Supporting Information 1

Summary documents of detailed literature searches for
ESGE QIC Pancreatobiliary Working Group performed by:

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SUCCESS RATE OF CANNULATION

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1.1 (A I) **Statement: Does experience of endoscopists influence the rate of deep cannulation of the common bile duct / pancreatic duct during ERCP in patients with native papillas?**

Population
Patients undergoing ERCP

Intervention
ERCP performed by experienced (n of procedures specialty or years of training) endoscopists
OR
ERCP performed in high volume centers

Control
ERCP performed by inexperienced endoscopists
OR
ERCP performed in non-high volume centers

Outcome
Success rate of **cannulation**

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Clinical Competence"[Mesh] OR "Education, Medical, Graduate"[Mesh] OR "Gastroenterology/education"[Mesh] OR (volume[Title/Abstract] AND (center[Title/Abstract] OR centers[Title/Abstract] OR hospital[Title/Abstract] OR hospitals[Title/Abstract] OR clinic[Title/Abstract] OR clinics[Title/Abstract])) OR ((Experience*[Title/Abstract] OR train*[Title/Abstract]) AND (endoscopist[Title/Abstract] OR endoscopists[Title/Abstract]))) **AND** ("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) **AND**

("Catheterization"[Mesh] OR cannulation[Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti))) **AND** ('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) **AND** ('cannulation'/exp OR cannulation:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)
#1   MeSH descriptor: [Clinical Competence] explode all trees
#2   MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3   MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4   (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5   (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6   #2 or #1 or #5 or #3 or #4
#7   MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#8   ERCP:ti,ab,kw (Word variations have been searched)
#9   #8 or #7
#10   MeSH descriptor: [Catheterization] explode all trees
#11   cannulation:ti,ab,kw (Word variations have been searched)
#12   #10 or #11
#13   #12 and #6 and #9

Primary studies

PubMed
("Clinical Competence"[Mesh] OR "Education, Medical, Graduate"[Mesh] OR "Gastroenterology/education"[Mesh] OR (volume[Title/Abstract] AND (center[Title/Abstract] OR centers[Title/Abstract] OR hospital[Title/Abstract] OR hospitals[Title/Abstract] OR clinic[Title/Abstract] OR clinics[Title/Abstract])) OR ((Experience*[Title/Abstract] OR train*[Title/Abstract]) AND (endoscopist[Title/Abstract] OR endoscopists[Title/Abstract]))) **AND** ("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) **AND** ("Catheterization"[Mesh] OR cannulation[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti))) **AND** ('endoscopic

retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) **AND** ('cannulation'/exp OR cannulation:ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1   MeSH descriptor: [Clinical Competence] explode all trees
#2   MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3   MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4   (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5   (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6   #2 or #1 or #5 or #3 or #4
#7   MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#8   ERCP:ti,ab,kw (Word variations have been searched)
#9   #8 or #7
#10   MeSH descriptor: [Catheterization] explode all trees
#11   cannulation:ti,ab,kw (Word variations have been searched)
#12   #10 or #11
#13   #12 and #6 and #9

Results

Results of the bibliographic searches
After removing duplicates, 269 articles (10 reviews and 259 primary studies) were found. Another study was found through references included in others clinical questions and another one was suggested by experts. One potentially relevant systematic review and 10 primary studies were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies
Five studies were excluded: two because the objective of the studies was no in the inclusion criteria: one assessed the technical proficiency needed to perform needle-knife pre-cut papillotomy (NKPP) in case of cannulation was unsuccessful within 20 minutes with standard ERCP (Fukatsu 2009); the other assessed risk factors of post ERCP pancreatitis (Nakai 2014); two because the intervention was not in the inclusion criteria: precut sphincterotomy (Akaraviputh 2008, Harewood 2002); two studies (Ekkelenkamp 2014, Verma 2007) because already included in the systematic review of Shahidi 2015.

Included studies
6 studies were finally included: one systematic review (Shahidi 2015) and 4 cohort studies (Chibbar 2014, Garrow 2009, Kapral 2008, Peng 2013) and 1 cross sectional (Oppong 2012). Data of two studies (Garrow 2009 and Chibbar 2014) were extracted from conference abstracts; evidence tables and quality assessment was not performed because not enough data were provided.

Table 1. Results of systematic review

Study	Number of ERCP	Number of endoscopist who performed ERCP	Intervention and control	Success rate of cannulation
Shahidi 2015	4477 ERCPs (4 studies) not specified whether all patients were with native papillas	53 trainees (4 studies)	ERCP training required to achieve procedural competency	**Pancreatic duct Cannulation:** 2 studies Threshold to define competency : success rates between 80% and 85% Competency achieved by between 70 and 160 ERCPs. On further stratification, only 1 study explicitly incorporated deep PD cannulation into their definition of competency. Competency was reached in this study by 160 ERCPs. **Common bile duct cannulation**: 4 studies Threshold to define competency success rates between 80% and 85% Competency achieved by between 160 and 400 ERCPs for 2 studies Of note, when explicitly evaluating deep CBD cannulation in cases with native papillary anatomy, only 1 study was able to reach competency ($\geq$80%), which occurred between 350 to 400 ERCPs.

Table2: Results of primary studies

Study	Number of ERCP	Number of endoscopist who performed ERCP	Intervention and control	Success rate of cannulation
Chibbar 2014	465 ERCPs: not specified whether all patients were with native papillas HVE =367 ERCPs LVE= 98 ERCPs	6 endoscopists (3 HVE and 3 LVE)	high volume ERCP (HVE) group performed at least 75 ERCPs / endoscopist / year *vs* low volume ERCP (LVE) group performed less than 75 ERCPs each during the year.	**Successful cannulation** LVE group =78.6% HVE group=91.0% (p=0.001, OR 2.8) Once adjusted for ERCP complexity, the OR for successful cannulation was 2.64 (p=0.002) between the HVE and LVE groups.
Garrow 2009	7896 ERCP cases; not specified whether all patients were with native papillas	59 doctors from 3 countries	Less experienced practitioners by <150 cases in the last year More experienced practitioners by <1000 total lifetime	**Biliary cannulation** Less experienced=94.0% More experienced=98.0% p<0.0001 **Minor papilla cannulation** Less experienced=82.1% More experienced=95.7% p<0.0001
Kapral 2008	3132 ERCPs not specified whether all patients were with native papillas 81.1% therapeutic procedures	2618 patients 89 endoscopists	< 50 ERCP per year (68 endoscopists) vs >50 ERCP per year (21 endoscopists)	**Cannulation rates** < 50 ERCP per year, % (n)=84.2 (978) >50 ERCP per year, % (n)=91.2 (2132) P<0.001

Oppong 2012	19848 ERCPs with cannulation attempts in patients with native papillas	66 endoscopists from US and UK	<100 ERCP a year (19 endoscopists) vs >100 ERCP per year (47 endoscopists)	**Cannulation rates ≥90%** < 100 ERCP per year, % =63.1 >100 ERCP per year, % =85.1 P=0.09
Peng 2013	13018 ERCPs in native papillae	85 endoscopists	Categories for the endoscopist's prior hands-on training volume: 0(no formal training)=40 (47.1%) 1–100= 6 (7.1%) 101–150=8 (9.4%) 151–200=5 (5.9%) 201–250=7 (8.2%) >250 procedures=19 (22.4%) Lifetime volume (estimated cumulative number of prior ERCPs) Median (range, IQR) 1200 (175–15000, 587–2500) Annual volume (estimated by number of ERCPs performed the preceding year) Median (range, IQR) 150 (10–940, 90–239)	**Overall deep biliary cannulation success rate** Annual volume p=0.01 ≤90: Reference 91-150: 1.28 (0.72-2.29) 151-239: 1.85 (0.95-3.60) >239: 2.79 (1.46-5.31)

Quality of evidence

Study limitations (risk of bias): yes (two conference abstracts; low quality systematic review; high quality for retrospective cohort).
Inconsistency of results: no
Indirectness of evidence: yes (all but two studies did not specify whether all patients were with native papilla)
Imprecision: no (included more than 25000 ERCP)
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as very low because evidence came from observational studies with study limitation and indirectness.

Conclusions

Success rate of cannulation is influenced by experience of endoscopists: less experienced endoscopists had significantly lower success rates for biliary cannulation
(**VERY LOW QUALITY OF EVIDENCE**).
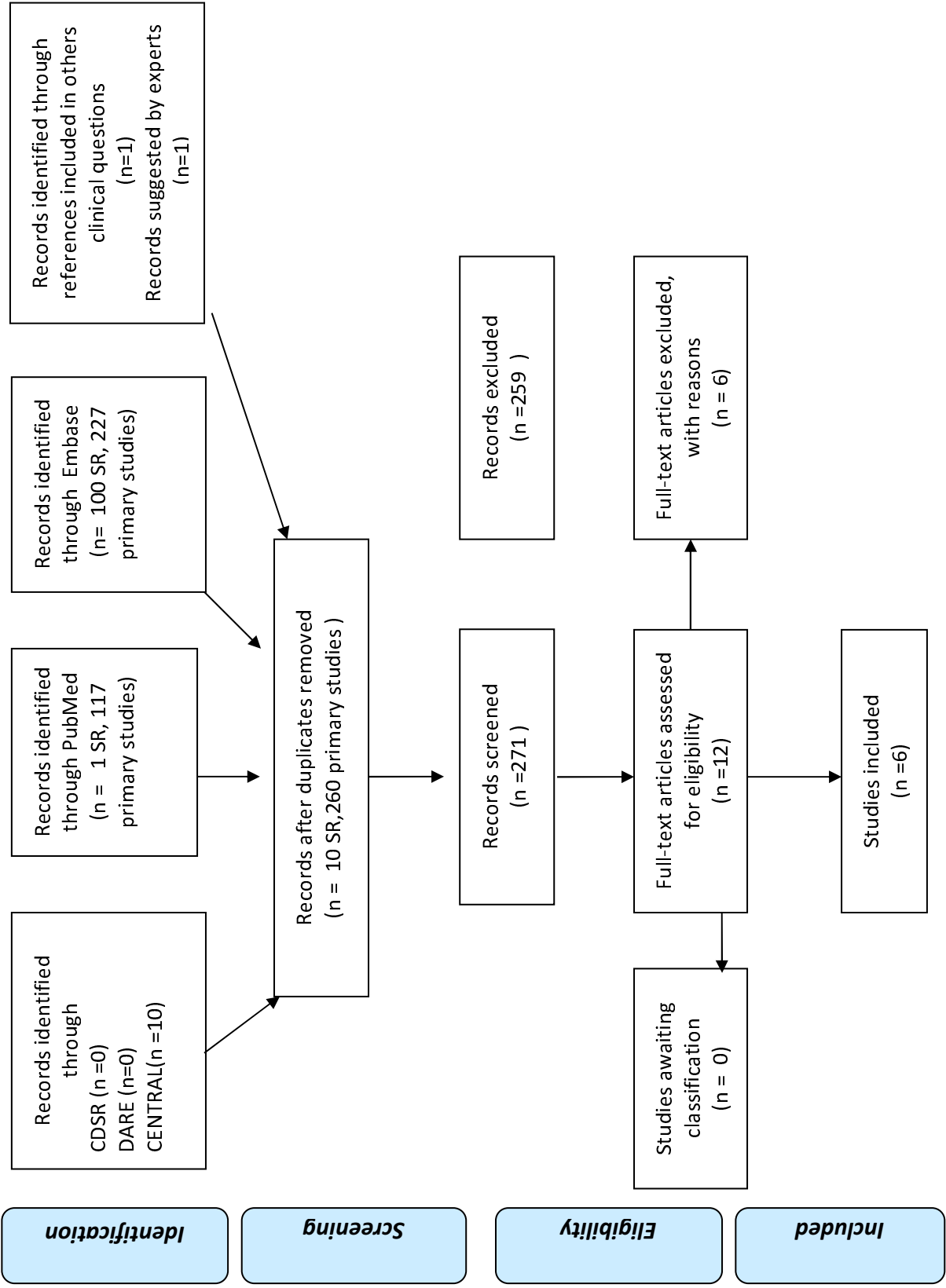
References

Included studies
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4. Oppong K.W., Romagnuolo J., Cotton P.B.Research: The ERCP quality network benchmarking project: A preliminary comparison of practice in UK and USA. Frontline Gastroenterology 2012 3:3 (157-161)
5. Peng, C.; Nietert, P. J.; Cotton, P. B.; Lackland, D. T., and Romagnuolo, J. Predicting native papilla biliary cannulation success using a multinational Endoscopic Retrograde Cholangiopancreatography (ERCP) Quality Network. BMC Gastroenterol. 2013; 13:147.
6. Shahidi N.; Ou G.; Telford J., and Enns R. When trainees reach competency in performing ERCP: A systematic review. Gastrointest. Endosc. 2015; 81(6):1337-1342;

Excluded studies

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2. Ekkelenkamp V.E.; Koch A.D.; Rauws E.A.J.; Borsboom G.J.J.M.; De Man R.A., and Kuipers E.J. Competence development in ERCP: The learning curve of novice trainees. Endoscopy. 2014; 46(11):949-955;
3. Fukatsu H.; Kawamoto H.; Harada R.; Tsutsumi K.; Fujii M.; Kato H.; Hirao K.; Nakanishi T.; Mizuno O.; Ogawa T.; Ishida E.; Okada H., and Sakaguchi K. Quantitative assessment of technical proficiency in performing needle-knife precut papillotomy. Surg. Endosc. Interv. Tech. 2009; 23(9):2066-2072;
4. Harewood G.C. and Baron T.H. An assessment of the learning curve for precut biliary sphincterotomy. Am. J. Gastroenterol. 2002; 97(7):1708-1712;
5. Nakai Y.; Isayama H.; Sasahira N.; Kogure H.; Sasaki T.; Yamamoto N.; Matsukawa M.; Saito K.; Umefune G.; Kawahata S.; Akiyama D.; Saito T.; Hamada T.; Takahara N.; Mizuno S.; Miyabayashi K.; Takahashi R.; Yamamoto K.; Mohri D.; Hirano K.; Tada M., and Koike K. Risk factors for post-ERCP pancreatitis in therapeutic biliary ERCP using wire-guided cannulation. Gastrointest. Endosc. 2014; 79(5):AB258;
6. Verma D.; Gostout C.J.; Petersen B.T.; Levy M.J.; Baron T.H., and Adler D.G. Establishing a true assessment of endoscopic competence in ERCP during training and beyond: a single-operator learning curve for deep biliary cannulation in patients with native papillary anatomy. Gastrointest. Endosc. 2007; 65(3):394-400;

PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n =0)
DARE (n=0)
CENTRAL(n =10)

Records identified
through PubMed
(n = 1 SR, 117
primary studies)

Records identified
through Embase
(n= 100 SR, 227
primary studies)

Records identified through
references included in others
clinical questions
(n=1)
Records suggested by experts
(n=1)

Screening

Records after duplicates removed
(n = 10 SR,260 primary studies)

Records screened
(n =271)

Records excluded
(n =259)

Eligibility

Full-text articles assessed
for eligibility
(n =12)

Full-text articles excluded,
with reasons
(n = 6)

Studies awaiting
classification
(n = 0)

Included

Studies included
(n =6)

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STONE EXTRACTION

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1.2 (AII) **Statement: Does experience of endoscopists influence the success rate of extraction of common bile duct (CBD)-stones of <1 cm during ERCP in patients with native papillas?**

Population
Patients with bile duct stones (synonym: choleodocholithiasis) undergoing ERCP

Intervention
ERCP performed by experienced (n of procedures specialty or years of training) endoscopists
OR
ERCP performed in high volume centers

Control
ERCP performed by inexperienced endoscopists
OR
ERCP performed in non-high volume centers

Outcome
Success rate of **stone extraction**

Bibliographic searches
Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Clinical Competence"[Mesh] OR "Education, Medical, Graduate"[Mesh] OR "Gastroenterology/education"[Mesh] OR (volume[Title/Abstract] AND (center[Title/Abstract] OR centers[Title/Abstract] OR hospital[Title/Abstract] OR hospitals[Title/Abstract] OR clinic[Title/Abstract] OR clinics[Title/Abstract])) OR ((Experience*[Title/Abstract] OR train*[Title/Abstract]) AND (endoscopist[Title/Abstract] OR endoscopists[Title/Abstract]))) **AND** ("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) **AND** (Choledocholithiasis[Text Word] OR (("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR

"Bile Duct" [Title/Abstract]) AND (stone*[Text Word] OR calculi[Text Word] OR calculus[Text Word]))) **AND** ("surgery" [Subheading] OR remov*[Title/Abstract] OR extract*[Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti))) **AND** ('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) **AND** (Choledocholithiasis:ab,ti OR 'common bile duct stone'/exp OR (('common bile duct'/exp OR CBD:ab,ti OR ' bile duct':ab,ti) AND (stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti))) **AND** (remov*:ab,ti OR extract*:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)
#1   MeSH descriptor: [Clinical Competence] explode all trees
#2   MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3   MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4   (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5   (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
        #6 #2 or #1 or #5 or #3 or #4
#7   MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#8   ERCP:ti,ab,kw (Word variations have been searched)
#9   #8 or #7
#10   CBD or bile duct:ti,ab,kw (Word variations have been searched)
#11   MeSH descriptor: [Common Bile Duct] explode all trees
#12   #10 or #11
#13   stone or calculus:ti,ab,kw (Word variations have been searched)
#14   #12 and #13
#15   Choledocholithiasis:ti,ab,kw (Word variations have been searched)
#16   MeSH descriptor: [Choledocholithiasis] explode all trees
#17   #14 or #15 or #16
#18   Any MeSH descriptor with qualifier(s): [Surgery - SU]
#19   extraction or removal:ti,ab,kw (Word variations have been searched)
#20   #18 or #19
#21   #9 and #5 and #17 and #20 Publication Year from 2000 to 2015

Primary studies

PubMed
("Clinical Competence"[Mesh] OR "Education, Medical, Graduate"[Mesh] OR "Gastroenterology/education"[Mesh] OR (volume[Title/Abstract] AND (center[Title/Abstract] OR centers[Title/Abstract] OR hospital[Title/Abstract] OR hospitals[Title/Abstract] OR clinic[Title/Abstract] OR clinics[Title/Abstract])) OR ((Experience*[Title/Abstract] OR

train*[Title/Abstract]) AND (endoscopist[Title/Abstract] OR endoscopists[Title/Abstract]))) **AND** ("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) **AND** (Choledocholithiasis[Text Word] OR (("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct" [Title/Abstract]) AND (stone*[Text Word] OR calculi[Text Word] OR calculus[Text Word]))) **AND** ("surgery" [Subheading] OR remov*[Title/Abstract] OR extract*[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti))) **AND** ('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) **AND** (Choledocholithiasis:ab,ti OR 'common bile duct stone'/exp OR (('common bile duct'/exp OR CBD:ab,ti OR ' bile duct':ab,ti) AND (stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti))) **AND** (remov*:ab,ti OR extract*:ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1   MeSH descriptor: [Clinical Competence] explode all trees
#2   MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3   MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4   (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5   (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6   #2 or #1 or #5 or #3 or #4
#7   MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#8   ERCP:ti,ab,kw (Word variations have been searched)
#9   #8 or #7
#10   CBD or bile duct:ti,ab,kw (Word variations have been searched)
#11   MeSH descriptor: [Common Bile Duct] explode all trees
#12   #10 or #11
#13   stone or calculus:ti,ab,kw (Word variations have been searched)
#14   #12 and #13
#15   Choledocholithiasis:ti,ab,kw (Word variations have been searched)
#16   MeSH descriptor: [Choledocholithiasis] explode all trees
#17   #14 or #15 or #16
#18   Any MeSH descriptor with qualifier(s): [Surgery - SU]
#19   extraction or removal:ti,ab,kw (Word variations have been searched)
#20   #18 or #19
#21   #9 and #5 and #17 and #20 Publication Year from 2000 to 2015

Results

Results of the bibliographic searches
After removing duplicates, 83 articles (1 reviews and 82 primary studies) were found. No potentially relevant systematic reviews were found; 6 primary studies were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies
Four studies were excluded: two studies because no outcome of interest (Cote 2012, Kalaitzakis 2015: the outcome was failed index ERCP procedure when percutaneous biliary drainage and/or (open, laparoscopic, or transcystic) common bile duct exploration was performed during the same (index) hospital episode); two studies because no comparison of interest (Swan 2013, Yiasemidou 2012).

Included studies
Two studies were finally included (Enochsson 2010, Garrow 2009).
Data of Garrow 2009 was extracted from conference abstracts; evidence tables and quality assessment was not performed because not enough data were provided.
Enochsson 2010 not specified the size of common bile duct (CBD) stones and whether all patients were with native papillas.

