOTAL KNEE REPLACEMENT/ARTHROPLASTY (TKR)

Main findings	Threshold volume	Quality of evidence
<p><u>Mortality:</u> - inverse relation with hospital volume (mix SS & NS)</p>	No threshold available.	<p>1) Fitness to support evidence: +++ 2) 3 primary studies^{138, 142, 143} Origin: 3/3 USA 3) Study period: Not specified 4) Inverse VOA is based on a mix of SS & NS primary studies <input type="checkbox"/> GRADE C evidence level</p>

NHS 1997¹⁸⁴

Main findings	Threshold volume	Quality of evidence
<p><u>Post-operative complication rate:</u> - inverse relation with hospital volume (>75% SS) <u>Length of stay:</u> - inverse relation (i.e. shorter LOS) with hospital volume (>75% SS)</p>	No threshold available.	<p>1) Fitness to support evidence: ++ 2) 3 primary studies^{142, 149, 215} Origin: 3/3 USA 3) Study period: 1985-1992 4) Inverse VOA is based on SS primary studies <input type="checkbox"/> GRADE C evidence level</p>

Conclusion on volume - outcome association for total knee replacement (TKR)

Main findings	Threshold volume	Quality of evidence
<p>INVERSE relation between: - hospital volume - mortality CONFLICTING results (i.e. mix of inverse and direct relation) for: - hospital volume – post-operative complication rate</p>	<p>Minimal hospital volume threshold: - lower threshold: 10 TKR per annum - upper threshold: 100 TKR per annum. These thresholds correspond with the majority of the thresholds in the SRs.</p>	<p>- 1 out of 7 SRs has Grade B evidence level^{168-171, 181, 184, 188} - 6 out of 7 SRs have Grade C evidence level^{168-171, 181, 184, 188}</p>

HIP FRACTURE SURGERY

Totality of systematic reviews

Total number of SRs	3 ^{170, 171, 184}
Publication date all SRs	1997-2003
Total number of studies included	8 ^{143, 156-158, 215, 216, 225, 241}
Study period all SRs	1972-1994
Outcome variables	In-hospital mortality ^{170, 171, 184} ; Length of stay ¹⁸⁴ .

Gandjour 2003¹⁷⁰

HIP FRACTURE SURGERY

Main findings

Mortality:
- inverse relation with hospital volume (mix SS & NS)

Threshold volume

High volume hospital >16.

Quality of evidence

- 1) Fitness to support evidence: +++
 - 2) 2 primary studies ^{156, 158}
 - Origin: 1/2 Germany, 1/2 Canada
 - 3) Study period: Not specified
 - 4) Inverse VOA is based on a mix of SS & NS primary studies
- GRADE C evidence level**

Halm 2002 ¹⁷¹

Main findings

Mortality:
- inverse relation with hospital volume (>75% SS)

Threshold volume

High volume hospital range 73 to 200,
Low volume hospital range 25 to 32.

Quality of evidence

- 1) Fitness to support evidence: +
 - 2) 2 primary studies ^{143, 156}
 - Origin: 1/2 USA, 1/2 Canada
 - 3) Study period: 1990-1994
 - 4) Inverse VOA is based on SS primary studies
- GRADE C evidence level**

NHS 1997 ¹⁸⁴

Main findings

In-hospital mortality:
- inverse relation with hospital volume (>75% SS)

Threshold volume

No threshold available.

Quality of evidence

- 1) Fitness to support evidence: ++
 - 2) 5 primary studies ^{157, 215, 216, 225, 241}
 - Origin: 5/5 USA
 - 3) Study period: 1972-1990
 - 4) Inverse VOA is based on SS primary studies
- GRADE C evidence level**

Conclusion on volume - outcome association for hip fracture surgery

Main findings

INVERSE relation between:
- hospital volume - mortality

Threshold volume

Threshold not possible.

Quality of evidence

- 3 out of 3 SRs have Grade C evidence level ^{170, 171, 184}
Cave!
Very few primary studies for each SR.