Study	Number of ERCP		Intervention	Success rate of stone extraction
Enochsson 2010	11,074 ERCPs	8088 patients in 51 hospitals.	High volume >1000 ERCP case/year low volume < 200 ERCP case /year Intermediate volume center (200-1000 ERCP)	**Successful Common bile duct stone extraction, %** Low-volume centers =72.5% High-volume centers =81.1% High-to low P value=0. 0008 Intermediate volume center= 77.8% High-to intermediate: P value=ns
Garrow 2009	7896 ERCP cases; not specified whether all patients were with native papillas	59 doctors from 3 countries	Less experienced practitioners by <150 cases in the last year More experienced practitioners by <1000 total lifetime	**Bile duct stone extraction (<10 mm)** Less experienced= 98% More experienced=100% p=0.001

Quality of evidence

Study limitations (risk of bias): yes
Inconsistency of results: no
Indirectness of evidence: yes: in both studies it was not specified whether all patients were with native papillas
Imprecision: no *(two studies with a total of 18970 ERCPs)*
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as very low because of evidence came from observational studies with study limitation and inconsistency .

Conclusions

For unspecified size of stones, high-volume canters had a slightly higher success rate of CBDS extraction than low-volume canters. Success rates for bile duct stone extraction <10 mm were higher in high volume centres
(**VERY LOW QUALITY OF EVIDENCE**)
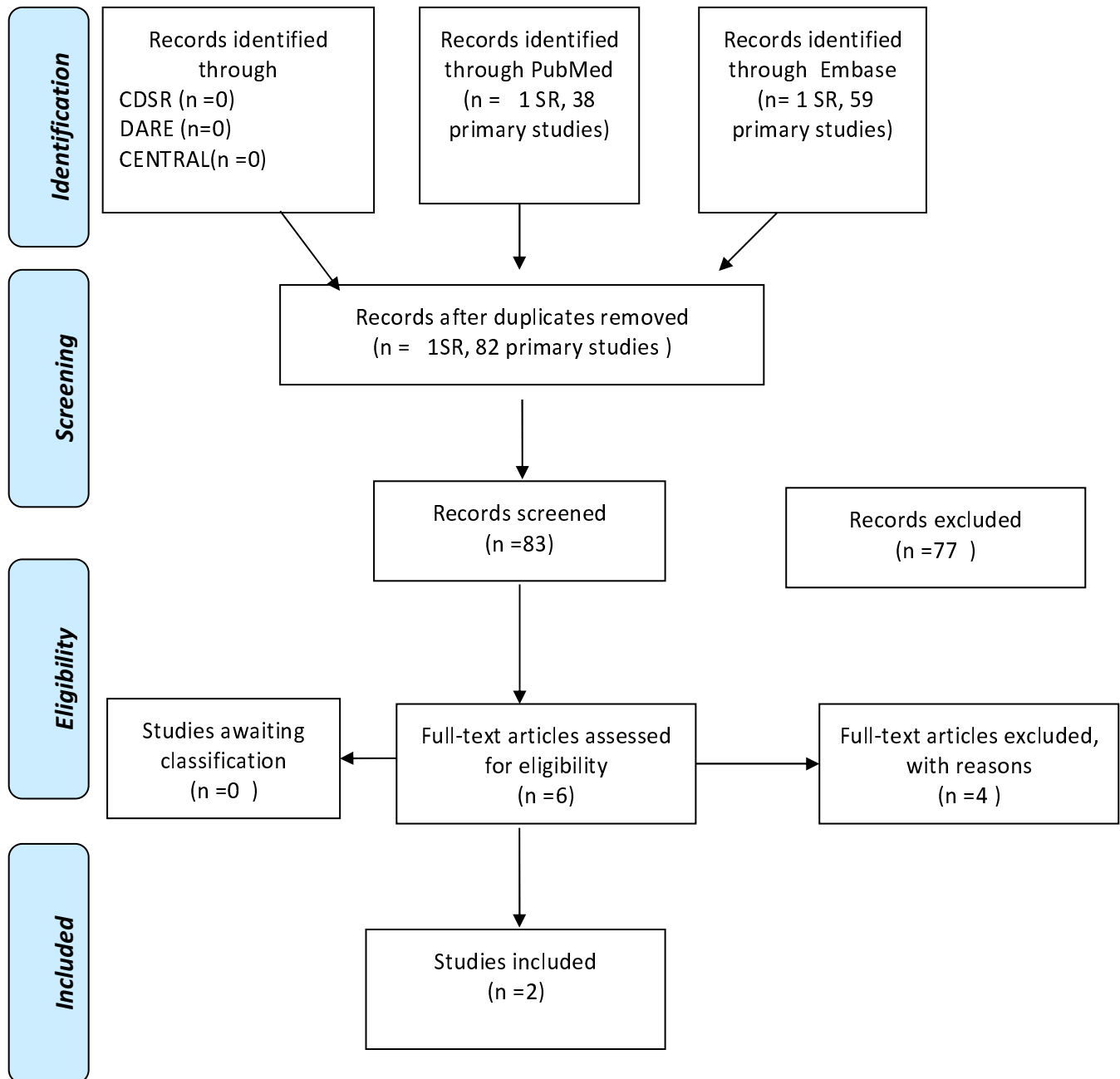
References

Included studies
1. Enochsson, L.; Swahn, F.; Arnelo, U.; Nilsson, M.; Lohr, M., and Persson, G. Nationwide, population-based data from 11,074 ERCP procedures from the Swedish Registry for Gallstone Surgery and ERCP. Gastrointest Endosc. 2010 Dec; 72(6):1175-84, 1184.e1-3.
2. Garrow D.A.; Romagnuolo J., and Cotton P.B. Comparing ERCP practice and outcomes by level of experience. Gastrointest. Endosc. 2009; 69(5):AB231;

Excluded studies
1. Cote, G. A.; Singh, S.; Bucksot, L. G.; Lazzell-Pannell, L.; Schmidt, S. E.; Fogel, E.; McHenry, L.; Watkins, J.; Lehman, G., and Sherman, S. Association between volume of endoscopic retrograde cholangiopancreatography at an academic medical center and use of pancreatobiliary therapy. Clin Gastroenterol Hepatol. 2012 Aug; 10(8):920-4.
2. Kalaitzakis E. and Toth E. Hospital Volume Status Is Related to Technical Failure and All-Cause Mortality Following ERCP for Benign Disease. Dig. Dis. Sci. 2015; 60(6):1793-1800;
3. Swan M.P.; Alexander S.; Barnes M.; Prewett E.; Croagh D., and Devonshire D.A. Endoscopic Papillary Large Balloon Dilation (EPLBD) in the management of large CBD stones; an Australian perspective. J. Gastroenterol. Hepatol. 2013; 2845;
4. Yiasemidou M. and Stock S. ERCP-can a small volume unit provide a satisfactory service? Gut. 2012; 61A286-A287;

PRISMA 2009 Flow Diagram

Identification

| Records identified through CDSR (n =0) DARE (n=0) CENTRAL(n =0) | Records identified through PubMed (n = 1 SR, 38 primary studies) | Records identified through Embase (n= 1 SR, 59 primary studies) |

Screening

Records after duplicates removed
(n = 1SR, 82 primary studies)

Records screened
(n =83)

Records excluded
(n =77)

Eligibility

Studies awaiting classification
(n =0)

Full-text articles assessed for eligibility
(n =6)

Full-text articles excluded, with reasons
(n =4)

Included

Studies included
(n =2)

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SUCCESS RATE OF STENT PLACEMENT

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Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro
Tumori- CPO Piemonte

1.3 (A III(a)) **Statement: Does experience of endoscopists influence the success rate of stent placement for biliary obstruction during ERCP -** *independent of the etiology of the stricture***?**

Population
Patients with bilary (= bile duct) stenosis (synonym: common bile duct stricture)

Intervention
ERCP performed by experienced (n of procedures specialty or years of training) endoscopists
OR
ERCP performed in high volume centers

Control
ERCP performed by inexperienced endoscopists
OR
ERCP performed in non-high volume centers

Outcome
Success rate of **stent placement**

1.4 (A III(b)) **Statement: Does experience of endoscopists influence the success rate of stent placementfor biliary** *benign* **obstruction**(e.g., cholangitis, pancreatitis, sclerosing papillitis, postoperative stenosis, stones) **during ERCP?**

Population
Patients with benign bilary stenosis

Intervention
ERCP performed by experienced (n of procedures specialty or years of training) endoscopists
OR
ERCP performed in high volume centers

Control
ERCP performed by inexperienced endoscopists
OR
ERCP performed in non-high volume centers

Outcome
Success rate of **stent placement**

1.5 (A III(c)) **Statement: Does experience of endoscopists influence the success rate of stent placementin patients with *bile duct cancer*?**

Population
Patients with bile duct cancer (synonym: extrahepatic biliary cancer)

Intervention
ERCP performed by experienced (n of procedures specialty or years of training) endoscopists
OR
ERCP performed in high volume centers

Control
ERCP performed by inexperienced endoscopists
OR
ERCP performed in non-high volume centers

Outcome
Success rate of **stent placement**

1.6 (A III(d)) **Statement: Does experience of endoscopists influence the success rate of stent placementin patients with *pancreatic cancer*?**

Population
Patients with pancreatic cancer

Intervention
ERCP performed by experienced (n of procedures specialty or years of training) endoscopists
OR
ERCP performed in high volume centers

Control
ERCP performed by inexperienced endoscopists
OR
ERCP performed in non-high volume centers

Outcome
Success rate of **stent placement**

Inclusion criteria for III (a - d):
- Extrahepatic biliary stricture (= obstruction is below the bifurcation)
- Common bile duct stenosis

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Clinical Competence"[Mesh] OR "Education, Medical, Graduate"[Mesh] OR "Gastroenterology/education"[Mesh] OR (volume[Title/Abstract] AND (center[Title/Abstract] OR centers[Title/Abstract] OR hospital[Title/Abstract] OR hospitals[Title/Abstract] OR clinic[Title/Abstract] OR clinics[Title/Abstract])) OR ((Experience*[Title/Abstract] OR train*[Title/Abstract]) AND (endoscopist[Title/Abstract] OR endoscopists[Title/Abstract]))) **AND** ("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) **AND** ("Stents"[Mesh] OR stent[Title/Abstract] OR stents[Title/Abstract]) **AND** ((("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct"[Title/Abstract] OR biliary[Title/Abstract] OR pancreatic[Title/Abstract]) AND (obstruct*[Title/Abstract] OR occlu*[Title/Abstract] OR stricture[Text Word] OR stenosis[Text Word] OR stone*[Text Word] OR calculi[Text Word] OR calculus[Text Word] OR cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign* [Title/Abstract] OR tumor [Title/Abstract] OR tumour [Title/Abstract] OR tumors [Title/Abstract] OR tumours [Title/Abstract] OR carcinom* [Title/Abstract])) OR ((obstruct*[Text Word] OR occlu*[Text Word]) AND benign[Title/Abstract]) OR "Cholangitis"[Mesh] OR Cholangitis[Title/Abstract] OR pancreatitis[Title/Abstract] OR "Pancreatitis"[Mesh] OR sclerosing papillitis[Title/Abstract] OR "Biliary Tract Neoplasms"[Mesh] OR "Pancreatic Neoplasms"[Mesh]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti))) **AND** ('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) **AND** ((('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti) AND (obstruct*:ab,ti OR occlu*:ab,ti OR stricture:ab,ti OR 'stenosis'/exp OR stenosis:ab,ti cancer OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti)) OR ((obstruct*:ab,ti OR occlu*:ab,ti) AND benign:ab,ti) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR pancreatitis:ab,ti OR Cholangitis:ab,ti OR 'cholangitis'/exp OR 'pancreatitis'/exp OR 'sclerosing papillitis':ab,ti) **AND** ('biliary stent'/exp OR stent:ab,ti OR stents:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and **Database of Abstracts of Reviews of Effects (DARE)**
#1   MeSH descriptor: [Clinical Competence] explode all trees
#2   MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3   MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]

#4   (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)

#5   (experienced or training) and endoscopist:ti,ab,kw: (Word variations have been searched)

#6   #2 or #1 or #5 or #3 or #4

#7   MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees

#8   ERCP:ti,ab,kw (Word variations have been searched)

#9   #8 or #7

#10   MeSH descriptor: [Stents] explode all trees

#11   stent:ti,ab,kw (Word variations have been searched)

#12   #10 or #11

#13   MeSH descriptor: [Common Bile Duct] explode all trees

#14   CBD or biliary or pancreatic or bile duct:ti,ab,kw (Word variations have been searched)

#15   obstruction or occlusion:ti,ab,kw (Word variations have been searched)

#16   cancer or neoplasm or malign or tumor or carcinoma or stricture or stenosis:ti,ab,kw (Word variations have been searched)

#17   #13 or #14

#18   #15 or #16

#19   #17 and #18

#20   benign:ti,ab,kw (Word variations have been searched)

#21   #15 and #20

#22   cholangitis or pancreatitis or sclerosing papillitis:ti,ab,kw (Word variations have been searched)

#23   MeSH descriptor: [Cholangitis] explode all trees

#24   MeSH descriptor: [Pancreatitis] explode all trees

#25   MeSH descriptor: [Biliary Tract Neoplasms] explode all trees

#26   MeSH descriptor: [Pancreatic Neoplasms] explode all trees

#27   #19 or #21 or #22 or #23 or #24 or #25 or #26

#28   #6 and #9 and #12and #27 Publication Year from 2000 to 2015

Primary studies

PubMed

("Clinical Competence"[Mesh] OR "Education, Medical, Graduate"[Mesh] OR "Gastroenterology/education"[Mesh] OR (volume[Title/Abstract] AND (center[Title/Abstract] OR centers[Title/Abstract] OR hospital[Title/Abstract] OR hospitals[Title/Abstract] OR clinic[Title/Abstract] OR clinics[Title/Abstract])) OR ((Experience*[Title/Abstract] OR train*[Title/Abstract]) AND (endoscopist[Title/Abstract] OR endoscopists[Title/Abstract]))) **AND** ("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) **AND** ("Stents"[Mesh] OR stent[Title/Abstract] OR stents[Title/Abstract]) **AND** ((("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct"[Title/Abstract] OR biliary[Title/Abstract] OR pancreatic[Title/Abstract]) AND (obstruct*[Title/Abstract] OR occlu*[Title/Abstract] OR stricture[Text Word] OR stenosis[Text Word] OR stone*[Text Word] OR calculi[Text Word] OR calculus[Text Word] OR cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign* [Title/Abstract] OR tumor [Title/Abstract] OR tumour [Title/Abstract] OR tumors [Title/Abstract] OR tumours [Title/Abstract] OR carcinom* [Title/Abstract])) OR ((obstruct*[Text Word] OR occlu*[Text Word]) AND benign[Title/Abstract]) OR "Cholangitis"[Mesh] OR Cholangitis[Title/Abstract] OR pancreatitis[Title/Abstract] OR "Pancreatitis"[Mesh] OR sclerosing papillitis[Title/Abstract] OR "Biliary Tract Neoplasms"[Mesh] OR "Pancreatic Neoplasms"[Mesh]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract]

OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti))) **AND** ('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) **AND** ((('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti) AND (obstruct*:ab,ti OR occlu*:ab,ti OR stricture:ab,ti OR 'stenosis'/exp OR stenosis:ab,ti cancer OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti)) OR ((obstruct*:ab,ti OR occlu*:ab,ti) AND benign:ab,ti) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR pancreatitis:ab,ti OR Cholangitis:ab,ti OR 'cholangitis'/exp OR 'pancreatitis'/exp OR 'sclerosing papillitis':ab,ti) **AND** ('biliary stent'/exp OR stent:ab,ti OR stents:ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)

#1   MeSH descriptor: [Clinical Competence] explode all trees
#2   MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3   MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4   (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5   (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6   #2 or #1 or #5 or #3 or #4
#7   MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#8   ERCP:ti,ab,kw (Word variations have been searched)
#9   #8 or #7
#10   MeSH descriptor: [Stents] explode all trees
#11   stent:ti,ab,kw (Word variations have been searched)
#12   #10 or #11
#13   MeSH descriptor: [Common Bile Duct] explode all trees
#14   CBD or biliary or pancreatic or bile duct:ti,ab,kw (Word variations have been searched)
#15   obstruction or occlusion:ti,ab,kw (Word variations have been searched)
#16   cancer or neoplasm or malign or tumor or carcinoma or stricture or stenosis:ti,ab,kw (Word variations have been searched)
#17   #13 or #14
#18   #15 or #16
#19   #17 and #18
#20   benign:ti,ab,kw (Word variations have been searched)
#21   #15 and #20
#22   cholangitis or pancreatitis or sclerosing papillitis:ti,ab,kw (Word variations have been searched)
#23   MeSH descriptor: [Cholangitis] explode all trees
#24   MeSH descriptor: [Pancreatitis] explode all trees
#25   MeSH descriptor: [Biliary Tract Neoplasms] explode all trees
#26   MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#27   #19 or #21 or #22 or #23 or #24 or #25 or #26
#28   #6 and #9 and #12and #27 Publication Year from 2000 to 2015

Results

<u>Results of the bibliographic searches</u>
After removing duplicates, 155 articles (3 reviews and 152 primary studies) were found. No potentially relevant systematic reviews were found; 4 primary studies were considered potentially relevant and acquired in full text. (See flow chart)

<u>Excluded studies</u>
Four studies were excluded: two because no outcome of interest (Chibbar 2014, Ekkelenkamp 2014); one because narrative review(Freeman 2005) and one because editorial (Freeman 2010).
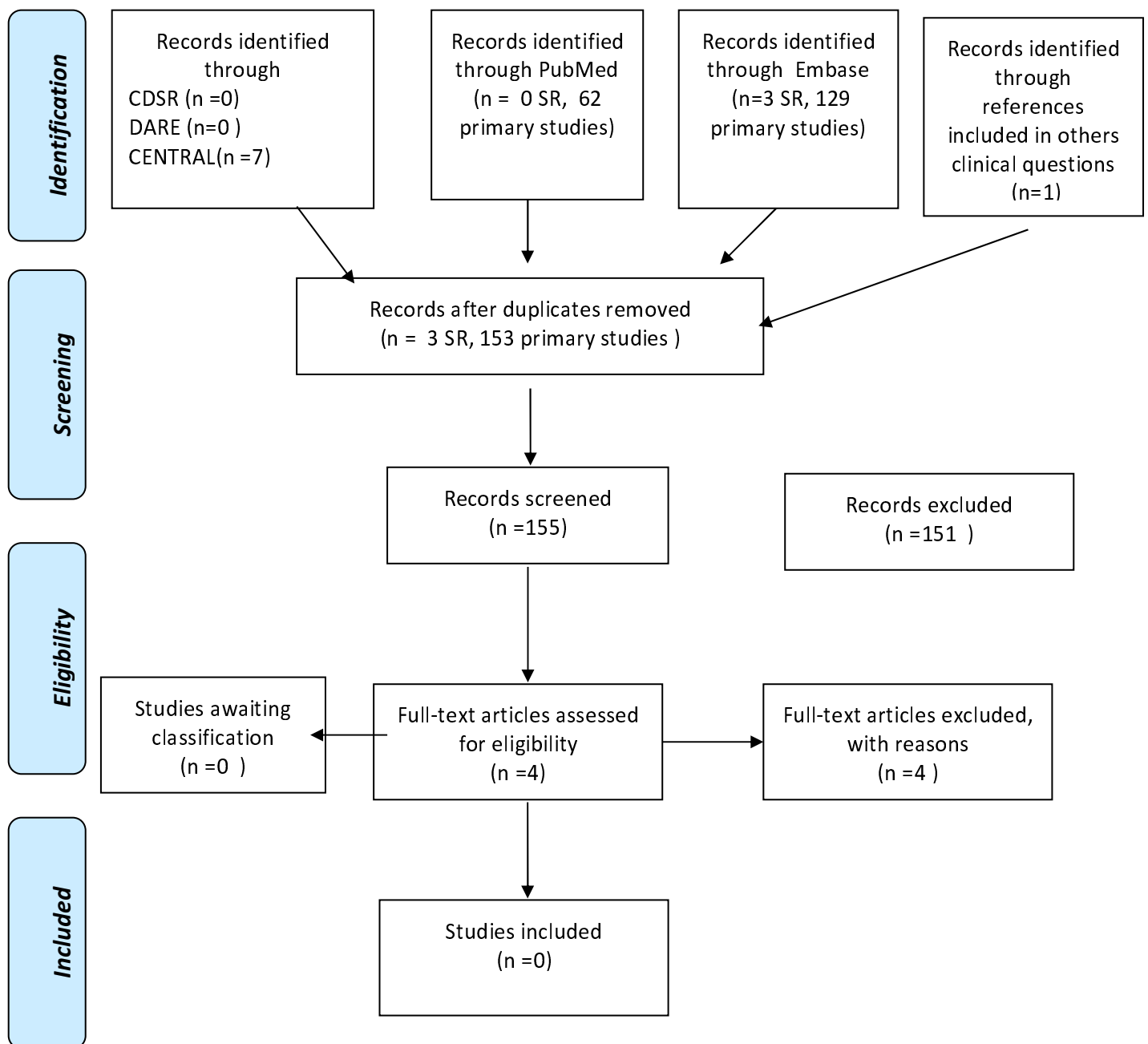
Conclusions

No conclusion can be drawn because no evidence was found.

References

<u>Excluded studies</u>
1. Ekkelenkamp V.E.; Koch A.D.; Rauws E.A.J.; Borsboom G.J.J.M.; De Man R.A., and Kuipers E.J. Competence development in ERCP: The learning curve of novice trainees. Endoscopy. 2014; 46(11):949-955;
2. Chibbar R.; D'Souza P.; Sandha G.; Zepeda-Gomez S.; Van Zanten S.V.; Teshima C.W., and Sultanian R.A. The impact of endoscopist case volume on ERCP outcomes: Experience at a Canadian tertiary centre. Gastroenterology. 2014; 146(5):S-388;
3. Freeman M.L. Pancreatic stents for prevention of post-ERCP pancreatitis: for everyday practice or for experts only? Gastrointest. Endosc. 2010; 71(6):940-944;
4. Freeman M.L. and Guda N.M. Endoscopic biliary and pancreatic sphincterotomy. Curr. Treat. Options Gastroenterol. 2005; 8(2):127-134;

PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n =0)
DARE (n=0)
CENTRAL(n =7)

Records identified through PubMed
(n = 0 SR, 62 primary studies)

Records identified through Embase
(n=3 SR, 129 primary studies)

Records identified through references included in others clinical questions (n=1)

Screening

Records after duplicates removed
(n = 3 SR, 153 primary studies)

Records screened
(n =155)

Records excluded
(n =151)

Eligibility

Studies awaiting classification
(n =0)

Full-text articles assessed for eligibility
(n =4)

Full-text articles excluded, with reasons
(n =4)

Included

Studies included
(n =0)

**S.C. Epidemiologia screening, registro tumori –
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POST-ERCP COMPLICATIONS

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Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

1.7 (A IV) **Statement: Does experience of endoscopists influence the prevention of complications following ERCP (% of patients suffering from post-ERCP complications)?**

Population
Patients undergoing ERCP

Intervention
ERCP performed by experienced (n of procedures specialty or years of training) endoscopists
OR
ERCP performed in high volume centers

Control
ERCP performed by inexperienced endoscopists
OR
ERCP performed in non-high volume centers

Outcome
Complications

Post-ERCP complications (short term complications), e.g.:
- bleeding (following sphincterotomy at ERCP, often immediately after sphinterotomy, sometimes also with delay if patient under anticoagulation-drugs)
- perforation(usually happening during ERCP)
- stent dislocation (migration, late complication)
- post-ERCP pancreatitis (immediately after ERCP)

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Clinical Competence"[Mesh] OR "Education, Medical, Graduate"[Mesh] OR "Gastroenterology/education"[Mesh] OR (volume[Title/Abstract] AND (center[Title/Abstract] OR centers[Title/Abstract] OR hospital[Title/Abstract] OR hospitals[Title/Abstract] OR clinic[Title/Abstract] OR clinics[Title/Abstract])) OR ((Experience*[Title/Abstract] OR train*[Title/Abstract]) AND (endoscopist[Title/Abstract] OR endoscopists[Title/Abstract]))) **AND** ("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) **AND** ("adverse effects"[Subheading] OR negative[Title/Abstract] OR adverse[Title/Abstract] OR side[Title/Abstract] OR complication[Text Word] OR complications[Title/Abstract] OR Safety[Text Word] OR "complications"[Subheading] OR "Hemorrhage"[Mesh] OR "Gastrointestinal Hemorrhage"[Mesh] OR hemorrhage[Title/Abstract] OR "Pancreatitis"[Text Word] OR Pancreatitis[Title/Abstract] OR perforation[Text Word] OR perforation[Title/Abstract] OR perforations[Title/Abstract] OR "Intestinal Perforation"[Mesh] OR bleeding[Text Word] OR bleeding[Title/Abstract] OR (("Stents"[Mesh] OR stent[Title/Abstract] OR stents[Title/Abstract]) AND (dislocation[Text Word] OR migration[Text Word]))) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti))) **AND** ('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) **AND** ('intestine perforation'/exp OR perforation:ab,ti OR perforations:ab,ti OR 'gastrointestinal hemorrhage'/exp OR bleeding:ab,ti OR Hemorrhage:ab,ti OR 'pancreatitis'/exp OR pancreatitis:ab,ti OR (('biliary stent'/exp OR stent:ab,ti OR stents:ab,ti) AND (dislocation:ab,ti OR migration:ab,ti)) OR 'side effect'/exp OR side:ab,ti OR 'adverse outcome'/exp OR adverse:ab,ti OR 'complication'/exp OR complication:ab,ti OR complications:ab,ti OR negative:ab,ti OR safety:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and **Database of Abstracts of Reviews of Effects (DARE)**
#1   MeSH descriptor: [Clinical Competence] explode all trees
#2   MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3   MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4   (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5   (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
      #6 #2 or #1 or #5 or #3 or #4

#7   MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees

#8   ERCP:ti,ab,kw (Word variations have been searched)

#9   #8 or #7

#10   Any MeSH descriptor with qualifier(s): [Adverse effects - AE, Complications - CO]

#11   Negative or adverse or side or complication or Safety:ti,ab,kw (Word variations have been searched)

#12   MeSH descriptor: [Hemorrhage] explode all trees

#13   MeSH descriptor: [Gastrointestinal Hemorrhage] explode all trees

#14   MeSH descriptor: [Pancreatitis] explode all trees

#15   MeSH descriptor: [Intestinal Perforation] explode all trees

#16   hemorrhage or Pancreatitis or perforation or bleeding:ti,ab,kw (Word variations have been searched)

#17   MeSH descriptor: [Stents] explode all trees

#18   stent:ti,ab,kw (Word variations have been searched)

#19   dislocation or migration:ti,ab,kw (Word variations have been searched)

#20   #17 or #18

#21   #20 and #19

#22   #10 or #11 or #12 or #13 or #14 or #15 or #16 or #21

#23   #22 and #9 and #6 Publication Year from 2000 to 2015

Primary studies

PubMed

("Clinical Competence"[Mesh] OR "Education, Medical, Graduate"[Mesh] OR "Gastroenterology/education"[Mesh] OR (volume[Title/Abstract] AND (center[Title/Abstract] OR centers[Title/Abstract] OR hospital[Title/Abstract] OR hospitals[Title/Abstract] OR clinic[Title/Abstract] OR clinics[Title/Abstract])) OR ((Experience*[Title/Abstract] OR train*[Title/Abstract]) AND (endoscopist[Title/Abstract] OR endoscopists[Title/Abstract]))) **AND** ("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) **AND** ("adverse effects"[Subheading] OR negative[Title/Abstract] OR adverse[Title/Abstract] OR side[Title/Abstract] OR complication[Text Word] OR complications[Title/Abstract] OR Safety[Text Word] OR "complications"[Subheading] OR "Hemorrhage"[Mesh] OR "Gastrointestinal Hemorrhage"[Mesh] OR hemorrhage[Title/Abstract] OR "Pancreatitis"[Text Word] OR Pancreatitis[Title/Abstract] OR perforation[Text Word] OR perforation[Title/Abstract] OR perforations[Title/Abstract] OR "Intestinal Perforation"[Mesh] OR bleeding[Text Word] OR bleeding[Title/Abstract] OR (("Stents"[Mesh] OR stent[Title/Abstract] OR stents[Title/Abstract]) AND (dislocation[Text Word] OR migration[Text Word]))) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti))) **AND** ('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) **AND** ('intestine perforation'/exp OR perforation:ab,ti OR perforations:ab,ti OR 'gastrointestinal hemorrhage'/exp OR bleeding:ab,ti OR Hemorrhage:ab,ti OR 'pancreatitis'/exp OR pancreatitis:ab,ti OR (('biliary stent'/exp OR stent:ab,ti OR stents:ab,ti) AND (dislocation:ab,ti OR migration:ab,ti)) OR 'side effect'/exp OR side:ab,ti OR

'adverse outcome'/exp OR adverse:ab,ti OR 'complication'/exp OR complication:ab,ti OR complications:ab,ti OR negative:ab,ti OR safety:ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1   MeSH descriptor: [Clinical Competence] explode all trees
#2   MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3   MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4   (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5   (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
        #6 #2 or #1 or #5 or #3 or #4
#7   MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#8   ERCP:ti,ab,kw (Word variations have been searched)
#9   #8 or #7
#10   Any MeSH descriptor with qualifier(s): [Adverse effects - AE, Complications - CO]
#11   Negative or adverse or side or complication or Safety:ti,ab,kw (Word variations have been searched)
#12   MeSH descriptor: [Hemorrhage] explode all trees
#13   MeSH descriptor: [Gastrointestinal Hemorrhage] explode all trees
#14   MeSH descriptor: [Pancreatitis] explode all trees
#15   MeSH descriptor: [Intestinal Perforation] explode all trees
#16   hemorrhage or Pancreatitis or perforation or bleeding:ti,ab,kw (Word variations have been searched)
#17   MeSH descriptor: [Stents] explode all trees
#18   stent:ti,ab,kw (Word variations have been searched)
#19   dislocation or migration:ti,ab,kw (Word variations have been searched)
#20   #17 or #18
#21   #20 and #19
#22   #10 or #11 or #12 or #13 or #14 or #15 or #16 or #21
#23   #22 and #9 and #6 Publication Year from 2000 to 2015

Results

Results of the bibliographic searches
After removing duplicates, 622 articles (20 reviews and 602 primary studies) were found. No potentially relevant systematic reviews were found; 22 primary studies were considered potentially relevant and acquired in full text. (See flow chart)

Excluded studies
16 studies were excluded: seven studies because outcome not in the inclusion criteria (Chennat 2010, Ekkelenkamp 2015, Garrow 2009, Kalaitzakis 2013, Kalaitzakis 2015, Nguyen 2010 (assess the association between likelihood of CCY and hospital volumes of CCY, pancreatitis, and endoscopic retrograde cholangio-pancreatography), Varadarajulu 2006); 5 studies because no comparison of interest assessed (Boudreau 2009, Nakai 2014, Rice 2010 (poster abstract of Rice 2011), Rice 2011, Swan 2009); one study because narrative review (Rabenstein 2002); one study

because no comparison and outcome of interest (Troendle 2014); two because same studies of studies already included (Enochsson 2010 Pancreatology: same study of Enochson 2010 Gastrointest. Endosc; Kapral J. Gastroenterol. Hepatol. Erkr. 2008: same study of Kapral 2008 Endoscopy but published in German language).

Included studies
Six studies were finally included (Chibbar 2015, Enochson 2010, Glomsaker 2013, Harewood 2002, Kapral 2008, Testoni 2010)

Data of Chibbar 2014 was extracted from conference abstracts; evidence tables and quality assessment was not performed because not enough data were provided.

Study	Number of ERCP	Number of endoscopist Number of patients	Intervention	Bleeding	Pancreatitis	Perforation	Other complications
Chibbar 2014	465 ERCPs: HVE =367 ERCPs LVE= 98 ERCPs	6 endoscopists (3 HVE and 3 LVE)	high volume ERCP (HVE) group performed at least 75 ERCPs/ endoscopist/ year *vs* low volume ERCP (LVE) group performed less than 75 ERCPs each during the year.				**Overall complication rate** HVE group= 5.2% LVE group = 7.1% (p=0.45, OR 0.71) adjusted for ERCP complexity, the OR for complication 0.59 between the HVE and LVE groups
Enochsson 2010	11,074 ERCPs	8088 patients in 51 hospitals.	High volume >1000 ERCPcase/year low volume < 200 ERCP case /year Intermediate volume center (200-1000 ERCP)	**Perioperative** High-volume centers =0.5% Low-volume centers = 0.4% High-to low P =ns Intermediate volume center= 0.7% High-to intermediate P = ns	High-volume centers =3.7% Low-volume centers = 2.4% High-to low P =0 .0123 Intermediate volume center= 2.4% High-to intermediate P = 0.0027	High-volume centers =0.3% Low-volume centers = 0.3% High-to low P =ns Intermediate volume center= 0.2% High-to intermediate	**Perioperative complications** High-volume centers =2.1% Low-volume centers = 3.1% High-to low P =0.0255 Intermediate volume center= 2.4% High-to intermediate

				Postoperative		P = ns	Postoperative Complications
				High-volume centers =1.1% Low-volume centers = 0.9% High-to low P =ns Intermediate volume center= 0.8% High-to intermediate P = ns			**Postoperative Complications** High-volume centers =11.2% Low-volume centers = 9.6% High-to low P =ns Intermediate volume center= 9.4% High-to intermediate P =0.0161
Glomsaker 2013	2808 ERCP (but 2675 procedures included in the multivariable regression analysis)	48 endoscopists	Volume centers: >150 ERCPs annually vs less		OR 1·70 (95%CI 1·08, 2·69)		Severe or fatal according to Cotton et al grade OR: 1·74 (95%CI 1·02, 2·98) Severe or fatal according to Dindo–Clavien grade OR: 2.45 (95%CI1.56, 3.84) Other complications OR: (OR 3·27, 2·00 to 5·43;

Note: The top row headers "P = ns" / "Postoperative" / "Postoperative Complications" appear as a continuation of a table from the previous page; the bold "Postoperative" heading appears in the fifth column and bold "Postoperative Complications" in the last column.

Harewood 2002	253 ERCP	253 consecutive patients who underwent precut biliary sphincterotomy one endoscopist	first 200 ERCP procedures vs subsequent 53 ERCP	Initial 200=2% Subsequent 53= 1% P=ns	Initial 200= 11% Subsequent 53=11% P=ns	Initial 200=0% Subsequent 53=0% p= ns	**Other (**any other adverse events related to the sphincterotomy procedure requiring hospitalization) Initial 200=2% Subsequent 53=2% P=ns **Overall Complication (% severe)** Initial 200= 16% (3) Subsequent 53=14% (2) P=ns
Kapral 2008	3132 ERCPs 81.1% therapeutic procedures	2618 patients 89 endoscopists	< 50 ERCP per year (68 endoscopists) vs >50 ERCP per year (21 endoscopists)	< 50 ERCP per year, % (n)=4.7(982) >50 ERCP per year, % (n)=3.2 (2128) P=ns	< 50 ERCP per year, % (n)=5.6(947) >50 ERCP per year, % (n)=4.9 (2098) P=ns	< 50 ERCP per year, % (n)=0.6 (974) >50 ERCP per year, % (n)=0.5 (2129) P=ns	**Cholangitis** < 50 ERCP per year, % (n)=2.8 (951) >50 ERCP per year, % (n)=1.5 (2102) P=0.022 **cardiopulmonary complications** < 50 ERCP per year, % (n)=1.6 (966) >50 ERCP per year, % (n)=0.6 (2112) P=0.014

						Overall complications < 50 ERCP per year, % (n)=13.6 (916) >50 ERCP per year, % (n)=10.2 (2035) P=0.007
Testoni 2010	3,635 ERCP	3,331 ERCPs were carried out by expert operators and 304 by less-experienced operators	ERCP volume high-volume centers vs low-volume centers. ERCP experience (endoscopist) low grade if the career-long total performance was fewer than 200 procedures and / or the current number < 40 per year		Low-ERCP volume (center) =OR 1.3 (95%CI 0.81 – 1.95) Low-ERCP experience (endoscopist) =OR 0.7 (95%CI 0.32 – 1.25)		

Quality of evidence

Study limitations (risk of bias): no(six studies of high quality and one conference abstract)
Inconsistency of results: no for bleeding and perforation, yes for pancreatitis and overall complications)
Indirectness of evidence: no
Imprecision: no (seven studies with greater of 21000 ERCP included)
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as low because evidence came from observational studies .

Conclusions

Overall complications

Overall complication rates were not significantly changed according to the level of experience or volume centers but one study showed that endoscopists with a case volume exceeding 50 ERCPs per year had lower overall complication rates. An increased risk of severe complications was observed in centres with an annual ERCP volume of more than 150 procedures
(**VERY LOW QUALITY OF EVIDENCE**).

Bleeding

Bleeding was not associated with experience of endoscopist or volume centers
(**LOW QUALITY OF EVIDENCE**).

Perforations

Perforations was not associated with experience of endoscopist or volume centers
(**LOW QUALITY OF EVIDENCE**).

Pancreatitis
when the cut off between high and low volume of ERCP per year is 200 or less ERCP per year , post-ERCP pancreatitis was not associated with the case volume of either the single endoscopist or the center according to all bu one study that found an increase in pancreatic when hospital volume was greater than 150/year. When the comparison is between very high-volume centers (>1000 ERCP case/year) and intermediate ((200-1000 ERCP)- and low-volume centers (< 200 ERCP case /year), higher frequency of pancreatitis were shown in high volume centers
(**VERY LOW QUALITY OF EVIDENCE**).

Other complications
Endoscopists with a case volume exceeding 50 ERCPs per year had lower rates of Cholangitis and cardiopulmonary complications
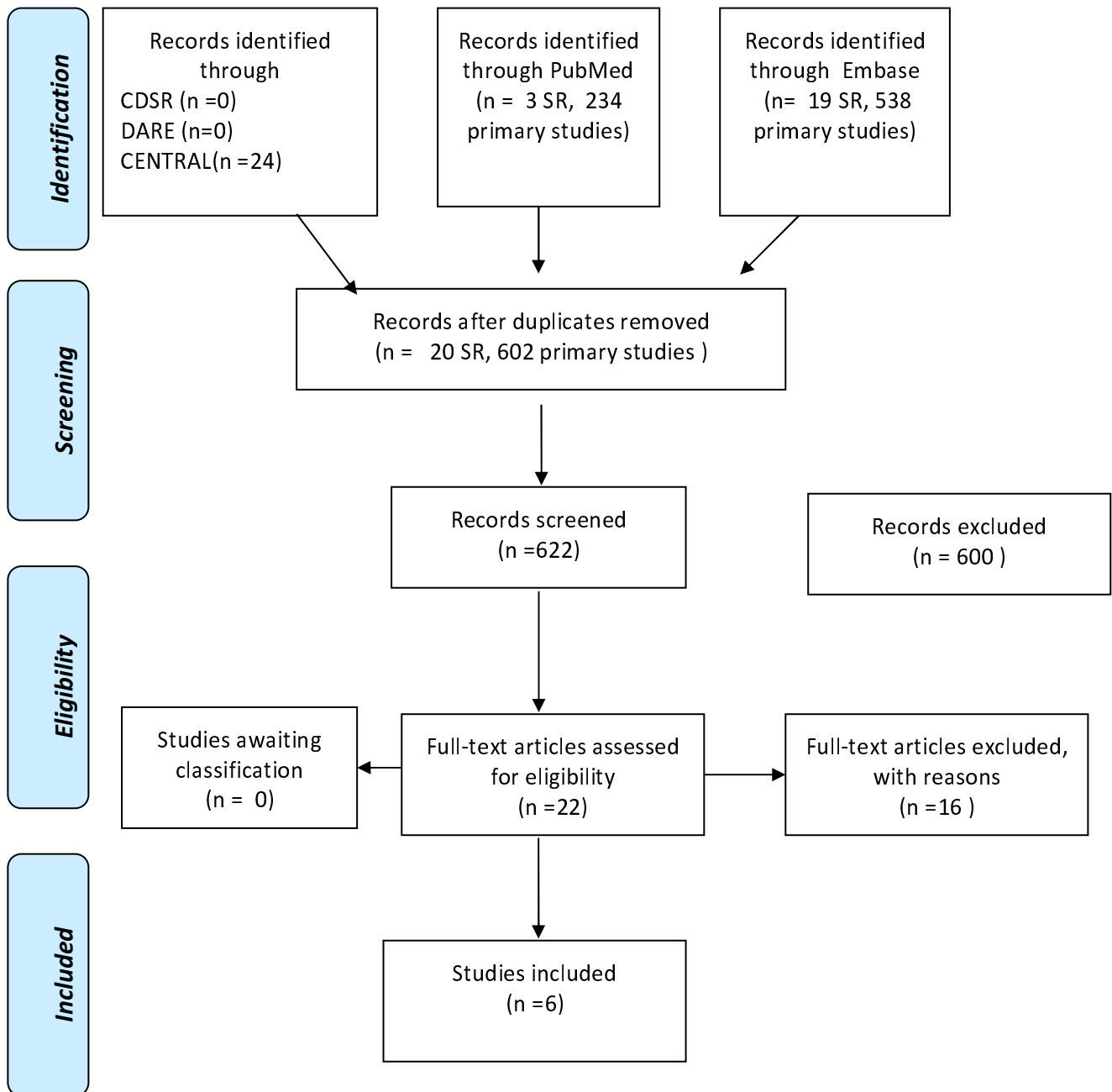(**LOW QUALITY OF EVIDENCE**).