Supplement Chapter III – Critical review of methods to assess the volume outcome relationship

APPENDIX 11 : SEARCH STRATEGY

Books: Two books were identified from Amazon:

1. Hospital Volume, Physician Volume, and Patient Outcomes: Assessing the Evidence (Paperback) by Harold S. Luft, Deborah W. Garnick, David H. Mark, Stephen J. McPhee.³⁰³
2. Volume-outcome and Its Impact on U.S. Health Care Markets (Gesundheitsoekonomische Beitrage) (Paperback) by Harald Seider.³⁰⁴

Database	Medline
Host	Pubmed
Date of search	17th October 2007
Years covered	No time limit
Search Strategy	In Chapter 3
Language restrictions	None

Results from specific searches:

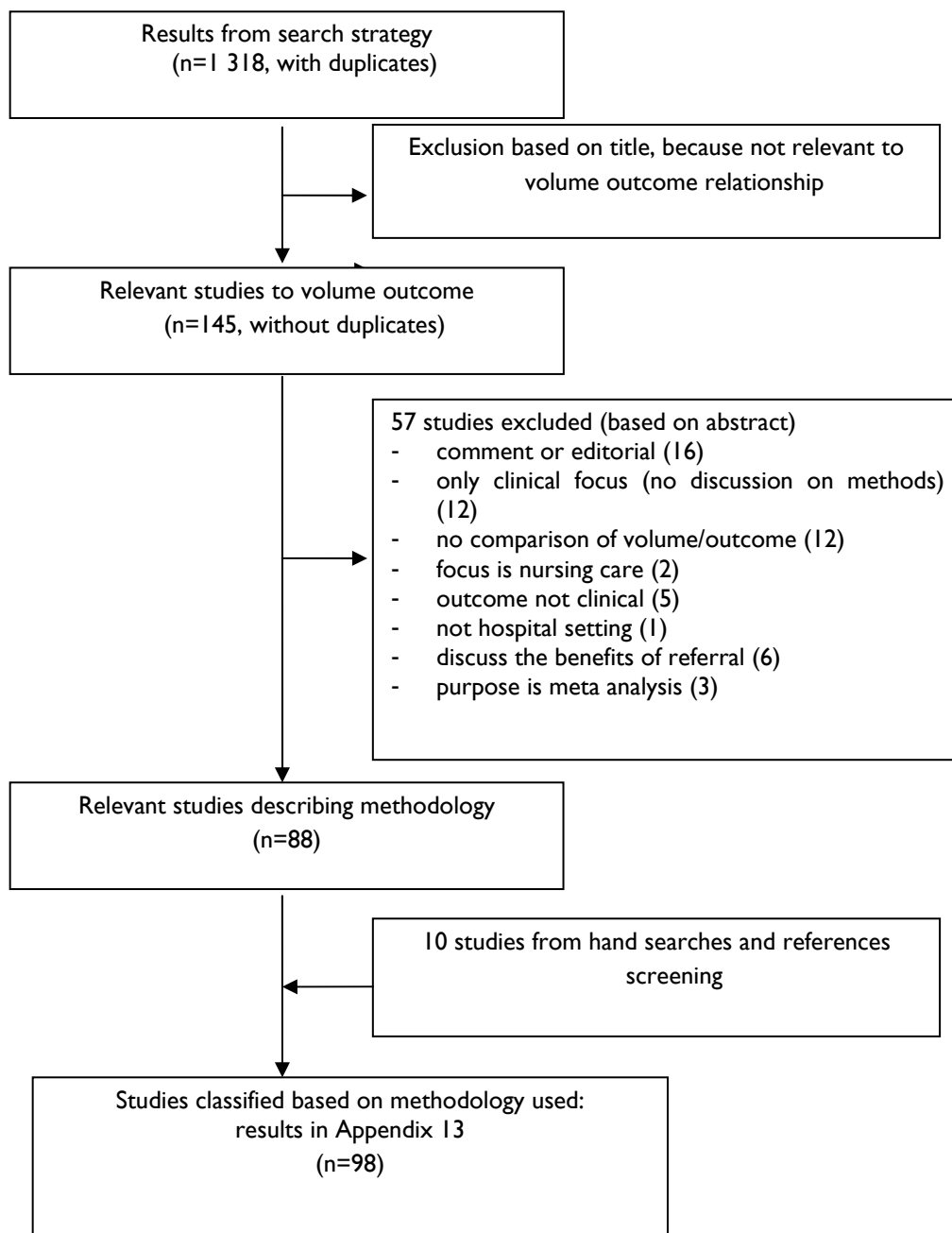
#	Specific Searches	Hits Medline	Relevant to volume outcome	With removal of duplicates
#4	statistics (reviews only) (MESH)	227	20	145
#7	case mix (MESH)	32	30	
#11	cluster (MESH)	56	4	
#48	causality (MESH)	368	66	
#49	longitudinal (MESH)	468	25	
#56	instrumental (text)	27	3	
#74	threshold (text)	125	22	
#77	selective referral (text)	15	14	