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PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n =0)
DARE (n=0)
CENTRAL(n =24)

Records identified through PubMed
(n = 3 SR, 234 primary studies)

Records identified through Embase
(n= 19 SR, 538 primary studies)

Screening

Records after duplicates removed
(n = 20 SR, 602 primary studies)

Records screened
(n =622)

Records excluded
(n = 600)

Eligibility

Studies awaiting classification
(n = 0)

Full-text articles assessed for eligibility
(n =22)

Full-text articles excluded, with reasons
(n =16)

Included

Studies included
(n =6)

S.C. Epidemiologia screening, registro tumori –
CPO Piemonte
Direttore: Dr. Nereo Segnan
via Cavour 31, 10123 Torino
tel. 011.6333881 - fax 011.6333861
www.cpo.it - email: info@cpo.it

STAGING CANCER DURING EUS

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

1.8 (A V(a)) **Does experience of endoscopists or teaching endoscopists in formal training programs**(e.g., GATE – „gastroenterological education-training endoscopy" (DGVS),Principals of Training in Gastrointestinal Endoscopy (ASGE),EFSUMB, DEGUM) **influence accurate *staging of esophageal cancer*(e.g., T-staging, documentation of lymph nodes, vascular infiltration, distant metastases) during EUS?**

Population
Patients with eosphageal cancer undergoing EUS

Intervention
EUS performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS perfomed by experienced endoscopist having undergone formal EUS training program
OR
EUS performed in high volume centers

Control
EUS performed by inexperienced endoscopists
OR
EUS performed by an endoscopist without formal EUS training program
OR
EUS performed in non-high volume centers

Outcome
accurate staging of esophageal cancer (according to the UICC staging system)

1.9 (A V(b)) **Does experience of endoscopists or teaching endoscopists in formal training programs** (e.g., GATE – „gastroenterological education-training endoscopy" (DGVS), Principals of Training in Gastrointestinal Endoscopy (ASGE),EFSUMB, DEGUM) **influence accurate** *staging of gastric cancer*(e.g., T-staging, documentation of lymph nodes, vascular infiltration, distant metastases) during EUS?

Population
Patients with gastric cancer undergoing EUS

Intervention
EUS performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS perfomed by experienced endoscopist having undergone formal EUS training program
OR
EUS performed in high volume centers

Control
EUS performed by inexperienced endoscopists
OR
EUS performed by an endoscopist without formal EUS training program
OR
EUS performed in non-high volume centers

Outcome
accurate staging of gastric cancer (according to the UICC staging system)

1.10 (A V(c)) **Does experience of endoscopists or teaching endoscopists in formal training programs** (e.g., GATE – „gastroenterological education-training endoscopy" (DGVS), Principals of Training in Gastrointestinal Endoscopy (ASGE),EFSUMB, DEGUM)**influence accurate** *staging of pancreatic cancer*(e.g., T-staging, documentation of lymph nodes, vascular infiltration, distant metastases) during EUS?

Population
Patients with pancreatic cancer undergoing EUS

Intervention
EUS performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS perfomed by experienced endoscopist having undergone formal EUS training program
OR
EUS performed in high volume centers

Control
EUS performed by inexperienced endoscopists
OR
EUS perfomed by an endoscopist without formal EUS training program
OR
EUS performed in non-high volume centers

Outcome
accurate staging of pancreatic cancer (according to the UICC staging system)

1.11 (A V(d)) **Does experience of endoscopists or teaching endoscopists in formal training programs** (e.g., GATE – „gastroenterological education-training endoscopy" (DGVS), Principals of Training in Gastrointestinal Endoscopy (ASGE),EFSUMB, DEGUM) **influences accurate** *staging of bile duct cancer*(**e.g., T-staging, documentation of lymph nodes, vascular infiltration, distant metastases) during EUS?**

Population
Patients with bile duct cancer (synonym: extrahepatic biliary cancer) undergoing EUS

Intervention
EUS performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS perfomed by experienced endoscopist having undergone formal EUS training program
OR
EUS performed in high volume centers

Control
EUS performed by inexperienced endoscopists
OR
EUS perfomed by an endoscopist without formal EUS training program
OR
EUS performed in non-high volume centers

Outcome
accurate staging of bile duct cancer (according to the UICC staging system)

1.12 (A V(e)) **Does experience of endoscopists or teaching endoscopists in formal training programs** (e.g., GATE – „gastroenterological education-training endoscopy" (DGVS), Principals of Training in Gastrointestinal Endoscopy (ASGE),EFSUMB, DEGUM) **influences accurate** *staging of rectal cancer* (**e.g., T-staging, documentation of lymph nodes, vascular infiltration, distant metastases) during EUS?**

Population
Patients with rectal cancer (synonym: extrahepatic biliary cancer) undergoing EUS

Intervention
EUS performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS perfomed by experienced endoscopist having undergone formal EUS training program
OR
EUS performed in high volume centers

Control

EUS performed by inexperienced endoscopists
OR
EUS perfomed by an endoscopist without formal EUS training program
OR
EUS performed in non-high volume centers

Outcome

accurate staging of rectal cancer (according to the UICC staging system)

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Clinical Competence"[Mesh] OR "Education, Medical, Graduate"[Mesh] OR "Gastroenterology/education"[Mesh] OR (volume[Title/Abstract] AND (center[Title/Abstract] OR centers[Title/Abstract] OR hospital[Title/Abstract] OR hospitals[Title/Abstract] OR clinic[Title/Abstract] OR clinics[Title/Abstract])) OR ((Experience*[Title/Abstract] OR train*[Title/Abstract]) AND (endoscopist[Title/Abstract] OR endoscopists[Title/Abstract])) OR ((GATE[Title/Abstract] OR DGVS[Title/Abstract] OR EFSUMB[Title/Abstract] OR DEGUM[Title/Abstract] OR ASGE[Title/Abstract]) AND (education[Title/Abstract] OR training[Title/Abstract] OR teach*[Title/Abstract]))) **AND** ("Endosonography"[Mesh] OR EUS[Title/Abstract]) **AND** ("Neoplasm Staging"[Mesh] OR stag*[Title/Abstract] OR infiltration[Title/Abstract] OR TNM[Title/Abstract] OR (("Lymph Nodes"[Mesh] OR "lymph node"[Title/Abstract] OR "lymph nodes"[Title/Abstract] OR "lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract]) AND (metastasis[Title/Abstract] OR metastases[Title/Abstract])) OR "Lymphatic Metastasis"[Mesh]) **AND** ((("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct"[Title/Abstract] OR biliary[Title/Abstract] OR pancreatic[Title/Abstract] OR rectal[Title/Abstract] OR gastric[Title/Abstract] OR esophageal[Title/Abstract] OR oesophageal[Title/Abstract]) AND (cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign* [Title/Abstract] OR tumor [Title/Abstract] OR tumour [Title/Abstract] OR tumors [Title/Abstract] OR tumours [Title/Abstract] OR carcinom* [Title/Abstract])) OR "Biliary Tract Neoplasms"[Mesh] OR "Pancreatic Neoplasms"[Mesh] OR "Gastrointestinal Neoplasms"[Mesh] OR "Rectal Neoplasms"[Mesh]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti)) OR ((GATE:ab,ti OR DGVS:ab,ti OR EFSUMB:ab,ti OR DEGUM:ab,ti OR ASGE:ab,ti) AND (education:ab,ti OR training:ab,ti OR teach*:ab,ti))) **AND** ('endoscopic echography'/exp OR EUS:ab,ti) **AND** ('cancer

staging'/exp OR stag*:ab,ti OR infiltration:ab,ti OR TNM:ab,ti OR (('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti) AND (metastasis:ab,ti OR metastases:ab,ti)) OR 'lymph node metastasis'/exp) **AND** ((('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti OR rectal:ab,ti OR gastric:ab,ti OR esophageal:ab,ti OR oesophageal:ab,ti) AND (cancer:ab,ti   OR neoplasm*:ab,ti OR malign*:ab,ti   OR tumor:ab,ti   OR tumour:ab,ti   OR tumors:ab,ti   OR tumours:ab,ti OR carcinom*:ab,ti)) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR 'rectum cancer'/exp OR 'esophagus cancer'/exp OR 'digestive system cancer'/exp) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and **Database of Abstracts of Reviews of Effects (DARE)**
#1   MeSH descriptor: [Clinical Competence] explode all trees
#2   MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3   MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4   (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5   (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6   (GATE or DGVS or EFSUMB or DEGUM or ASGE) and (education or training or teaching):ti,ab,kw (Word variations have been searched)
#7   #6 or #5 or #4 or #3 or #2or #1
#8   MeSH descriptor: [Endosonography] explode all trees
#9   EUS:ti,ab,kw (Word variations have been searched)
#10   #8 or #9
#11   MeSH descriptor: [Neoplasm Staging] explode all trees
#12   MeSH descriptor: [Lymphatic Metastasis] explode all trees
#13   MeSH descriptor: [Lymph Nodes] explode all trees
#14   lymph node:ti,ab,kw (Word variations have been searched)
#15   metastasis:ti,ab,kw (Word variations have been searched)
#16   #13 or #14
#17   #16 and #15
#18   staging or infiltration or TNM:ti,ab,kw (Word variations have been searched)
#19   #17 or #18 or #11 or #12
#20   MeSH descriptor: [Common Bile Duct] explode all trees
#21   CBD or biliary or pancreatic or bile duct or rectal or gastric or esphageal:ti,ab,kw (Word variations have been searched)
#22   cancer or neoplasm or malign or tumor or carcinoma:ti,ab,kw (Word variations have been searched)
#23   #20 or #21
#24   #23 and #22
#25   MeSH descriptor: [Biliary Tract Neoplasms] explode all trees
#26   MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#27   MeSH descriptor: [Gastrointestinal Neoplasms] explode all trees
#28   MeSH descriptor: [Rectal Neoplasms] explode all trees
#29   #24 or #28 or #27 or #25 or #26
#30   #29 and #19 and #7 and #10 Publication Year from 2000 to 2015

Primary studies

PubMed

("Clinical Competence"[Mesh] OR "Education, Medical, Graduate"[Mesh] OR "Gastroenterology/education"[Mesh] OR (volume[Title/Abstract] AND (center[Title/Abstract] OR centers[Title/Abstract] OR hospital[Title/Abstract] OR hospitals[Title/Abstract] OR clinic[Title/Abstract] OR clinics[Title/Abstract])) OR ((Experience*[Title/Abstract] OR train*[Title/Abstract]) AND (endoscopist[Title/Abstract] OR endoscopists[Title/Abstract])) OR ((GATE[Title/Abstract] OR DGVS[Title/Abstract] OR EFSUMB[Title/Abstract] OR DEGUM[Title/Abstract] OR ASGE[Title/Abstract]) AND (education[Title/Abstract] OR training[Title/Abstract] OR teach*[Title/Abstract]))) **AND** ("Endosonography"[Mesh] OR EUS[Title/Abstract]) **AND** ("Neoplasm Staging"[Mesh] OR stag*[Title/Abstract] OR infiltration[Title/Abstract] OR TNM[Title/Abstract] OR (("Lymph Nodes"[Mesh] OR "lymph node"[Title/Abstract] OR "lymph nodes"[Title/Abstract] OR "lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract]) AND (metastasis[Title/Abstract] OR metastases[Title/Abstract])) OR "Lymphatic Metastasis"[Mesh]) **AND** ((("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct"[Title/Abstract] OR biliary[Title/Abstract] OR pancreatic[Title/Abstract] OR rectal[Title/Abstract] OR gastric[Title/Abstract] OR esophageal[Title/Abstract] OR oesophageal[Title/Abstract]) AND (cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign* [Title/Abstract] OR tumor [Title/Abstract] OR tumour [Title/Abstract] OR tumors [Title/Abstract] OR tumours [Title/Abstract] OR carcinom* [Title/Abstract])) OR "Biliary Tract Neoplasms"[Mesh] OR "Pancreatic Neoplasms"[Mesh] OR "Gastrointestinal Neoplasms"[Mesh] OR "Rectal Neoplasms"[Mesh]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti)) OR ((GATE:ab,ti OR DGVS:ab,ti OR EFSUMB:ab,ti OR DEGUM:ab,ti OR ASGE:ab,ti) AND (education:ab,ti OR training:ab,ti OR teach*:ab,ti))) **AND** ('endoscopic echography'/exp OR EUS:ab,ti) **AND** ('cancer staging'/exp OR stag*:ab,ti OR infiltration:ab,ti OR TNM:ab,ti OR (('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti) AND (metastasis:ab,ti OR metastases:ab,ti)) OR 'lymph node metastasis'/exp) **AND** ((('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti OR rectal:ab,ti OR gastric:ab,ti OR esophageal:ab,ti OR oesophageal:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti)) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR 'rectum cancer'/exp OR 'esophagus cancer'/exp OR 'digestive system cancer'/exp) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1   MeSH descriptor: [Clinical Competence] explode all trees
#2   MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3   MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]

#4   (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5   (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6   (GATE or DGVS or EFSUMB or DEGUM or ASGE) and (education or training or teaching):ti,ab,kw (Word variations have been searched)
#7   #6 or #5 or #4 or #3 or #2or #1
#8   MeSH descriptor: [Endosonography] explode all trees
#9   EUS:ti,ab,kw (Word variations have been searched)
#10   #8 or #9
#11   MeSH descriptor: [Neoplasm Staging] explode all trees
#12   MeSH descriptor: [Lymphatic Metastasis] explode all trees
#13   MeSH descriptor: [Lymph Nodes] explode all trees
#14   lymph node:ti,ab,kw (Word variations have been searched)
#15   metastasis:ti,ab,kw (Word variations have been searched)
#16   #13 or #14
#17   #16 and #15
#18   staging or infiltration or TNM:ti,ab,kw (Word variations have been searched)
#19   #17 or #18 or #11 or #12
#20   MeSH descriptor: [Common Bile Duct] explode all trees
#21   CBD or biliary or pancreatic or bile duct or rectal or gastric or esphageal:ti,ab,kw (Word variations have been searched)
#22   cancer or neoplasm or malign or tumor or carcinoma:ti,ab,kw (Word variations have been searched)
#23   #20 or #21
#24   #23 and #22
#25   MeSH descriptor: [Biliary Tract Neoplasms] explode all trees
#26   MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#27   MeSH descriptor: [Gastrointestinal Neoplasms] explode all trees
#28   MeSH descriptor: [Rectal Neoplasms] explode all trees
#29   #24 or #28 or #27 or #25 or #26
#30   #29 and #19 and #7 and #10 Publication Year from 2000 to 2015

Results

Results of the bibliographic searches
After removing duplicates, 112 articles (6 reviews and 106 primary studies) were found. No potentially relevant systematic reviews were found; 5 primary studies were considered potentially relevant and acquired in full text (See flow chart).

Included studies
Five studies were finally included (Carmody 2000, Harewood 2002, Morris 2011, Marusch 2011, van Vliet 2006).

Clinical question A_V. (a)

One study (van Vliet 2006) assessing accurate staging of esophageal cancer was included.

Study	Patients	Intervention	T stage-accuracy	N stage-accuracy	M stage-accuracy
Van Vliet 2006	244 patients underwent EUS followed by esophageal resection without neoadjuvant chemo- or radiotherapy.	low-volume center: EUS performed by (4 senior and 5 junior endoscopists with fewer than 50 EUS staging procedures per year High volume Centers found by literature search : higher than 50 per year	Overall Low-volume center (EUS probe passage)= 54% (94/173) Low-volume center (no EUS probe passage)= 69% (49/71) High-volume centers= 68%-89% T1 Low-volume center (EUS probe passage)= 21% (9/43) Low-volume center (no EUS probe passage) =- High-volume centers=33%-100% T2 Low-volume center (EUS probe passage)= 25% (10/40) Low-volume center (no EUS probe passage) 0% (0/6) High-volume centers 12.5%-84% T3 Low-volume center (EUS probe passage)= 85% (75/88) Low-volume center (no EUS probe passage) 79% (49/62) High-volume centers 75%-94%	Low-volume center (EUS probe passage)= 64% (110/171) Low-volume center (no EUS probe passage) =51% (33/65) High-volume centers, %=70-84	Low-volume center (EUS probe passage)= 92% (157/171) Low-volume center (no EUS probe passage) =88% (57/65) High-volume centers, %=81-97

			T4 Low-volume center (EUS probe passage) 0% (0/2) Low-volume center (no EUS probe passage) 0% (0/3) High-volume centers 50%-100%		

Quality of evidence

Study limitations (risk of bias): no
Inconsistency of results: no
Indirectness of evidence: no
Imprecision: yes (only one study with 244 patients)
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as moderate because of imprecision

Conclusions

Staging in low volume centres is less accurate than staging performed in high volume (**MODERATE QUALITY OF EVIDENCE**)

Clinical question A V. (b)

No studies were found assessing this clinical question.

Conclusions

No conclusion can be drawn about the association between accurate staging of gastric cancer and experience or training programs of endoscopists because no evidence was found.

Clinical question A V. (c)

One study (Harewood 2002) assessing accurate staging of pancreatic cancer was included.

Study	Patients	Intervention	Accuracy
Harewood 2002	20 patients with pancreatic masses underwent EUS-FNA 3 endosonographers	Group A (n=9): patients examined by initial experience which included a formal training period of 2 months Group B (n=11): patients examined by later experience subsequent to "hands-on" training	**Accuracy** based on the original pathology interpretation. Group A= 33% (3/9) Group B= 91% (10/11) p =0.004 vs. group A multivariate analysis : variable predictive of an accurate EUS-FNA result : endosonographer experience OR = 3.0 (95% CI 1.1-8.4)

Quality of evidence

Study limitations (risk of bias): no
Inconsistency of results: no
Indirectness of evidence: no
Imprecision: yes (only one study with 20 patients)
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as low because of imprecision

Conclusions

Staging at the initial endosonographer experience is less accurate than staging performed after formal training
(**LOW QUALITY OF EVIDENCE**)

Clinical question A V. (d)

No studies were found assessing this clinical question.

Conclusions

No conclusion can be drawn about the association between accurate staging of bile duct cancer and experience or training programs of endoscopists because no evidence was found.

Clinical question A V. (e)

Three study (Carmody 2000, Morris 2011, Marusch 2011) assessing accurate staging of rectal cancer were included.

Study	Patients	Intervention	T stage-accuracy	N stage-accuracy	Other
Carmody, 2000	41 patients with a diagnosis of a rectal neoplasm undergoing a TRUS examination	1-12 examinations vs 13-24 examinations vs 25-36 examinations performed by the same operator	**Accuracy of Depth Invasion(T)** 1-12=58% 13-24=92% 25-36=83% Initial 12 examinations=58% Last 24 examinations=87% p= 0.048		**Overall Accuracy of TN stage** 1-12=58% 13-24=92% 25-36=75%
Marusch 2011	7096 patients with rectal carcinoma who did not receive neoadjuvant radio-chemotherapy after EUS	**hospital volume** ≤10EUS/year Vs 11-30EUS/year Vs >30EUS/year	**uT-pT correspondence by hospital volume, %** ≤10EUS/year=63.2% (95%CI 61.5%-64.9%) 11-30 EUS/year=64.6% (95%CI 62.9%-66.2%) >30EUS/year =73.1% (95%CI 69.4%-76.5%) **Under staging by hospital volume, %** ≤10EUS/year=17.3% (95%CI 16.0%-18.7%) 11-30EUS/year=19.5% (95%CI 18.1%-20.8%) >30EUS/year =13.5% (95%CI 10.9%-16.5%)		

			Over staging by hospital volume, % ≤10EUS/year=19.4% (95%CI 18.1%-20.9%) 11-30EUS/year=16.0% (95%CI 14.8%-17.3%) >30EUS/year=13.3% (95%CI 10.8%-16.3%)		
Morris 2011	272 patients with rectal adenocarcinoma assessed by ERUS 233 were assessable for T-stage and 142 for N-stage	All examinations performed by a single operator Time period 1: 1 year; 40 patients examined Time period 2: 3 years: 110 patients examined Time period 3: 3 years: 122 patients examined	**T-stage** correct Time Period 1 =32/39 Time Period 2=79/96 Time Period 3=80/98 Accuracy, % Time Period 1=82.1 Time Period 2=82.3 Time Period 3=81.6 P:0.99	**N-stage** Correct Time Period 1=20/24 Time Period 2=38/56 Time Period 3=46/62 Accuracy, % Time Period 1=83.3 Time Period 2=67.9 Time Period 3=74.2 P:0.31	

Quality of evidence

Study limitations (risk of bias): yes (not all patients received the reference standard and were included in the analysis
Inconsistency of results: no
Indirectness of evidence: yes (two studies compared accuracy of examinations performed by only one endosonographer)
Imprecision: no
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as low because of study limitations and indirectness

Conclusions

Accuracy of staging of rectal cancer does not seem to be strongly correlated with endosonographer experience, nor by hospital volume
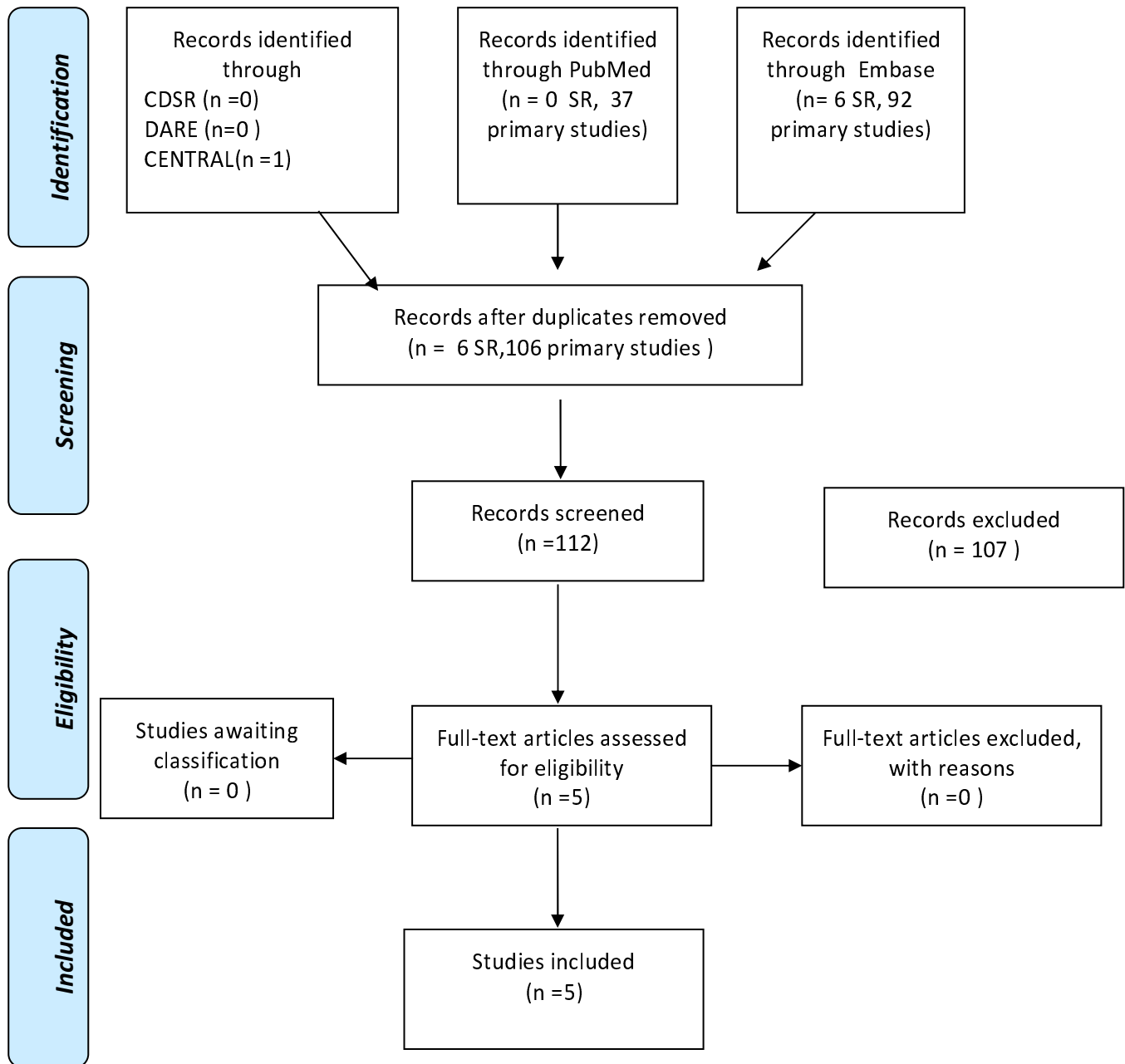(**LOW QUALITY OF EVIDENCE**)

References

Included studies
1. Carmody, B. J. and Otchy, D. P. Learning curve of transrectal ultrasound. Dis Colon Rectum. 2000 Feb; 43(2):193-7.
2. Harewood, G. C.; Wiersema, L. M.; Halling, A. C.; Keeney, G. L.; Salamao, D. R., and Wiersema, M. J. Influence of EUS training and pathology interpretation on accuracy of EUS-guided fine needle aspiration of pancreatic masses. Gastrointest Endosc. 2002 May; 55(6):669-73.
3. Morris, O. J.; Draganic, B., and Smith, S. Does a learning curve exist in endorectal two-dimensional ultrasound accuracy? Tech Coloproctol. 2011 Sep; 15(3):301-11
4. Marusch F.; Ptok H.; Sahm M.; Schmidt U.; Ridwelski K.; Gastinger I., and Lippert H. Endorectal ultrasound in rectal carcinoma do the literature results really correspond to the realities of routine clinical care? Endoscopy. 2011; 43(5):425-431
5. van Vliet E.P.M.; Eijkemans M.J.C.; Poley J.-W.; Steyerberg E.W.; Kuipers E.J., and Siersema P.D. Staging of esophageal carcinoma in a low-volume EUS center compared with reported results from high-volume centers. Gastrointest. Endosc. 2006; 63(7):938-947

PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n =0)
DARE (n=0)
CENTRAL(n =1)

Records identified through PubMed
(n = 0 SR, 37 primary studies)

Records identified through Embase
(n= 6 SR, 92 primary studies)

Screening

Records after duplicates removed
(n = 6 SR,106 primary studies)

Records screened
(n =112)

Records excluded
(n = 107)

Eligibility

Studies awaiting classification
(n = 0)

Full-text articles assessed for eligibility
(n =5)

Full-text articles excluded, with reasons
(n =0)

Included

Studies included
(n =5)

S.C. Epidemiologia screening, registro tumori –
CPO Piemonte
Direttore: Dr. Nereo Segnan
via Cavour 31, 10123 Torino
tel. 011.6333881 - fax 011.6333861
www.cpo.it - email: info@cpo.it

AZIENDA OSPEDALIERO - UNIVERSITARIA
Città della Salute e della Scienza di Torino

CPO
Centro di Riferimento per l'Epidemiologia
e la Prevenzione Oncologica in Piemonte

IDENTIFICATION OF DEFINED LANDMARKS

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

1.13 (A VI) **Does experience of endoscopists or teaching endoscopists in formal training programs** (e.g., GATE – „gastroenterological education-training endoscopy" (DGVS), Principals of Training in Gastrointestinal Endoscopy (ASGE),EFSUMB, DEGUM)**influence the quality performance of EUS** (% of examinations with well documented **depiction of relevant structures**, specific for the indication of EUS) ? (Esophageal cancer: visualization of the tumor, mediastinum (lymph nodes), gastroesophageal junction, celiac axis (lymph nodes) and left lobe of the liver (to rule out metastatic disease). Diseases of the pancreato-biliary system: Visualization of the entire pancreas (signs of chronic pancreatitis, pancreatic cyst) pancreatic duct, common bile duct (stricture, dilation, stones). Rectal cancer: visualization of the tumor :location, extention, infiltration of surrounding structures; visualization of surrounding structures: genitourinary structures, iliacvessels,sphincter apparatus, lymph nodes)

Population
Patients undergoing EUS

Intervention
EUS performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS perfomed by experienced endoscopist having undergone formal EUS training program
OR
EUS performed in high volume centers

Control
EUS performed by inexperienced endoscopists
OR
EUS perfomed by an endoscopist without formal EUS training program
OR
EUS performed in non-high volume centers

Outcome
Identification of **defined landmarks**

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

<u>PubMed</u>
("Clinical Competence"[Mesh] OR "Education, Medical, Graduate"[Mesh] OR "Gastroenterology/education"[Mesh] OR (volume[Title/Abstract] AND (center[Title/Abstract] OR centers[Title/Abstract] OR hospital[Title/Abstract] OR hospitals[Title/Abstract] OR clinic[Title/Abstract] OR clinics[Title/Abstract])) OR ((Experience*[Title/Abstract] OR train*[Title/Abstract]) AND (endoscopist[Title/Abstract] OR endoscopists[Title/Abstract])) OR ((GATE[Title/Abstract] OR DGVS[Title/Abstract] OR EFSUMB[Title/Abstract] OR DEGUM[Title/Abstract] OR ASGE[Title/Abstract]) AND (education[Title/Abstract] OR training[Title/Abstract] OR teach*[Title/Abstract]))) **AND** ("Endosonography"[Mesh] OR EUS[Title/Abstract]) **AND** ((("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct"[Title/Abstract] OR biliary[Title/Abstract] OR pancreatic[Title/Abstract] OR rectal[Title/Abstract] OR gastric[Title/Abstract] OR esophageal[Title/Abstract] OR oesophageal[Title/Abstract]) AND (cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign* [Title/Abstract] OR tumor [Title/Abstract] OR tumour [Title/Abstract] OR tumors [Title/Abstract] OR tumours [Title/Abstract] OR carcinom* [Title/Abstract] OR "Lymph Nodes"[Mesh] OR "lymph node"[Title/Abstract] OR "lymph nodes"[Title/Abstract] OR "lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract])) OR "Biliary Tract Neoplasms"[Mesh] OR "Pancreatic Neoplasms"[Mesh] OR "Gastrointestinal Neoplasms"[Mesh] OR "Rectal Neoplasms"[Mesh] OR pancreatitis[Title/Abstract] OR "Pancreatitis"[Mesh] OR "Esophagogastric Junction"[Mesh] OR (("Lymph Nodes"[Mesh] OR "lymph node"[Title/Abstract] OR "lymph nodes"[Title/Abstract] OR "lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract]) AND (mediastinum[Title/Abstract] OR "celiac axis"[Title/Abstract])) OR "Pancreatic Cyst"[Mesh] OR "pancreatic cyst"[Title/Abstract] OR "pancreatic cysts"[Title/Abstract] OR (("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct" [Title/Abstract]) AND (stone*[Text Word] OR calculi[Text Word] OR calculus[Text Word] OR stricture[Text Word] OR stenosis[Text Word] OR dilation[Text Word])) OR (sphincter[Title/Abstract] AND apparatus[Title/Abstract]) OR (iliac[Title/Abstract] AND (vessel [Title/Abstract] OR vessels[Title/Abstract])) OR (genitourinary[Title/Abstract] AND (structures[Title/Abstract] OR structure[Title/Abstract])) OR (("Liver"[Mesh] OR liver[Title/Abstract]) AND "left lobe" [Title/Abstract])) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

<u>Embase</u>
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti)) OR ((GATE:ab,ti OR DGVS:ab,ti OR EFSUMB:ab,ti OR DEGUM:ab,ti OR ASGE:ab,ti) AND (education:ab,ti OR training:ab,ti OR teach*:ab,ti))) **AND** ('endoscopic echography'/exp OR EUS:ab,ti) **AND** (((('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti OR rectal:ab,ti OR gastric:ab,ti OR esophageal:ab,ti OR oesophageal:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR 'lymph node'/exp OR 'lymph node':ab,ti OR 'lymph

nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti)) OR pancreatitis:ab,ti OR 'pancreatitis'/exp OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR 'rectum cancer'/exp OR 'esophagus cancer'/exp OR 'digestive system cancer'/exp OR 'mediastinum lymph node'/exp OR (('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti) AND ('celiac axis':ab,ti OR mediastinum:ab,ti)) OR 'pancreas cyst'/exp OR 'pancreatic cyst':ab,ti OR 'pancreatic cysts':ab,ti OR (('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti) AND (stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti OR stricture:ab,ti OR stenosis:ab,ti)) OR (sphincter:ab,ti AND apparatus:ab,ti) OR (iliac:ab,ti AND (vessel:ab,ti OR vessels:ab,ti)) OR (genitourinary:ab,ti AND (structures:ab,ti OR structure:ab,ti)) OR (('liver'/exp OR liver:ab,ti) AND 'left lobe':ab,ti)) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and **Database of Abstracts of Reviews of Effects (DARE)**

#1   MeSH descriptor: [Clinical Competence] explode all trees
#2   MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3   MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4   (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5   (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6   (GATE or DGVS or EFSUMB or DEGUM or ASGE) and (education or training or teaching):ti,ab,kw (Word variations have been searched)
#7   #6 or #5 or #4 or #3 or #2or #1
#8   MeSH descriptor: [Endosonography] explode all trees
#9   EUS:ti,ab,kw (Word variations have been searched)
#10   #8 or #9
#11   MeSH descriptor: [Common Bile Duct] explode all trees
#12   CBD or biliary or pancreatic or bile duct or rectal or gastric or esphageal:ti,ab,kw (Word variations have been searched)
#13   #11 or #12
#14   cancer or neoplasm or malign or tumor or carcinoma:ti,ab,kw (Word variations have been searched)
#15   MeSH descriptor: [Lymph Nodes] explode all trees
#16   lymph node:ti,ab,kw (Word variations have been searched)
#17   #14 or #15 or #16
#18   #13 and #17
#19   MeSH descriptor: [Esophagogastric Junction] explode all trees
#20   pancreatitis:ti,ab,kw (Word variations have been searched)
#21   MeSH descriptor: [Biliary Tract Neoplasms] explode all trees
#22   MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#23   MeSH descriptor: [Gastrointestinal Neoplasms] explode all trees
#24   MeSH descriptor: [Rectal Neoplasms] explode all trees
#25   MeSH descriptor: [Pancreatitis] explode all trees
#26   #15 or #16
#27   mediastinum or celic axis:ti,ab,kw (Word variations have been searched)
#28   #26 and #27
#29   MeSH descriptor: [Pancreatic Cyst] explode all trees
#30   pancreatic cyst:ti,ab,kw (Word variations have been searched)
#31   CBD or bile duct:ti,ab,kw (Word variations have been searched)

#32   stone or calculus or stricture or stenosis or dilation:ti,ab,kw (Word variations have been s searched)

#33   (#11 or #31) and #32

#34   sphincter apparatus:ti,ab,kw or iliac vessels:ti,ab,kw or genitourinary structures:ti,ab,kw or liver and left lobe:ti,ab,kw (Word variations have been searched)

#35   #34 or #33 or #28 or #29 or #30 or #25 or #24 or #23 or #22 or #21 or #20 or #19 or #18

#36   #10 and #7 and #35 Publication Year from 2000 to 2015

Primary studies

PubMed

("Clinical Competence"[Mesh] OR "Education, Medical, Graduate"[Mesh] OR "Gastroenterology/education"[Mesh] OR (volume[Title/Abstract] AND (center[Title/Abstract] OR centers[Title/Abstract] OR hospital[Title/Abstract] OR hospitals[Title/Abstract] OR clinic[Title/Abstract] OR clinics[Title/Abstract])) OR ((Experience*[Title/Abstract] OR train*[Title/Abstract]) AND (endoscopist[Title/Abstract] OR endoscopists[Title/Abstract])) OR ((GATE[Title/Abstract] OR DGVS[Title/Abstract] OR EFSUMB[Title/Abstract] OR DEGUM[Title/Abstract] OR ASGE[Title/Abstract]) AND (education[Title/Abstract] OR training[Title/Abstract] OR teach*[Title/Abstract]))) **AND** ("Endosonography"[Mesh] OR EUS[Title/Abstract]) **AND** (((("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct"[Title/Abstract] OR biliary[Title/Abstract] OR pancreatic[Title/Abstract] OR rectal[Title/Abstract] OR gastric[Title/Abstract] OR esophageal[Title/Abstract] OR oesophageal[Title/Abstract]) AND (cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign* [Title/Abstract] OR tumor [Title/Abstract] OR tumour [Title/Abstract] OR tumors [Title/Abstract] OR tumours [Title/Abstract] OR carcinom* [Title/Abstract] OR "Lymph Nodes"[Mesh] OR "lymph node"[Title/Abstract] OR "lymph nodes"[Title/Abstract] OR "lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract])) OR "Biliary Tract Neoplasms"[Mesh] OR "Pancreatic Neoplasms"[Mesh] OR "Gastrointestinal Neoplasms"[Mesh] OR "Rectal Neoplasms"[Mesh] OR pancreatitis[Title/Abstract] OR "Pancreatitis"[Mesh] OR "Esophagogastric Junction"[Mesh] OR (("Lymph Nodes"[Mesh] OR "lymph node"[Title/Abstract] OR "lymph nodes"[Title/Abstract] OR "lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract]) AND (mediastinum[Title/Abstract] OR "celiac axis"[Title/Abstract])) OR "Pancreatic Cyst"[Mesh] OR "pancreatic cyst"[Title/Abstract] OR "pancreatic cysts"[Title/Abstract] OR (("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct" [Title/Abstract]) AND (stone*[Text Word] OR calculi[Text Word] OR calculus[Text Word] OR stricture[Text Word] OR stenosis[Text Word] OR dilation[Text Word])) OR (sphincter[Title/Abstract] AND apparatus[Title/Abstract]) OR (iliac[Title/Abstract] AND (vessel [Title/Abstract] OR vessels[Title/Abstract])) OR (genitourinary[Title/Abstract] AND (structures[Title/Abstract] OR structure[Title/Abstract])) OR (("Liver"[Mesh] OR liver[Title/Abstract]) AND "left lobe" [Title/Abstract])) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti)) OR ((GATE:ab,ti OR DGVS:ab,ti OR EFSUMB:ab,ti OR DEGUM:ab,ti OR ASGE:ab,ti) AND (education:ab,ti OR training:ab,ti OR teach*:ab,ti))) **AND** ('endoscopic echography'/exp OR EUS:ab,ti) **AND**

(((('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti OR rectal:ab,ti OR gastric:ab,ti OR esophageal:ab,ti OR oesophageal:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR 'lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti)) OR pancreatitis:ab,ti OR 'pancreatitis'/exp OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR 'rectum cancer'/exp OR 'esophagus cancer'/exp OR 'digestive system cancer'/exp OR 'mediastinum lymph node'/exp OR (('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti) AND ('celiac axis':ab,ti OR mediastinum:ab,ti)) OR 'pancreas cyst'/exp OR 'pancreatic cyst':ab,ti OR 'pancreatic cysts':ab,ti OR (('common bile duct'/exp OR CBD:ab,ti OR ' bile duct':ab,ti) AND (stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti OR stricture:ab,ti OR stenosis:ab,ti)) OR (sphincter:ab,ti AND apparatus:ab,ti) OR (iliac:ab,ti AND (vessel:ab,ti OR vessels:ab,ti)) OR (genitourinary:ab,ti AND (structures:ab,ti OR structure:ab,ti)) OR (('liver'/exp OR liver:ab,ti) AND 'left lobe':ab,ti)) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)

#1	MeSH descriptor: [Clinical Competence] explode all trees
#2	MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3	MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4	(center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5	(experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6	(GATE or DGVS or EFSUMB or DEGUM or ASGE) and (education or training or teaching):ti,ab,kw (Word variations have been searched)
#7	#6 or #5 or #4 or #3 or #2or #1
#8	MeSH descriptor: [Endosonography] explode all trees
#9	EUS:ti,ab,kw (Word variations have been searched)
#10	#8 or #9
#11	MeSH descriptor: [Common Bile Duct] explode all trees
#12	CBD or biliary or pancreatic or bile duct or rectal or gastric or esphageal:ti,ab,kw (Word variations have been searched)
#13	#11 or #12
#14	cancer or neoplasm or malign or tumor or carcinoma:ti,ab,kw (Word variations have been searched)
#15	MeSH descriptor: [Lymph Nodes] explode all trees
#16	lymph node:ti,ab,kw (Word variations have been searched)
#17	#14 or #15 or #16
#18	#13 and #17
#19	MeSH descriptor: [Esophagogastric Junction] explode all trees
#20	pancreatitis:ti,ab,kw (Word variations have been searched)
#21	MeSH descriptor: [Biliary Tract Neoplasms] explode all trees
#22	MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#23	MeSH descriptor: [Gastrointestinal Neoplasms] explode all trees
#24	MeSH descriptor: [Rectal Neoplasms] explode all trees
#25	MeSH descriptor: [Pancreatitis] explode all trees
#26	#15 or #16
#27	mediastinum or celic axis:ti,ab,kw (Word variations have been searched)
#28	#26 and #27

#29   MeSH descriptor: [Pancreatic Cyst] explode all trees
#30   pancreatic cyst:ti,ab,kw (Word variations have been searched)
#31   CBD or bile duct:ti,ab,kw (Word variations have been searched)
#32   stone or calculus or stricture or stenosis or dilation:ti,ab,kw (Word variations have been searched)
#33   (#11 or #31) and #32
#34   sphincter apparatus:ti,ab,kw or iliac vessels:ti,ab,kw or genitourinary structures:ti,ab,kw or liver and left lobe:ti,ab,kw (Word variations have been searched)
#35   #34 or #33 or #28 or #29 or #30 or #25 or #24 or #23 or #22 or #21 or #20 or #19 or #18
#36   #10 and #7 and #35 Publication Year from 2000 to 2015

Results

Results of the bibliographic searches
After removing duplicates, 367 articles (11 reviews and 356 primary studies) were found. No potentially relevant systematic reviews were found; 8 primary studies were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies
All the eight studies were excluded: five studies because no outcome of interest (Camody 2000, Harewood 2002, Kachare 2014, Mertz 2004, Morris 2011); one because no comparison of interest (Quinton 2014); one because no intervention of interest: EUS elastography (Soares 2015); one because letter without useful data (Jadav 2013).