The whole search strategy is given in the table below (in green #1, the initial search strategy from Appendix I without the restriction to reviews and meta analyses, in yellow #46 a simplified version of it, removing “frequency” or “quantity”.

Search	Most Recent Queries	Time	Result
#77	Search #1 AND "selective referral"	07:18:13	15
#76	Select 23 document(s)	07:17:10	23
#74	Search #46 AND threshold	07:16:45	125
#72	Select 23 document(s)	07:06:19	23
#56	Search #1 AND INSTRUMENTAL	07:05:58	27
#71	Select 20 document(s)	06:55:00	20
#4	Search #1 AND #3	06:54:38	7452
#70	Search #1 AND methodology	06:45:12	4202
#69	Search #46 AND (#66 OR cutoff OR cut-off)	06:44:42	122
#68	Search #46 AND #66	06:42:25	1
#64	Search #1 AND threshold	06:41:47	585
#67	Search #1 AND #66	06:41:01	3
#66	Search "Threshold Limit Values"[Mesh]	06:40:26	288

#55	Select 25 document(s)	06:04:41	25
#49	Search #46 AND #3 AND #26	06:04:16	466
#54	Select 66 document(s)	05:40:28	66
#48	Search #46 AND #3 AND #22	05:39:47	368
#51	Select 1 document(s)	05:24:38	1
#47	Search #46 AND #3	05:13:22	2845
#46	Search (volume[Title] NOT lung volume[Title] NOT "Respiratory Function Tests"[Mesh] NOT "Cardiac Volume"[Mesh] NOT "Blood Volume"[Mesh]) AND ("Outcome Assessment (Health Care)"[Mesh] OR outcome[Title] OR outcomes[Title] OR regionalization[Title] OR "Quality Indicators, Health Care/statistics and numerical data"[Mesh] OR "Quality Indicators, Health Care/utilization"[Mesh] OR "Health Care Quality, Access, and Evaluation"[Mesh] OR "Length of Stay/statistics and numerical data"[Mesh] OR "Recovery of Function"[Mesh] OR "Intraoperative Complications"[Mesh] OR "complications"[Subheading] OR "Hospital Mortality"[Mesh] OR "Fatal Outcome"[Mesh] OR "Survival Rate"[Mesh] OR "Utilization Review"[Mesh] OR "Health Resources"[Mesh]) AND "humans"[MeSH Terms]	05:12:28	6512
#1	Search (volume[Title] OR frequency[Title] OR quantity[Title] OR case load[Title] NOT lung volume[Title] NOT "Respiratory Function Tests"[Mesh] NOT "Cardiac Volume"[Mesh] NOT "Blood Volume"[Mesh]) AND ("Outcome Assessment (Health Care)"[Mesh] OR outcome[Title] OR outcomes[Title] OR regionalization[Title] OR "Quality Indicators, Health Care/statistics and numerical data"[Mesh] OR "Quality Indicators, Health Care/utilization"[Mesh] OR "Health Care Quality, Access, and Evaluation"[Mesh] OR "Length of Stay/statistics and numerical data"[Mesh] OR "Recovery of Function"[Mesh] OR "Intraoperative Complications"[Mesh] OR "complications"[Subheading] OR "Hospital Mortality"[Mesh] OR "Fatal Outcome"[Mesh] OR "Survival Rate"[Mesh] OR "Utilization Review"[Mesh] OR "Health Resources"[Mesh]) AND "humans"[MeSH Terms]	05:11:23	19341
#23	Search #4 AND #22	05:10:30	1593
#45	Select 31 document(s)	05:08:41	31
#7	Search #4 AND #6	05:04:03	32
#43	Select 4 document(s)	05:02:14	4
#11	Search #4 AND #10	05:00:46	56
#41	Select 30 document(s)	04:52:38	30
#39	Search #4 AND (#6 OR #10 OR #22 OR #26)	04:41:37	2430
#27	Search #4 AND #26	04:25:09	1094
#26	Search "Longitudinal Studies"[Mesh]	04:24:31	574541
#22	Search "Causality"[Mesh]	04:21:41	330037
#10	Search "Cluster Analysis"[Mesh]	04:16:32	16374
#6	Search ("Diagnosis-Related Groups"[Mesh] OR "Risk Adjustment"[Mesh])	04:09:00	9298
#3	Search "Statistics"[Mesh]	04:07:41	1177704