Included studies
No studies were retrieved fulfilling the inclusion criteria .
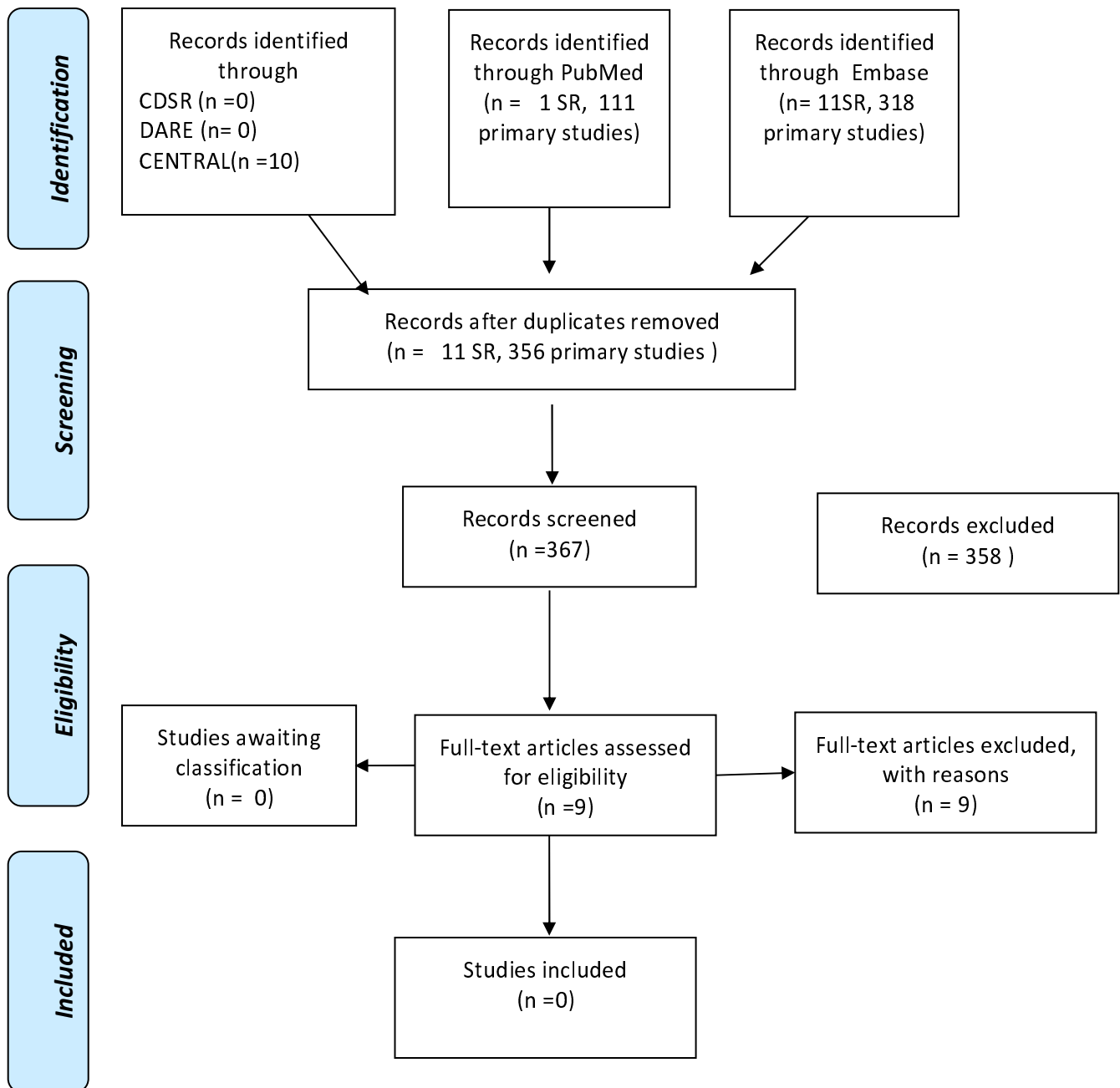
Conclusions

No conclusion can be drawn about the influence experience or training of endoscopists on the quality performance of EUS (% of examinations with well documented depiction of relevant structures, specific for the indication of EUS) because no evidence was found.

References

Excluded studies
1. Carmody, B. J. and Otchy, D. P. Learning curve of transrectal ultrasound. Dis Colon Rectum. 2000 Feb; 43(2):193-7.
2. Jadav, A. M.; Mumbi, C., and Brown, S. R. Does a learning curve exist in endorectal two-dimensional ultrasound accuracy? Tech Coloproctol. 2013 Feb; 17(1):125.
3. Harewood, G. C.; Wiersema, L. M.; Halling, A. C.; Keeney, G. L.; Salamao, D. R., and Wiersema, M. J. Influence of EUS training and pathology interpretation on accuracy of EUS-guided fine needle aspiration of pancreatic masses. Gastrointest Endosc. 2002 May; 55(6):669-73.
4. Kachare S.D.; Kaul A.G.; Fitzgerald T.L., and Zervos E.E. Increasing institutional experience and expertise improves diagnostic yield of endoscopic ultrasound (EUS) in solid pancreatic tumors. HPB. 2014; 1673;
5. Mertz, H. and Gautam, S. The learning curve for EUS-guided FNA of pancreatic cancer. Gastrointest Endosc. 2004 Jan; 59(1):33-7.
6. Morris, O. J.; Draganic, B., and Smith, S. Does a learning curve exist in endorectal two-dimensional ultrasound accuracy? Tech Coloproctol. 2011 Sep; 15(3):301-11.
7. Quinton S.; Srivastava A.K.; Kahrilas I.J.; Keefer L., and Komanduri S. "Breaking the bad news": A survey of practice patterns in disclosing a pancreatic cancer diagnosis amongst us endosonographers. Gastrointest. Endosc. 2014; 79(5):AB193;
8. Soares J.-B.; Iglesias-Garcia J.; Gon+°alves B.; Lindkvist B.; Lari+_o-Noia J.; Bastos P.; Caetano A.C.; Ferreira A.; Pimentel-Nunes P.; Lopes L.; Moutinho-Ribeiro P., and Dominguez-Mu+_oz J.E. Interobserver agreement of EUS elastography in the evaluation of solid pancreatic lesions. Endoscopic Ultrasound. 2015; 4(3):244-249
9. van Vliet E.P.M.; Eijkemans M.J.C.; Poley J.-W.; Steyerberg E.W.; Kuipers E.J., and Siersema P.D. Staging of esophageal carcinoma in a low-volume EUS center compared with reported results from high-volume centers. Gastrointest. Endosc. 2006; 63(7):938-947;

PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n =0)
DARE (n= 0)
CENTRAL(n =10)

Records identified through PubMed
(n = 1 SR, 111 primary studies)

Records identified through Embase
(n= 11SR, 318 primary studies)

Screening

Records after duplicates removed
(n = 11 SR, 356 primary studies)

Records screened
(n =367)

Records excluded
(n = 358)

Eligibility

Studies awaiting classification
(n = 0)

Full-text articles assessed for eligibility
(n =9)

Full-text articles excluded, with reasons
(n = 9)

Included

Studies included
(n =0)

**S.C. Epidemiologia screening, registro tumori –
CPO Piemonte**
Direttore: Dr. Nereo Segnan
via Cavour 31, 10123 Torino
tel. 011.6333881 - fax 011.6333861
www.cpo.it - email: info@cpo.it

ADEQUATE SAMPLING OF PATIENTS UNDERGOING EUS-FNA

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro
Tumori- CPO Piemonte

1.14 (A VII (a)). **Does experience of endoscopists or teaching endoscopists in formal training programs** (e.g., GATE – „gastroenterological education-training endoscopy" (DGVS), Principals of Training in Gastrointestinal Endoscopy (ASGE),EFSUMB, DEGUM) **influence the quality performance of EUS-FNA (adequate sampling (sampling sufficient enough for quantity and quality,diagnostic rates, sensitivity, accuracy) of** *solid masses* (e.g. tumor, lymph node)?

Population
Patients with solid masses (esophagus, mediastinum, stomach, pancreas, bile duct system, rectum: tumor, lymph nodes) undergoing EUS-FNA

Intervention
EUS-FNA performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS-FNA perfomed by experienced endoscopist having undergone formal EUS training program
OR
EUS-FNA performed in high volume centers

Control
EUS-FNA performed by inexperienced endoscopists
OR
EUS-FNA perfomed by an endoscopist without formal EUS training program
OR
EUS-FNA performed in non-high volume centers

Outcome
Adequate sampling(sampling sufficient enough for quantity and quality,diagnostic rates, sensitivity, accuracy) of **solid masses**(diagnosing cancer vs. benign lesion)

1.15 (A VII(b)). **Does experience of endoscopists or teaching endoscopists in formal training programs** (e.g., GATE – „gastroenterological education-training endoscopy" (DGVS), Principals of Training in Gastrointestinal Endoscopy (ASGE),EFSUMB, DEGUM)**influence the quality performance of EUS-FNA (adequate sampling (sampling sufficient enough for quantity and quality,diagnostic rates, sensitivity, accuracy) of** *inflammation* **(e.g.,autoimmune pancreatitis)?**

Population
Patients with *inflammation*(e.g., autoimmune pancreatitis)undergoing EUS-FNA

Intervention
EUS-FNA performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS-FNA perfomed by experienced endoscopist having undergone formal EUS training program
OR
EUS-FNA performed in high volume centers

Control
EUS-FNA performed by inexperienced endoscopists
OR
EUS-FNA perfomed by an endoscopist without formal EUS training program
OR
EUS-FNA performed in non-high volume centers

Outcome
Adequate sampling(sampling sufficient enough for quantity and quality,diagnostic rates, sensitivity, accuracy) of inflammation

Bibliographic searches
Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Clinical Competence"[Mesh] OR "Education, Medical, Graduate"[Mesh] OR "Gastroenterology/education"[Mesh] OR (volume[Title/Abstract] AND (center[Title/Abstract] OR centers[Title/Abstract] OR hospital[Title/Abstract] OR hospitals[Title/Abstract] OR clinic[Title/Abstract] OR clinics[Title/Abstract])) OR ((Experience*[Title/Abstract] OR train*[Title/Abstract]) AND (endoscopist[Title/Abstract] OR endoscopists[Title/Abstract])) OR ((GATE[Title/Abstract] OR DGVS[Title/Abstract] OR EFSUMB[Title/Abstract] OR DEGUM[Title/Abstract] OR ASGE[Title/Abstract]) AND (education[Title/Abstract] OR training[Title/Abstract] OR teach*[Title/Abstract]))) **AND** ("Endosonography"[Mesh] OR "Biopsy, Fine-Needle"[Mesh] OR ("endoscopic ultrasound" [Title/Abstract] AND fine[Title/Abstract] AND needle[Title/Abstract]) OR (EUS[Title/Abstract] AND FNA[Title/Abstract])) **AND** (sampling[Text Word] OR samplings[Title/Abstract] OR "Specimen Handling"[Mesh] OR specimen [Text Word] OR specimens[Title/Abstract] OR "pathology" [Subheading]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract]

OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti)) OR ((GATE:ab,ti OR DGVS:ab,ti OR EFSUMB:ab,ti OR DEGUM:ab,ti OR ASGE:ab,ti) AND (education:ab,ti OR training:ab,ti OR teach*:ab,ti))) **AND** ('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) **AND** ('laboratory diagnosis'/exp OR sampling:ab,ti OR sampling:ab,ti OR specimens:ab,ti OR specimens:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)
#1   MeSH descriptor: [Clinical Competence] explode all trees
#2   MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3   MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4   (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5   (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6   (GATE or DGVS or EFSUMB or DEGUM or ASGE) and (education or training or teaching):ti,ab,kw (Word variations have been searched)
#7   #6 or #5 or #4 or #3 or #2or #1
#8   MeSH descriptor: [Endosonography] explode all trees
#9   MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#10   endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#11   EUS and FNA:ti,ab,kw (Word variations have been searched)
#12   #8 or #9 or #10 or #11
#13   MeSH descriptor: [Specimen Handling] explode all trees
#14   specimen or sampling:ti,ab,kw (Word variations have been searched)
#15   #13 or #14
#16   #15 and #12 and #7 Publication Year from 2000 to 2015

Primary studies

PubMed

("Clinical Competence"[Mesh] OR "Education, Medical, Graduate"[Mesh] OR "Gastroenterology/education"[Mesh] OR (volume[Title/Abstract] AND (center[Title/Abstract] OR centers[Title/Abstract] OR hospital[Title/Abstract] OR hospitals[Title/Abstract] OR clinic[Title/Abstract] OR clinics[Title/Abstract])) OR ((Experience*[Title/Abstract] OR train*[Title/Abstract]) AND (endoscopist[Title/Abstract] OR endoscopists[Title/Abstract])) OR ((GATE[Title/Abstract] OR DGVS[Title/Abstract] OR EFSUMB[Title/Abstract] OR DEGUM[Title/Abstract] OR ASGE[Title/Abstract]) AND (education[Title/Abstract] OR training[Title/Abstract] OR teach*[Title/Abstract]))) **AND** ("Endosonography"[Mesh] OR "Biopsy, Fine-Needle"[Mesh] OR ("endoscopic ultrasound" [Title/Abstract] AND fine[Title/Abstract] AND needle[Title/Abstract]) OR (EUS[Title/Abstract] AND FNA[Title/Abstract])) **AND** (sampling [Text Word] OR samplings[Title/Abstract] OR "Specimen Handling"[Mesh] OR specimen [Text Word] OR specimens[Title/Abstract] OR "pathology" [Subheading]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti)) OR ((GATE:ab,ti OR DGVS:ab,ti OR EFSUMB:ab,ti OR DEGUM:ab,ti OR ASGE:ab,ti) AND (education:ab,ti OR training:ab,ti OR teach*:ab,ti))) **AND** ('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) **AND** ('laboratory diagnosis'/exp OR sampling:ab,ti OR sampling:ab,ti OR specimens:ab,ti OR specimens:ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)

#1   MeSH descriptor: [Clinical Competence] explode all trees
#2   MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3   MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4   (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5   (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6   (GATE or DGVS or EFSUMB or DEGUM or ASGE) and (education or training or teaching):ti,ab,kw (Word variations have been searched)
#7   #6 or #5 or #4 or #3 or #2or #1
#8   MeSH descriptor: [Endosonography] explode all trees
#9   MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#10   endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#11   EUS and FNA:ti,ab,kw (Word variations have been searched)
#12   #8 or #9 or #10 or #11
#13   MeSH descriptor: [Specimen Handling] explode all trees
#14   specimen or sampling:ti,ab,kw (Word variations have been searched)
#15   #13 or #14

#16   #15 and #12 and #7 Publication Year from 2000 to 2015

Results

Results of the bibliographic searches
After removing duplicates, 226 articles (4 reviews and 222 primary studies) were found. No potentially relevant systematic reviews were found; 16 primary studies were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies
Eleven studies were excluded: six because no outcome of interest (Eloubeidi 2005, Groth 2008, Harewood 2000, Lin 2008, Mertz 2004,Varadarajulu 2015); two because no comparison of interest (Lankarani 2011, Nteene 2012); one because patients not in the inclusion criteria (breast) (Feoli 2008); one because comparison and outcome not in the inclusion criteria (Kemp 2010); one commentary of excluded studies (Navani 2011).

Included studies
5 studies were finally included (DePew 2012, Houlton 2011, Nayar 2011, Piramanayagam 2014, Wahidi 2014).

Clinical question A VII. (a)

All five studies provided data on adequate sampling of solid masses. The location of sampling is heterogeneous..

Data of Piramanayagam 2014 was extracted from conference abstracts; evidence tables and quality assessment was not performed because not enough data were provided.

Study	Patients	Intervention	Sampling	sampling adequacy
DePew 2012	1275 patients 1304 endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) procedures 10 proceduralists resulting in 2414 LN biopsies	procedures performed annually by each proceduralist	mediastinal and hilar lymph nodes	Average number of EBUS-TBNA procedures performed annually by each proceduralist was not associated with a difference in sampling adequacy p:0.21
Houlton 2011	790 patients thyroid FNA interpreted at the 3 hospital Centers FNAs were performed by 134 physicians and interpreted by 16 pathologists	Low-volume clinicians (<20 FNAs performed) =125 clinicians high-volume clinicians (≥20 FNAs performed) =9 clinicians	thyroid	**Non diagnostic results, %** High volume clinicians(mean FNAs performed=45)=16% Low volume clinicians(mean FNAs performed=3.1)=15% P=0.47
Nayar 2011	228 consecutive patients with solid pancreatic Lesions EUS-FNA	<u>Comparison 1</u> First 80 cases of a single endoscopist (KO1) who did not receive any hands-on training (independent practice 2003/2004) vs same endoscopist (KO2) after having performed over 500	Pancreas	**Inadequate sampling** Comparison 1 KO1: 13/80 (16.25%) KO2: 4/68 (6%) P: 0.02 Comparison 2 KO2: 4/68 (6%) MN: 8/80 (10%) P. 0.37

		EUS-FNA (2007/2008) <u>Comparison 2</u> KO2 (not receive any hands-on training but performed over 500 EUS-FNA) vs single endoscpoist MN (12-month fellowship: a period of observation followed by hands-on training.)		
Piramanayaga m 2014	132 EUS FNA	one-week, intensive, short-term, hands-on EUS training program on tissue acquisition no prior EUS experience	pancreatic-biliary malignancy, metastatic cancer, luminal cancer, granulomatous/ benign lymph nodes, chronic pancreatitis/benign disease	**overall rate of non-diagnostic specimens** First 18 months=34.2% Second 18 months=18.2% P=0.03
Wahidi 2014	13 pulmonary trainees from three training programs and were observed over a 2-year period	Before EBUS-TBNA, all participants had to complete 30 conventional bronchoscopies, an EBUS-specific didactic curriculum, and a simulation session with a plastic airway model.	mediastinal, hilar, and peri-bronchial structures	**% Endoscopist who complete the essential** **steps of EBUS-TNBA and perform the procedure successfully with adequate tissue sampling** average of five procedures (95% CI, 2-7)=25% After 9 procedures (95% CI, 4-13)=50% after 13 procedures(95% CI, 7-16)=75%

Quality of evidence

Study limitations (risk of bias): no (5 case series studies)
Inconsistency of results: yes (studies assessing the impact of case volume on adequacy did not find an association; studies assessing the impact of experience (n .of cases analysed) found an association)
Indirectness of evidence: no
Imprecision: no
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as very low because of inconsistency and observational data.

Conclusions

Case volume did not seem to have a significant impact on non diagnostic results and inadequate sampling.
Rate of non diagnostic samples decrease with the increase of the number of procedures performed and after a formal training programs
(**VERY LOW QUALITY OF EVIDENCE**).

Clinical question A VII. (b)
No studies were found assessing this clinical question.

Conclusions

No conclusion can be drawn about the association between adequate sampling of inflammation and experience or training programs of endoscopists because no evidence was found.
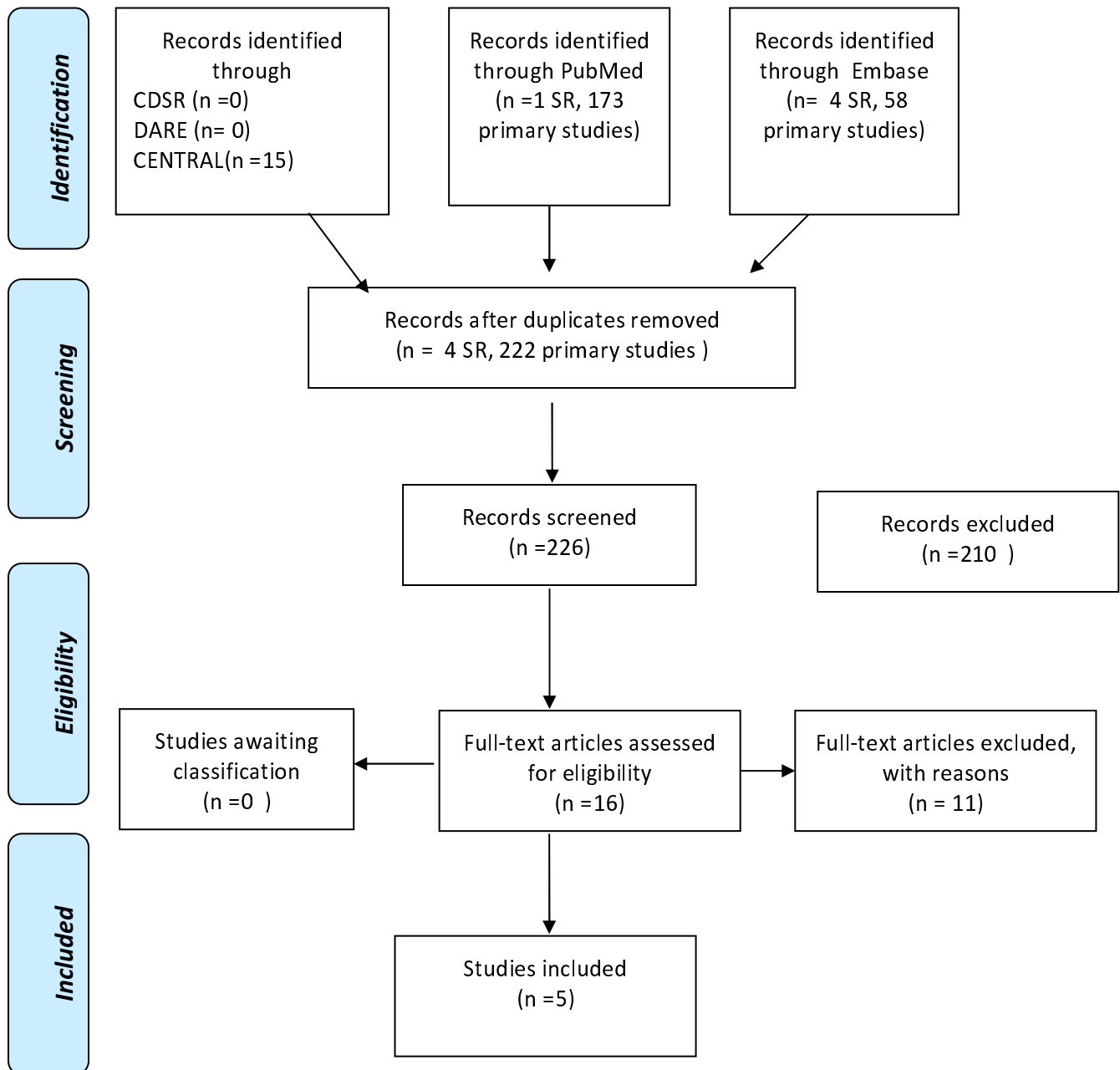
References
<u>Included studies</u>
1. DePew, Z. S.; Edell, E. S.; Midthun, D. E.; Mullon, J. J.; Bungum, A. O.; Decker, P. A., and Maldonado, F. Endobronchial ultrasound-guided transbronchial needle aspiration: determinants of sampling adequacy. J Bronchology Interv Pulmonol. 2012 Oct; 19(4):271-6.
2. Houlton, J. J.; Sun, G. H.; Fernandez, N.; Zhai, Q. J.; Lucas, F., and Steward, D. L. Thyroid fine-needle aspiration: does case volume affect diagnostic yield and interpretation? Arch Otolaryngol Head Neck Surg. 2011 Nov; 137(11):1136-9.
3. Nayar, M.; Joy, D.; Wadehra, V., and Oppong, K. Effect of dedicated and supervised training on achieving competence in EUS-FNA of solid pancreatic lesions. Scand J Gastroenterol. 2011 Jul; 46(7-8):997-1003.
4. Piramanayagam P.; Bang J.Y.; Varadarajulu S., and Palaniswamy K.R. What is the impact of a one-week, intensive, hands-on eus training program on tissue acquisition? Gastrointest. Endosc. 2014; 79(5):AB202-AB203;
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PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n =0)
DARE (n= 0)
CENTRAL(n =15)