APPENDIX 12 : GRAPHICAL FLOW OF SELECTION OF ARTICLES



APPENDIX 13 : CLASSIFICATION OF STATISTICAL METHODS USED TO ANALYZE THE VOLUME OUTCOME RELATIONSHIP

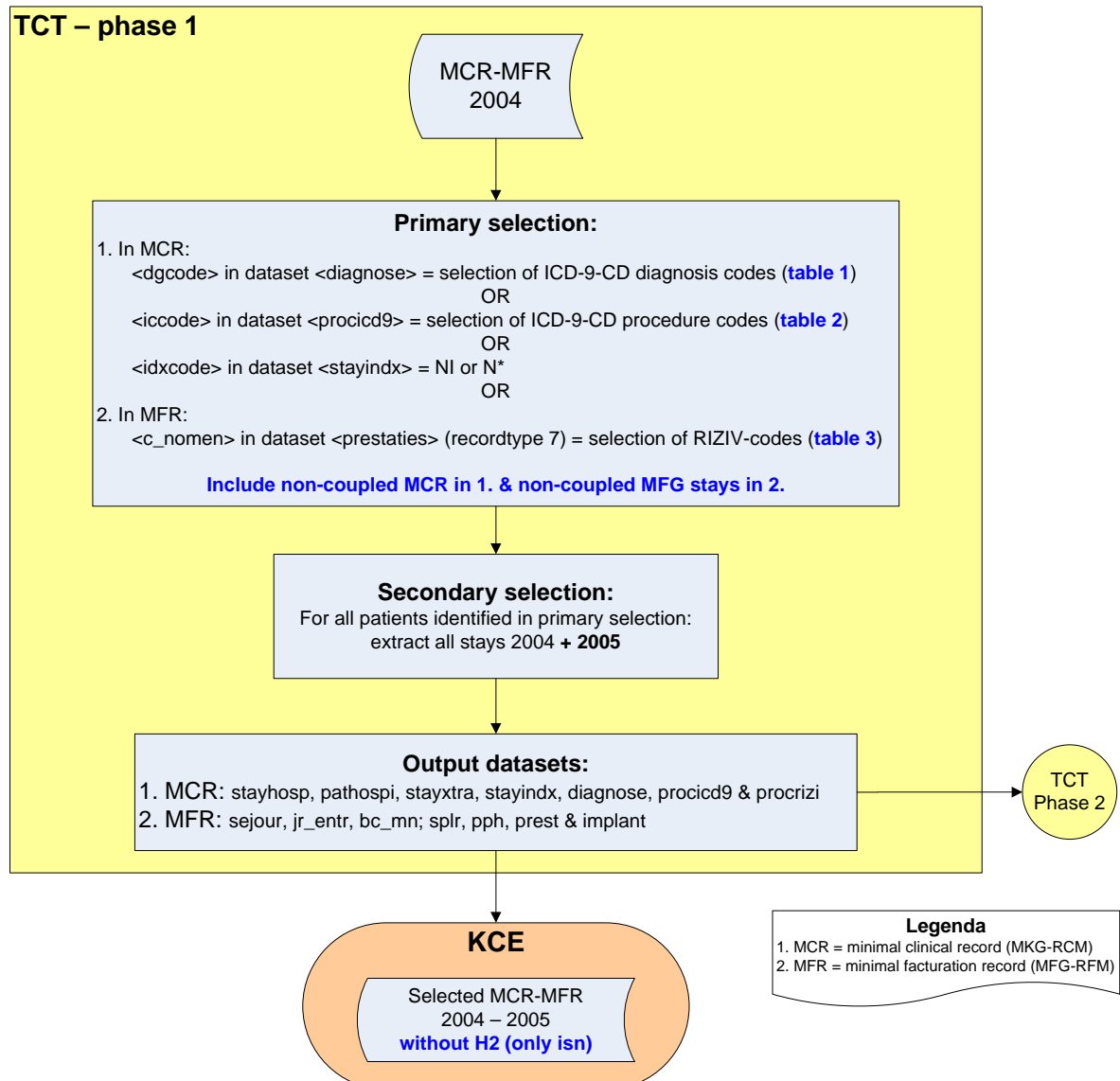
Statistical Method		Author, year and reference	N refs
CROSS SECTIONAL DESIGN			
Graphical presentation	Funnel plots	Spiegelhalter, 2005 ³⁰⁵	1
Group by volume and compare outcomes, with risk adjustments		Choti, 1998 ³⁰⁶ Freixinet, 2006 ⁸⁴ Gouma, 2000 ³⁵ Hannan, 1997 ²⁸⁵ Kastrati, 1998 ²⁸⁸ Mustafa, 2005 ³⁰⁷ Peck, 2001 ⁹¹ Shook, 1996 ²⁹⁸ Simunovic, 2000 ²³⁵ Solomon, 1996 ³⁰⁸ Taylor, 1997 ¹⁴³ Tepas, 1998 ³⁰⁹ Vakili, 2001 ¹²² Tjarda van Heek, 2005 ¹⁸⁹ Zacharias 2005 ³¹⁰ Courcoulas, 2003 ³¹¹ Khuri, 2005 ³¹²	17
Regression methods	Logistic regression, volume categorized	Axelrod, 2004 ³¹³ Cooper, 2000 ³¹⁴ Cowan, 2003 ³¹⁵ Dimick, 2003 ³¹⁶ Dimick, 2003 ⁴⁷ Dimick, 2002 ³¹⁷ Glance, 2003 ¹⁰² Gutierrez, 2007 ³¹⁸ Hannan, 1998 ³¹⁹ Hannan, 2005 ¹¹⁰ Heller, 2007 ³²⁰ Holt, 2007 ³²¹ Iapichino, 2004 ³²² Jain, 2004 ³²³ Jollis, 1997 ²⁸⁷ Katz, 2007 ³²⁴ Kimmel, 1995 ²⁹⁰ Lee, 2006 ³²⁵ Manheim, 1998 ²⁵⁶ Marrie, 2003 ³²⁶ McGrath, 1998 ²⁹³ Migliore, 2007 ²⁴ Moscucci, 2005 ¹¹¹ Mulwijk, 2007 ³²⁷ Rouvelas, 2007 ²⁵ Simunovic, 1999 ²¹⁰ Smink, 2004 ³²⁸ Smith, 2007 ³²⁹ Smith, 2004 ³³⁰ Teig, 2007 ³³¹ Thompson, 2007 ²⁹ Tracy, 2006 ³³²	42

Statistical Method		Author, year and reference	N refs
		Tucker, 2002 ³³³ Weller, 2006 ³³⁴ Damhuis, 2002 ³³⁵ Allareddy, 2007 ³³⁶ Urbach, 2004 ³³⁷ Hannan, 1989 ²¹⁷ Begg, 1998 ⁸⁰ Birkmeyer, 2003 ³ Birkmeyer, 2006 ³³⁸ Gammie, 2007 ¹⁰⁶	
	Logistic regression, volume continuous	Bazzani, 2007 ³³⁹ Blatier, 2001 ³⁴⁰ Peterson, 2004 ¹⁰⁴ Wen, 1996 ³⁴¹ Eckstein, 2007 ³⁴² Wetzel ³⁴³ Christian, 2003 ⁴ Spiegelhalter, 2002 ³⁴⁴	8
	Cox regression (survival analysis), volume categorical	Durairaj, 2005 ³⁴⁵ Fang, 2006 ³⁴⁶ Hosenpud, 1994 ¹³⁰ Ioka, 2005 ³⁴⁷ Meyerhardt, 2003 ⁵⁵ Meyerhardt, 2004 ²³³ Roohan, 1998 ⁷⁰ Schurman, 1999 ³⁴⁸ de Noronha, 2003 ³⁴⁹	9
	Poisson regression	Harmon, 1999 ²¹⁸ Shroyer, 1996 ²⁷⁹	2
Specific to correlation coefficient		Betensky, 2006 ³⁵⁰	1
Specific to clustering methods		Panageas, 2003 ³⁵¹ Panageas, 2007 ³⁵² Urbach, 2005 ⁸⁹	3
Simultaneous equations models		Luft, 1980 ³⁵³ Luft, 1987 ²²⁴	2
Instrumental variables		Tsai, 2006 ³⁵⁴ Gowrisankaran G., 2004 ³⁵⁵ Hughes, 1988 ¹⁵⁷ Picone, 2005 ³⁵⁶ Marcin, 2005 ³⁵⁷	5
LONGITUDINAL DESIGN			
Hospital fixed effects ?		Farley, 1992 ²⁶⁷ Hamilton, 1998 ¹⁵⁶ Hannan, 1992 ³⁵⁸ Hannan, 1995 ²⁷¹ Hamilton, 1997 ³⁵⁹	5