Records identified through PubMed
(n =1 SR, 173 primary studies)

Records identified through Embase
(n= 4 SR, 58 primary studies)

Screening

Records after duplicates removed
(n = 4 SR, 222 primary studies)

Records screened
(n =226)

Records excluded
(n =210)

Eligibility

Studies awaiting classification
(n =0)

Full-text articles assessed for eligibility
(n =16)

Full-text articles excluded, with reasons
(n = 11)

Included

Studies included
(n =5)

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MANAGEMENT OF PATIENTS UNDERGOING EUS-FNA

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Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro
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1.16 (A VIII). **Does experience of endoscopists or teaching endoscopists in formal training programs** (e.g., GATE – „gastroenterological education-training endoscopy" (DGVS), Principals of Training in Gastrointestinal Endoscopy (ASGE),EFSUMB, DEGUM) **influence the management of patients undergoing EUS-FNA** (e.g., tissue sampling of both primary tumor and lesion outside of primary field)**?**

Population
Patients undergoing EUS-FNA

Intervention
EUS-FNA performed by experienced (n of procedures specialty or years of training) endoscopists
OR
EUS-FNA perfomed by experienced endoscopist having undergone formal EUS training program
OR
EUS-FNA performed in high volume centers

Control
EUS-FNA performed by inexperienced endoscopists
OR
EUS-FNA perfomed by an endoscopist without formal EUS training program
OR
EUS-FNA performed in non-high volume centers

Outcome
Percentage of examinations in which **EUS-FNA** would **change** the **patient management** (e.g., tissue sampling of both primary tumor and lesion outside of primary field)

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Clinical Competence"[Mesh] OR "Education, Medical, Graduate"[Mesh] OR "Gastroenterology/education"[Mesh] OR (volume[Title/Abstract] AND (center[Title/Abstract] OR centers[Title/Abstract] OR hospital[Title/Abstract] OR hospitals[Title/Abstract] OR clinic[Title/Abstract] OR clinics[Title/Abstract])) OR ((Experience*[Title/Abstract] OR train*[Title/Abstract]) AND (endoscopist[Title/Abstract] OR endoscopists[Title/Abstract])) OR ((GATE[Title/Abstract] OR DGVS[Title/Abstract] OR EFSUMB[Title/Abstract] OR DEGUM[Title/Abstract] OR ASGE[Title/Abstract]) AND (education[Title/Abstract] OR training[Title/Abstract] OR teach*[Title/Abstract]))) **AND** ("Endosonography"[Mesh] OR "Biopsy, Fine-Needle"[Mesh] OR ("endoscopic ultrasound" [Title/Abstract] AND fine[Title/Abstract] AND needle[Title/Abstract]) OR (EUS[Title/Abstract] AND FNA[Title/Abstract])) **AND** ("Patient Care Management"[Mesh] OR management[Title/Abstract] OR impact[Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti)) OR ((GATE:ab,ti OR DGVS:ab,ti OR EFSUMB:ab,ti OR DEGUM:ab,ti OR ASGE:ab,ti) AND (education:ab,ti OR training:ab,ti OR teach*:ab,ti))) **AND** ('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) **AND** ('patient care'/exp OR management:ab,ti OR impact:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and **Database of Abstracts of Reviews of Effects (DARE)**
#1   MeSH descriptor: [Clinical Competence] explode all trees
#2   MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3   MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4   (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5   (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6   (GATE or DGVS or EFSUMB or DEGUM or ASGE) and (education or training or teaching):ti,ab,kw (Word variations have been searched)
#7   #6 or #5 or #4 or #3 or #2or #1
#8   MeSH descriptor: [Endosonography] explode all trees
#9   MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#10   endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#11   EUS and FNA:ti,ab,kw (Word variations have been searched)
#12   #8 or #9 or #10 or #11
#13   MeSH descriptor: [Patient Care Management] explode all trees
#14   patient management or impact:ti,ab,kw (Word variations have been searched)
#15   #13 or #14
#16   #7 and #12 and #15 Publication Year from 2000 to 2015

Primary studies

PubMed
("Clinical Competence"[Mesh] OR "Education, Medical, Graduate"[Mesh] OR "Gastroenterology/education"[Mesh] OR (volume[Title/Abstract] AND (center[Title/Abstract] OR centers[Title/Abstract] OR hospital[Title/Abstract] OR hospitals[Title/Abstract] OR clinic[Title/Abstract] OR clinics[Title/Abstract])) OR ((Experience*[Title/Abstract] OR train*[Title/Abstract]) AND (endoscopist[Title/Abstract] OR endoscopists[Title/Abstract])) OR ((GATE[Title/Abstract] OR DGVS[Title/Abstract] OR EFSUMB[Title/Abstract] OR DEGUM[Title/Abstract] OR ASGE[Title/Abstract]) AND (education[Title/Abstract] OR training[Title/Abstract] OR teach*[Title/Abstract]))) **AND** ("Endosonography"[Mesh] OR "Biopsy, Fine-Needle"[Mesh] OR ("endoscopic ultrasound" [Title/Abstract] AND fine[Title/Abstract] AND needle[Title/Abstract]) OR (EUS[Title/Abstract] AND FNA[Title/Abstract])) **AND** ("Patient Care Management"[Mesh] OR management[Title/Abstract] OR impact[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase
('clinical competence'/exp OR 'medical education'/exp OR (volume:ab,ti AND (center:ab,ti OR centers:ab,ti OR hospital:ab,ti OR hospitals:ab,ti OR clinic:ab,ti OR clinics:ab,ti)) OR ((train*:ab,ti OR Experience*:ab,ti) AND (endoscopist:ab,ti OR endoscopists:ab,ti)) OR ((GATE:ab,ti OR DGVS:ab,ti OR EFSUMB:ab,ti OR DEGUM:ab,ti OR ASGE:ab,ti) AND (education:ab,ti OR training:ab,ti OR teach*:ab,ti))) **AND** ('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) **AND** ('patient care'/exp OR management:ab,ti OR impact:ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1   MeSH descriptor: [Clinical Competence] explode all trees
#2   MeSH descriptor: [Education, Medical, Graduate] explode all trees
#3   MeSH descriptor: [Gastroenterology] explode all trees and with qualifier(s): [Education - ED]
#4   (center or hospital or clinic) and volume:ti,ab,kw (Word variations have been searched)
#5   (experienced or training) and endoscopist:ti,ab,kw (Word variations have been searched)
#6   (GATE or DGVS or EFSUMB or DEGUM or ASGE) and (education or training or teaching):ti,ab,kw (Word variations have been searched)
#7   #6 or #5 or #4 or #3 or #2or #1
#8   MeSH descriptor: [Endosonography] explode all trees
#9   MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#10   endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#11   EUS and FNA:ti,ab,kw (Word variations have been searched)
#12   #8 or #9 or #10 or #11
#13   MeSH descriptor: [Patient Care Management] explode all trees
#14   patient management or impact:ti,ab,kw (Word variations have been searched)
#15   #13 or #14
#16   #7 and #12 and #15 Publication Year from 2000 to 2015

Results

<u>Results of the bibliographic searches</u>
After removing duplicates, 167 articles (5 reviews and 162 primary studies) were found. Other five studies were suggested by authors. No potentially relevant systematic reviews were found; 13 primary studies were considered potentially relevant and acquired in full text (See flow chart).

<u>Excluded studies</u>
Thirteen studies were excluded: four studies because no outcome of interest (Houlton 2011, Lankarani 2011, Pyramanayagan 2014, Varadarajulu 2015); five because no comparison of interest (Bluen 2012, Chong 2005, Del Vecchio Blanco 2015, Mortensen 2001, Shami 2004); one because no intervention of interest (Feoli 2008); one because editorial (Kahaleh 2013); one because letter without useful data (Hirdes 2011); one because narrative review without useful data (Scheiman 2008)
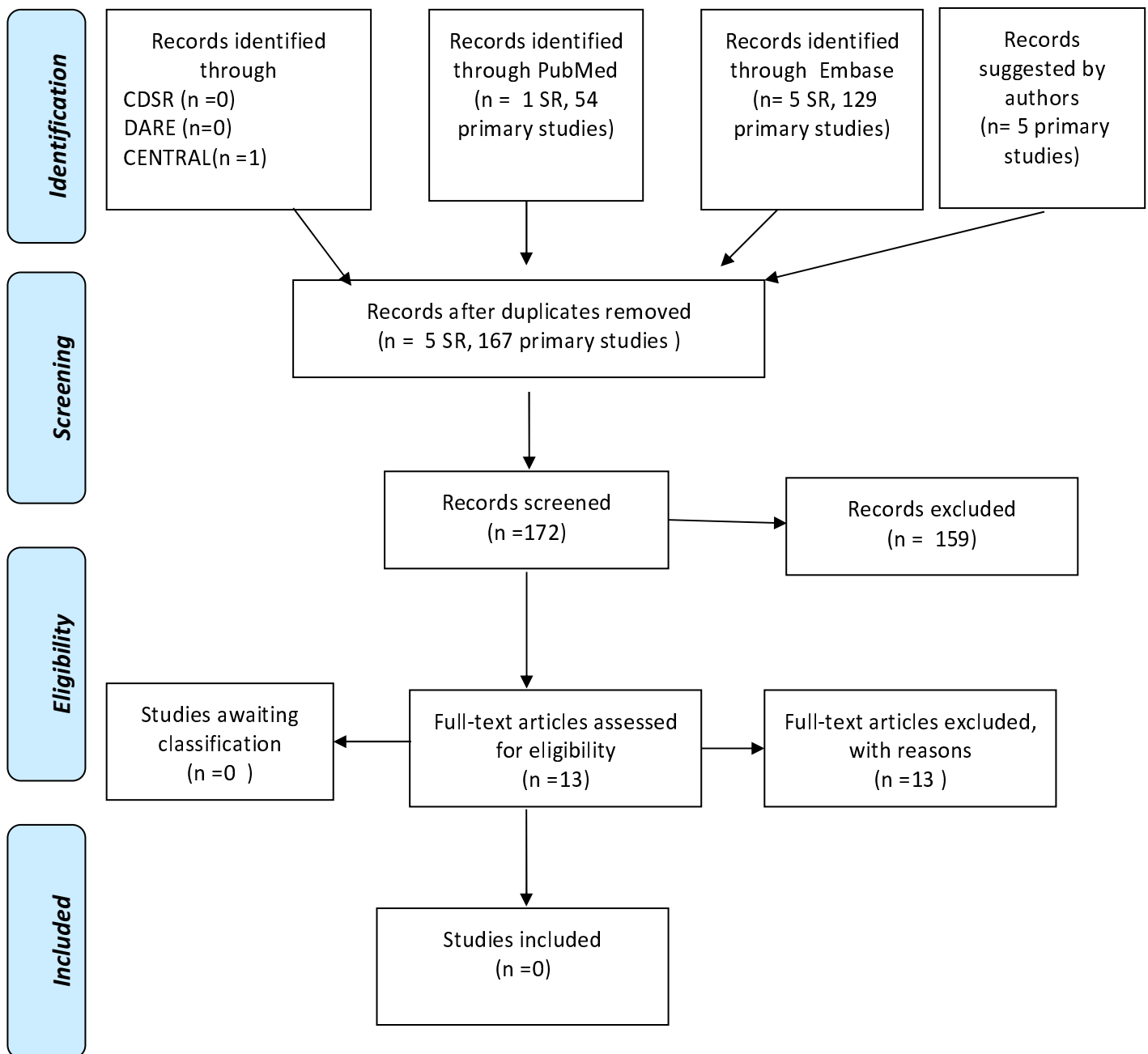
Conclusions

No conclusion can be drawn about the influence experience or training of endoscopists on the management of patients undergoing EUS-FNA because no evidence was found.

References

Excluded studies

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4. Feoli, F.; Paesmans, M., Van Eeckhout, P. Fine needle aspiration cytology of the breast: impact of experience on accuracy, using standardized cytologic criteria. Acta Cytol. 2008 Mar-2008 Apr 30; 52(2):145-51.
5. Hirdes, M. M, Vleggaar, F. P. Performance of EUS-FNA for mediastinal lymphadenopathy: impact on patient management and costs in low-volume EUS centers. Surg Endosc. 2011 Sep; 25(9):3124-5.
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11. Scheiman JM. Management of cystic lesions of the pancreas. J Gastrointest Surg. 2008;12:405-7.
12. Shami VM, Parmar KS, Waxman I. Clinical impact of endoscopic ultrasound and endoscopic ultrasound-guided fine-needle aspiration in the management of rectal carcinoma. Dis Colon Rectum. 2004;47:59-65.
13. Varadarajulu, S.; Holt, B. A.; Bang, J. Y.; Hasan, M. K.; Logue, A.; Tamhane, A.; Hawes, R. H., Hebert-Magee, S. Training endosonographers in cytopathology: improving the results of EUS-guided FNA. Gastrointest Endosc. 2015 Jan; 81(1):104-10.

PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n =0)
DARE (n=0)
CENTRAL(n =1)

Records identified through PubMed
(n = 1 SR, 54 primary studies)

Records identified through Embase
(n= 5 SR, 129 primary studies)

Records suggested by authors
(n= 5 primary studies)

Screening

Records after duplicates removed
(n = 5 SR, 167 primary studies)

Records screened
(n =172)

Records excluded
(n = 159)

Eligibility

Studies awaiting classification
(n =0)

Full-text articles assessed for eligibility
(n =13)

Full-text articles excluded, with reasons
(n =13)

Included

Studies included
(n =0)

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SUCCESS RATE OF CANNULATION

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Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

1.17. Frequency with which cannulation of biliary duct in patients with native major papillae without surgically altered anatomy undergoing ERCP for extraction of common bile duct stones is achieved.

Population
patients with native major papillae without surgically altered anatomy undergoing ERCP

Intervention
deep cannulation of biliary duct

Control
None

Outcome
achieved cannulation rate

Bibliographic searches
Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 29/6/2016 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) **AND** ("Catheterization"[Mesh] OR cannulation[Title/Abstract] OR "biliary cannulation"[Text Word]) **AND** ("Ampulla of Vater"[Mesh] OR (native[Title/Abstract] AND (papilla[Title/Abstract] OR papillae[Title/Abstract]))) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase

('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) **AND** (('cannulation'/exp AND 'bile duct'/exp) OR cannulation:ab,ti) **AND** ('Vater papilla'/exp OR (native:ab,ti AND (papilla:ab,ti OR papillae:ab,ti))) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and **Database of Abstracts of Reviews of Effects (DARE)**

#1   MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#2   ERCP:ti,ab,kw (Word variations have been searched)
#3   #1 or #2
#4   MeSH descriptor: [Catheterization] explode all trees
#5   cannulation:ti,ab,kw (Word variations have been searched)
#6   biliary cannulation:ti,ab,kw (Word variations have been searched)
#7   #4 or #5 or #6
#8   MeSH descriptor: [Ampulla of Vater] explode all trees
#9   native papilla:ti,ab,kw (Word variations have been searched)
#10   #8 or #9
#11   #7 and #3 and #10   Publication Year from 2000 to 2016

Primary studies

PubMed

("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) **AND** ("Catheterization"[Mesh] OR cannulation[Title/Abstract] OR "biliary cannulation"[Text Word]) **AND** ("Ampulla of Vater"[Mesh] OR (native[Title/Abstract] AND (papilla[Title/Abstract] OR papillae[Title/Abstract]))) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) **AND** (('cannulation'/exp AND 'bile duct'/exp) OR cannulation:ab,ti) **AND** ('Vater papilla'/exp OR (native:ab,ti AND (papilla:ab,ti OR papillae:ab,ti))) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)

#1   MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#2   ERCP:ti,ab,kw (Word variations have been searched)
#3   #1 or #2
#4   MeSH descriptor: [Catheterization] explode all trees
#5   cannulation:ti,ab,kw (Word variations have been searched)
#6   biliary cannulation:ti,ab,kw (Word variations have been searched)
#7   #4 or #5 or #6
#8   MeSH descriptor: [Ampulla of Vater] explode all trees

#9   native papilla:ti,ab,kw (Word variations have been searched)
#10   #8 or #9
#11   #7 and #3 and #10   Publication Year from 2000 to 2016

Results

Results of the bibliographic searches
After removing duplicates, 246 articles (5 reviews and 241 primary studies) were found. 51 primary studies were considered potentially relevant and acquired in full text. (See flow chart).
A sample size of 100 patients was used as a cut off for inclusion.

Excluded studies
23 articles were excluded: 1 because no population of interest (Skinner 2014); 1 because ERCP was performed by trainees (Pan 2015); 17 because conference abstracts (Alburquerque 2013 United Eur. Gastroenterol. J, Alburquerque 2013 Gastrointest. Endosc, Ansstas 2009, Cha 2011, Chiba 2013, Cote 2010, Familiari 2012, Familiari Gastrointest. Endosc. 2012, Georgopoulos 2013, Holt 2015 Gastrointest. Endosc, Lee 2010, Mariani 2016, Morgado 2016, Nakai 2014, Nakai 2016, Romagnuolo 2012, Skinner 2014 Gastrointest. Endosc); 1 because conference abstract of already included study (Holt 2015); 1 because reported the results only for the subgroup of patients (n: 46) with Periampullary diverticula (Tyagi 2009); 1 (Coelho-Prabhu 2012) because reported the results only for the subgroup of patients (n: 78) who received precut sphincterotomy with a converted needle knife; 1 because reported the results only for the subgroup of patients (n: 50) with double-guide-wire method (Grönroos 2011).

Awaiting assessment
For study (Ahmad 2005) it was impossible to retrieve the full text.

Included studies
27 studies were finally included (Bailey 2008,Cote 2010, Fukatsu 2008, Geraci 2013, Halttunen 2013, Halttunen 2014, Holt 2016, Huang 2015, Ito 2014, Katsinelos 2008, Kawakami 2012, Kubota 2013, Lopes 2014, Miao 2015, Nakai 2015, Panteris 2008, Park 2012, Parlak 2015, Peng 2013, Rajnakova 2003, Ramesh 2014, Sasahira 2015 , Testoni 2011, Tham 2004,Tsuchiya 2015, Vihervaara 2012, Zhang 2016).