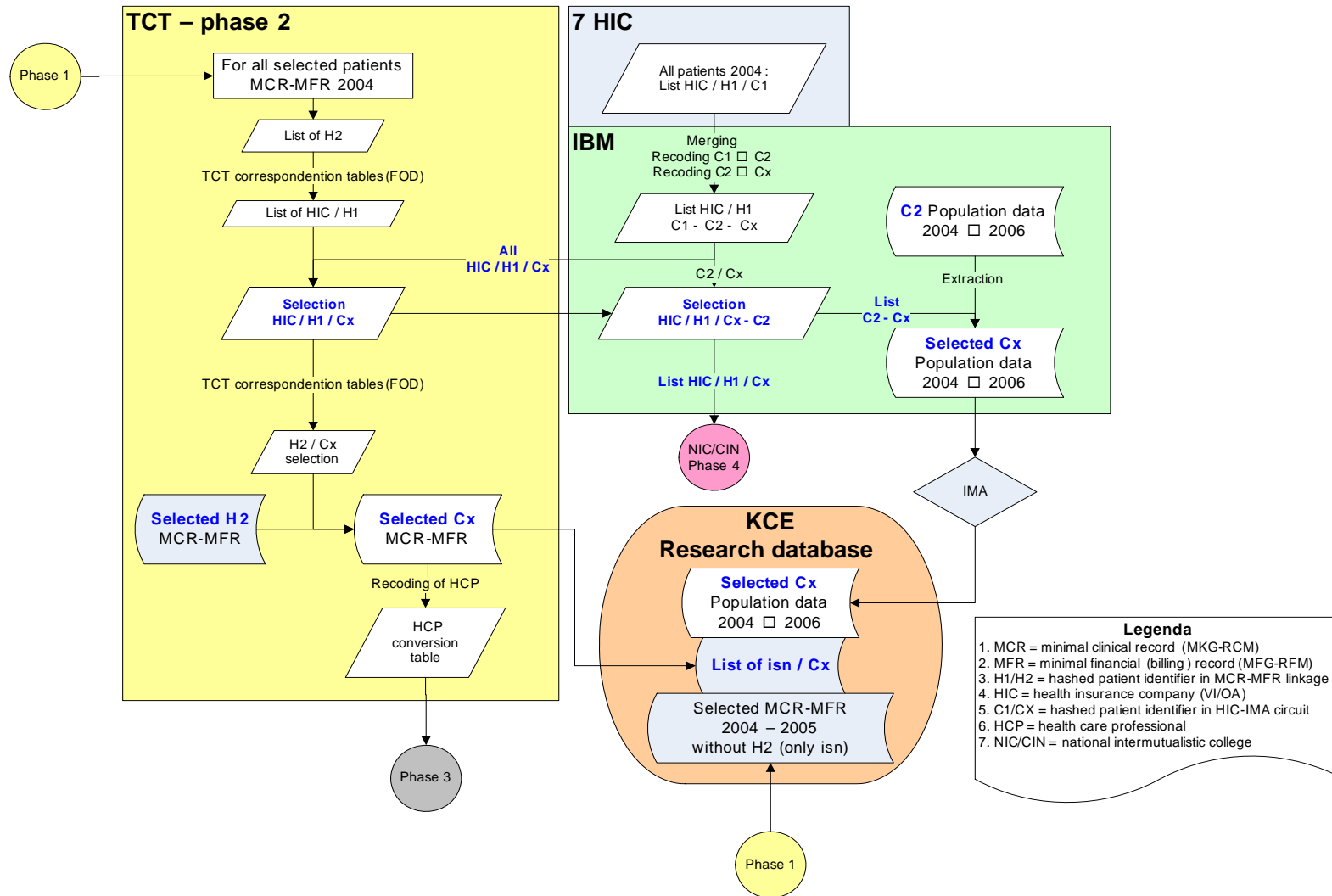
Supplement Chapter IV – Methods applied for the analyses

APPENDIX 14 : LINKING OF MCD-MFD, IMA-AIM DATA AND BCR IN FOUR PHASES

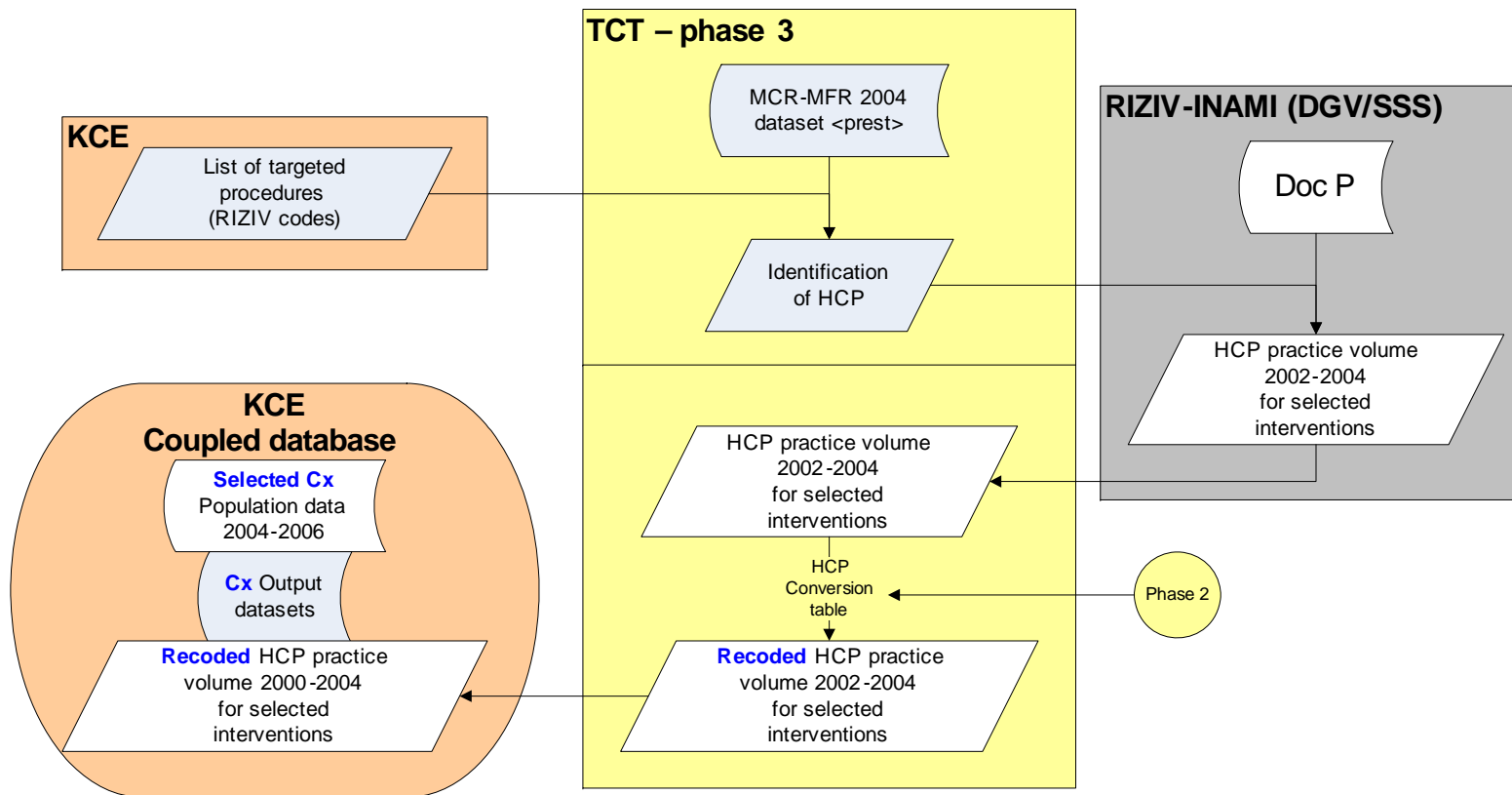
Phase I - Selection



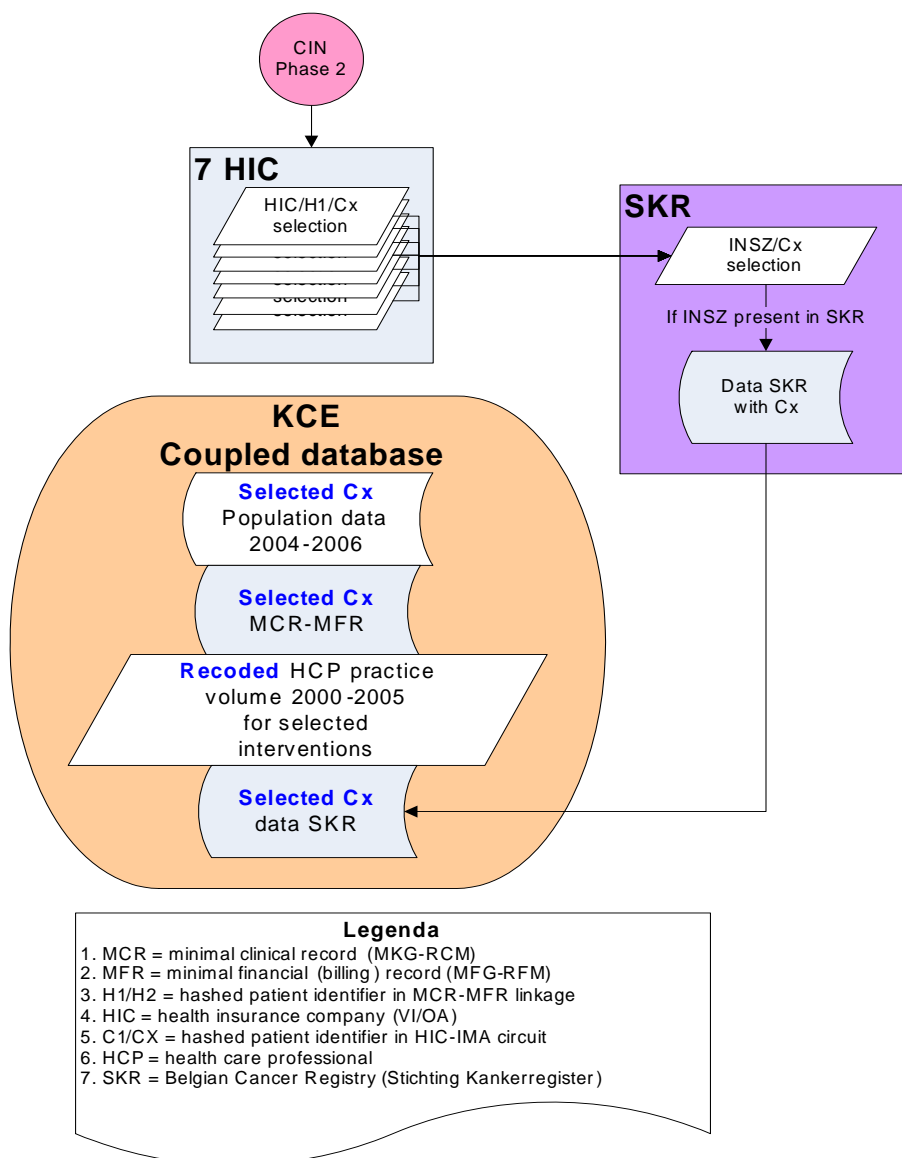
Phase 2 – Coupling IMA data



Phase 3 – HCP practice volume



Phase 4 – Additional data cancer patients



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