Study	N and characteristic of patients undergoing ERCP	Years of recruitments Setting	Intervention	Cannulation rate
Bailey 2008 (RCT)	413 patients with native papilla	between August 2003 and April 2006 tertiary referral University hospital Australia	cannulation with either sphincterotome and contrast injection (n:211) or sphincterotome and guide-wire cannulation (n; 202)	Overall: 97.3%
Cote 2010	1544 patients with a native papilla that could be reached by using a duodenoscope	between January 2006 and April 2008 Two tertiary care, academic medical centers, USA	first technique: standard techniques without a pre-cut sphincterotomy or stent placement. second technique in case of failure: a 0.025- or 0.035-inch guidewire is advanced to the level of the mid pancreatic body to allow placement of a soft polyethylene stent. If cannulation is unsuccessful after several minutes, a precut sphincterotomy is performed over the PD stent	first techniques: 1452/1544 (94%) adding second technique: 1523/1544 (98.6%)
Fukatsu 2008	501 consecutive patients with an intact duodenal papilla	Between October 2002 and February 2006 University Hospital, Japan	Standard procedure: cannulation using standard manoeuvres needle-knife pre-cut papillotomy (NKPP) when Standard procedure was unsuccessful within 20 min	Standard procedure: 421/501 (84.03%) adding NKPP: 76/80 (95%) Overall: 497/501 (99.2%)

| Geraci 2013 | 500 consecutive ERCPs | Between January 2008 and December 2012

surgical endoscopy unit, Italy | Biliary cannulation was attempted by using a standard three-lumen sphincterotome after the intravenous administration of hyoscine butylbromide 20mg. When biliary cannulation was not achieved by standard sphincterotome, we used hydrophilic guidewire or needle-knife pre-cut papillotomy with or without a pancreatic stent. | With intra-diverticula ampulla (IA): 81/81 (100%)

Without intra-diverticula ampulla (IA): 412/419 (98%)

<u>Overall</u>: 493/500 (98.6%) |
|---|---|---|---|---|
| Halttunen 2013 | 100 patients with native papilla | Between June 2011 and February 2012

University Central Hospital, Helsinki | 0.025-inch guide wire and sphincterotome group (n = 50) 0.035-inch guide wire and sphincterotome group (n = 50). | <u>0.025-inch guide wire</u> and sphincterotome group: 40/50 (80%)

<u>0</u>.035-inch guide wire and sphincterotome group: 40/50 (80%)

<u>Overall</u>: 80/100 (80%) |
| Halttunen 2014 (RCT) | 907 consecutive patients with native papilla | Between 1 January 2010 and 31 May 2011

10 Scandinavian endoscopy units | <u>first technique</u>: wire-guided cannulation (WGC) with a straight hydrophilic wire preloaded in a sphincterotome (67.6%), followed by catheter cannulation with (14.3) or without (13.3) a guide wire. <u>second technique in case of failure</u>: J-tip wires, needle knife (NKS) both in the precut and fistula technique, precut sphincterotomy with or without guide wire in the pancreatic duct, and pancreatic stenting | <u>First technique</u>: 679/907 (74.9%)

<u>Adding second technique</u>: 883/907 (97.4%) |

Holt 2016	524 consecutive patients with native papilla	Between November 1, 2013 and September 22, 2014 single tertiary-care center, USA	<u>Standard cannulation technique</u> was defined as biliary cannulation by using a sphincterotome or cannula, with or without device exchange or wire tip or contrast material guidance. <u>Advanced cannulation techniques</u> included cannulation beside a pancreatic wire or stent, needle-knife access papillotomy over a pancreatic stent or performed freehand, cannulation through a duodenal stent, and back-loading of the duodenoscope over a duodenal wire to pass a luminal stricture	<u>Standard cannulation technique</u>: 451/524 (86%) <u>Adding advanced cannulation techniques</u> :515/524 (98.3%)
Huang 2015 (RCT)	279 patients with native papilla undergoing consecutive therapeutic ERCP	Between January 2013 and December 2014 Hospital, China	double-guidewire technique group ,DWT (n=137) trans-pancreatic sphincterotomy group TPS (n=142)	DWT: 119/137(86.9%) TPS: 129/142 (90.8%) <u>Overall:</u> 248/279 (88.9%)
Ito 2014	146 patients with difficult biliary cannulation who underwent cannulation	Between December 2004 and April 2012 Hospital, Japan	cannula/ sphincterotome under guidance of injected contrast with P-GW (SGT: single-guidewire technique); SGT was done with a 0.025-inch guidewire If biliary cannulation with SGT was unsuccessful, (double-guide-wire technique) DGT was attempted. Other techniques such as pre-cut	<u>SGT</u>: 102/146 (69.9%) <u>adding DGT</u>: 120/146 (82.2%) <u>adding pre-cut sphincterotomy</u>: 126/146 (86.3%)

			sphincterotomy, second ERCP, or a substitutional modality were also added at the discretion of the endoscopist and according to the tolerance of the patient for the procedure	
Katsinelos 2008 (RCT)	332 patients	Between June 2006 and December 2006

Two tertiary referral centers, Greece | standard ERCP catheter (n: 165)

hydrophilic guide-wire (HGW) (n: 167)

If cannulation had not succeeded after 10 minutes with the technique assigned at randomization, a further attempt was made for an additional 10 minutes using the alternative technique | <u>primary success rate of selective CBD cannulation</u>

standard ERCP catheter: 89/165 (53.9%)
HGW: 136/167 (81.4%)

Successful crossover cannulation
standard ERCP catheter: 40/74 (54.0%)
HGW:4/31 (12.9%)

<u>Overall</u>: 269/332 (81.0%) |
| Kawakami 2012 (RCT) | 400 consecutive patients with naive papillae who were candidates for ERCP | Between September 2009 and March 2010

15 referral endoscopy units, Japan | ERCP catheter with contrast medium (C group:101)

ERCP catheter with guide-wire (C+ GW group: 102)

Sphincterotome with contrast medium (S group: 100)

Sphincterotome with guide-wire (S+GW group:97) | C group: 72/101 (71.3%
C+GW group: 75/102 (73.5%)
S group: 68/100 (68%)
S+GW group: 67/97 (69.1%)

<u>Overall</u>: 282/400 (70.5%) |
| Kubota 2013 | 134 patients who underwent needle-knife sphincterotomy (NKS) | Between May 2004 and July 2011

two-centers (university and Medical | Needle-knife precut papillotomy without pancreatic stent (NKPP) (n:36 patients)

Needle-knife precut | <u>NKPP</u>: 31/36 (86.1%)

NKPP-SIPS: 95/98 (96.9 %)

<u>Overall</u>: 126/134 (94.0%) |

		Center), Japan	papillotomy with a small incision using a layer-by-layer method over a pancreatic stent (NKPP-SIPS) (n: 98 patients)	
Lopes 2014	1087 consecutive patients with naive papilla	Between November 2006 and December 2010 affiliated university hospital., Portugal	Standard method with a triple lumen sphincterotome preloaded with contrast and a guide-wire If cannulation was unsuccessful after 12–15 min, a NKF was performed using a needle knife	Standard methods: 883 /1087 (81%) adding NKF:1049/1087 (96%)
Miao 2015	1059 patients	Between May 2012 and April 2013 Hospital, China	Standard method: A duodenoscope was inserted into the duodenal papilla. A catheter was then inserted via the papilla In the case of failing to enter the bile duct but repeated (more three times) insertion of the catheter into the pancreatic duct, a pancreatic guide-wire or plastic stent was placed, and bile duct cannulation was attempted again (n: 163). If the guide-wire repeatedly entered the pancreatic duct but failed to enter the bile duct a Pre-cut papillotomy was performed (n:69)	896/1059 (84.6%) adding the assistance of a pancreatic guide-wire or plastic stent: 990/1059 (93.5%) adding pre-cut papillotomy: 1057/1059 (99.8%.)
Nakai 2015	800 Consecutive patients with a native papilla undergoing therapeutic ERCP	Between January 2008 and October 2013	Wire-guided cannulation (WGC) In cases of difficult cannulation, the	WGC: 564/800(70.5%) adding DGW: 121/800 (15.1%) or PGW: 41/800 (5.1%),

	by using WGC	Academic center, Japan	method and timing of rescue techniques were determined at the discretion of the endoscopists: -contrast material–assisted cannulation, -a double-guide-wire (DGW) technique, -a pancreatic duct guide-wire (PGW) technique, -or a percutaneous trans-hepatic biliary drainage–assisted rendezvous technique. Prophylactic PD stent placement was performed at the discretion of the endoscopists.	or contrast material–assisted cannulation: 39/800 (4.9%) or PTBD rendezvous: 4/800 (0.5%) Final cannulation rate: 96.1%
Panteris 2008	601 undergoing ERCP: 117 with Periampullary diverticula (PAD) and 484 without PAD	Between May 2001 and December 2006 General Hospital, Greece	Cannulation was attempted by using a sphincterotome after the administration of 20 mg Buscopan	patients with PAD: 111/117 (94.9%) Patients without PAD: 459/484 (94.8%) Overall: 570/601 (94.8%)
Park 2012	154 patients with difficult cannulation: 33 with PAD, 121 without PAD	Between December 2005 and October 2010 Department of internal Medicine, Korea	needle-knife fistulotomy	with PAD: 31/33 (93.9%) without PAD: 107/121 /88.4%) Overall: 138 / 154 (89.6%).
Parlak 2015	1201 patients with naive papilla. 222 (18.5%) had peripapillary diverticulum PPD	recruitment period not reported Reference clinic, hospital, Turkey	In the presence of PPD, a sphincterotome or ERCP catheter installed with guide-wire was used for the cannulation attempt. The guidewire easily entered into the pancreatic duct, instead of the common bile duct,;	Without Peripapillary Diverticulum: 947/979 (97%) With PPD: 210/222 (95%) Overall: 1157/1201 (96.3%)

			then the guide-wire was left there. After that, with the help of another guide-wire-installed sphincterotome standing next to the previously placed guide-wire in the pancreatic duct, the cannulation of biliary system was tried to be completed. In the presence of deep-seated, crooked papilla without orifice observed or catheter unapproachable papilla, to reveal papillary orifice, a 5-F ERCP catheter was used to give the right position to papilla and to adjust the suitable cannulation angle. Then, the cannulation was attempted with another 5-F ERCP catheter or 5-F sphincterotome with the guide-wire passed through endoscope . In patients, who failed in the cannulation attempts with any of the 2 methods at each of the 5 trials, if a guide-wire stayed in the pancreatic duct, cannulation was achieved by precut with standard sphincterotomy over the wire previously left in the pancreatic duct with transpancreatic septotomy or with	

			fistulotomy technique by a needle-knife sphincterotome.	
Peng 2013	13018 patients with native papilla	Between March 28, 2007 and May 18, 2011 web-based registry, ERCP practices worldwide	Conventional deep biliary cannulation without pre-cut Cannulation with pre-cut	<u>Conventional</u> (without precut): 10903/12142 (89.8%) <u>with Pre-cut</u> sphincterotomy: 745/876 (85.1%) <u>Overall</u>:11648/13018 (95.6%)
Rajnakova 2003	626 patients with native papilla	Between January 1991 and December 1996	ERCP; no further information provided	592/626 (94.6%)
Ramesh 2014	243 patients underwent 3Fr or 5Fr pancreatic stent placement following sphincterotomy for manometry-proven sphincter of Oddi dysfunction (SOD).	Between 2002 and 2012 Hospital, Florida (USA)	3Fr stent placement (n=133) 5Fr stent placement (n=110)	<u>3Fr stent</u> 133/133 (100%) <u>5Fr stent</u> 110/110 (100%) <u>Overall:</u> 243/243 (100%)
Sasahira 2015 (RCT)	274 patients with naive papilla who underwent ERCP and a guidewire was unintentionally inserted n the main pancreatic duct within 10 attempts and 10 minutes . Patients were ecluded if selective bile duct cannulation was achieced on the first advances oft h eguidewire into the papilla , or if neithr duct was cannulated within 10 attempts and 10 minutes	Between April 2011 and June 2012 multicenter trial Japan	Double wire guide technique (EDG) (n:137) repeated use of single guide-wire cannulation (RSG) (n.137)	<u>RSG:</u> 133/137 (97%) <u>EDG:</u>134/137 (97.8%) <u>Overall:</u> 267/274 (97.4%)

| Testoni 2011 | 2003 patients who had undergone endoscopic retrograde cholangio-pancreatography | Between 2000 and 2008

tertiary referral centre, Italy | Pre-cut sphincterotomy | Without pre-cut: 1717/1834(93.6%)
With precutting:161 /170 94.7

Overall: 1878/2003 (93.7%) |
|---|---|---|---|---|
| Tham 2004 | 344 consecutive patients undergoing ERCP:
With periampullary diverticula (n=83) Without periampullary diverticula (n=261) | recruitment period not reported

Division of gastroenterology UK | ERCP performed with standard technique | With periampullary diverticula:78/83 (94%)

Without periampullary diverticula:245/261 (94%)

Overall: 323/344 (94%) |
| Tsuchiya 2015 (RCT) | 131 patients who required selective biliary cannulation of the native papilla | Between May 2012 and February 2013

Multicenter, hospitals, Japan | J-tip guide-wire (groups J), n=66

angled-tip guide-wire groups (groups A), n=65
If biliary cannulation was not achieved within 10 min, the guide-wire was changed to another type and the insertion was continued for another 10 min (cross-over method). | Success rate of first GW
J group: 56/66 (84.8%)
A group: 52/65 (80%)
Final success rate after switching to other guide-wire
J group:66/66 (100%)
A group: 65/65 (100%) |
| Vihervaara 2012 | 105 consecutive patients admitted for ERCP with intended biliary cannulation and with unhindered access to a native papilla | 2009

University Hospital, finland | conventional wire-guided method with cannula and guide-wire.

If this conventional cannulation method failed and the guide-wire more than once passed into the pancreatic duct, the double-guidewire method was used. If the double-guide-wire–assisted cannulation failed in terms of biliary | Cannula with guide-wire: 84/105 (80%)
Adding Double-guide-wire technique: 97/105 (92.4%)
Adding Needle-knife technique: 104/105 (99%) |

			cannulation or if the guide-wire entered neither the bile duct nor the pancreatic duct, the needle-knife–assisted cannulation, which according to us means a needle-knife fistulotomy, was the last option	
Zhang 2016	1130 consecutive patients with intact papilla who were established as candidates for therapeutic ERCP	Between January 2008 and March 2015 tertiary referral center, China	conventional group with repeated cannulation trials in patients with difficult bile duct cannulation; wire-guided cannulation technique with a sphincterotome preloaded with a 0.035-inch guide-. (n=532) NKPF group : NKPF in case of difficult biliary cannulation (n=598)	<u>conventional group</u>: 483/532 (90.8 %) <u>NKPF group</u>: 591/598 (98.8 %) <u>Overall</u>: 1074/1130 (95%)

Conclusions

Achieved cannulation rate ranged from 70.5% and 100% (median: 96%, mean 91.4%).

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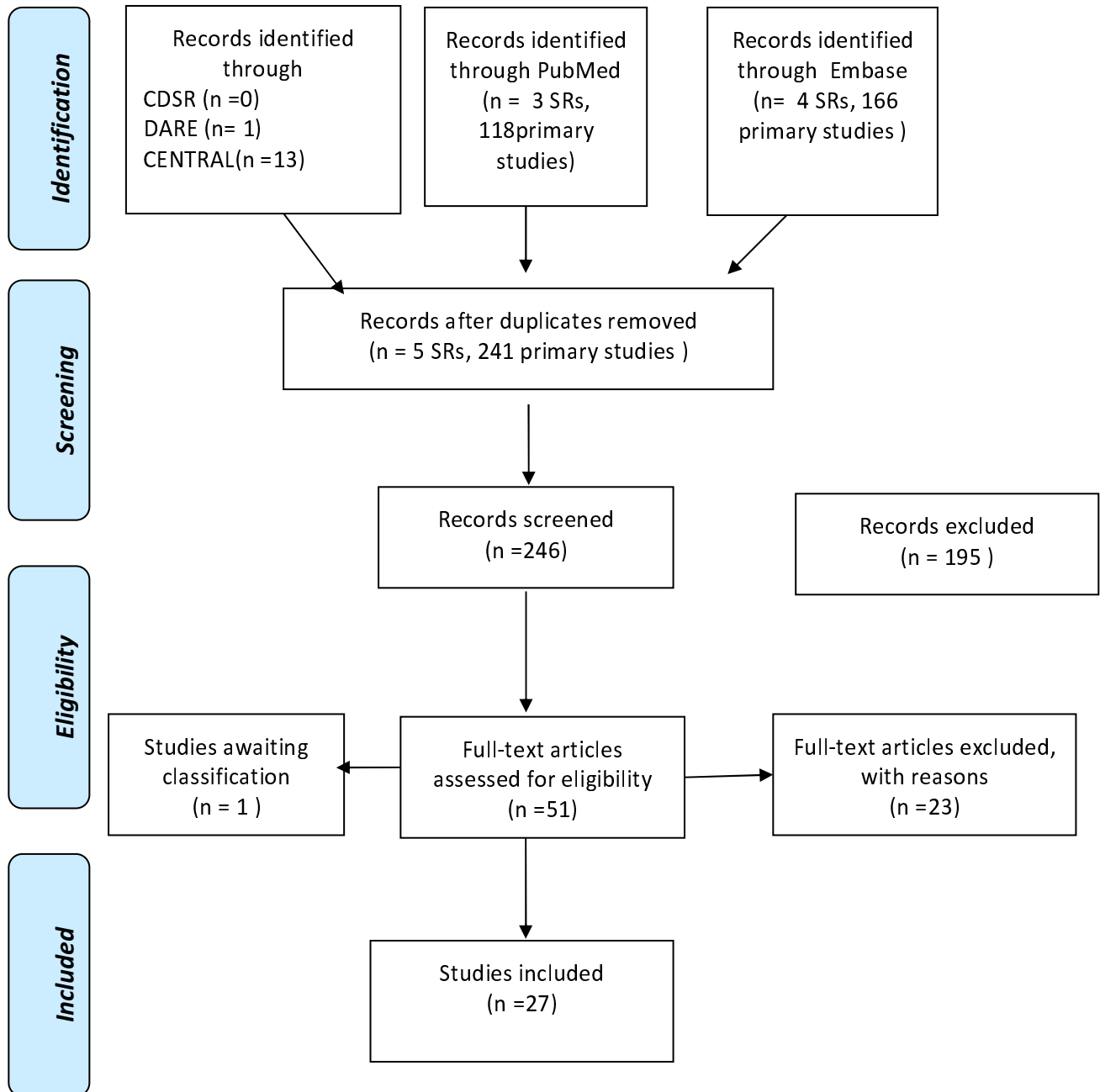
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PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n =0)
DARE (n= 1)
CENTRAL(n =13)

Records identified through PubMed
(n = 3 SRs, 118primary studies)

Records identified through Embase
(n= 4 SRs, 166 primary studies)

Screening

Records after duplicates removed
(n = 5 SRs, 241 primary studies)

Records screened
(n =246)

Records excluded
(n = 195)

Eligibility

Studies awaiting classification
(n = 1)

Full-text articles assessed for eligibility
(n =51)

Full-text articles excluded, with reasons
(n =23)

Included

Studies included
(n =27)

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STONE EXTRACTION

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Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

1.18. Frequency with which extraction of common bile duct stones of <1cm in patients with native major papillae without surgically altered anatomy undergoing ERCP is achieved.

Population
patients with native major papillae without surgically altered anatomy undergoing ERCP for extraction of common bile duct stones

Intervention
extraction of common bile duct stones of <1 cm

Control
none

Outcome
achieved extraction rate

Bibliographic searches
Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 29/6/2016 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
 ("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) **AND** ("surgery" [Subheading] OR remov*[Title/Abstract] OR extract*[Title/Abstract]) **AND** (Choledocholithiasis[Text Word] OR (("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct" [Title/Abstract]) AND (stone*[Text Word] OR calculi[Text Word] OR calculus[Text Word]))) **AND** ("Ampulla of Vater"[Mesh] OR (native[Title/Abstract] AND (papilla[Title/Abstract] OR papillae[Title/Abstract]))) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) **AND** (Choledocholithiasis:ab,ti OR 'common bile duct stone'/exp OR (('common bile duct'/exp OR CBD:ab,ti OR ' bile duct':ab,ti) AND (stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti))) **AND** (remov*:ab,ti OR extract*:ab,ti) **AND** ('Vater papilla'/exp OR (native:ab,ti AND (papilla:ab,ti OR papillae:ab,ti))) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)

#1   MeSH descriptor: [Ampulla of Vater] explode all trees
#2   native papilla:ti,ab,kw (Word variations have been searched)
#3   #1 or #2
#4   MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#5   ERCP:ti,ab,kw (Word variations have been searched)
#6   #5 or #6
#7   CBD or bile duct:ti,ab,kw (Word variations have been searched)
#8   MeSH descriptor: [Common Bile Duct] explode all trees
#9   #7 or #8
#10   stone or calculus:ti,ab,kw (Word variations have been searched)
#11   #9 and #10
#12   Choledocholithiasis:ti,ab,kw (Word variations have been searched)
#13   MeSH descriptor: [Choledocholithiasis] explode all trees
#14   #11 or #12 or #13
#15   Any MeSH descriptor with qualifier(s): [Surgery - SU]
#16   extraction or removal:ti,ab,kw (Word variations have been searched)
#17   #15or #16
#18   #3 and #6 and #17 and #14 Publication Year from 2000 to 2015

Primary studies

PubMed

("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) **AND** (Choledocholithiasis[Text Word] OR (("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct" [Title/Abstract]) AND (stone*[Text Word] OR calculi[Text Word] OR calculus[Text Word]))) **AND** ("surgery" [Subheading] OR remov*[Title/Abstract] OR extract*[Title/Abstract]) **AND** ("Ampulla of Vater"[Mesh] OR (native[Title/Abstract] AND (papilla[Title/Abstract] OR papillae[Title/Abstract]))) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

(Choledocholithiasis:ab,ti OR 'common bile duct stone'/exp OR (('common bile duct'/exp OR CBD:ab,ti OR ' bile duct':ab,ti) AND (stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti))) **AND** (remov*:ab,ti OR extract*:ab,ti) **AND** ('Vater papilla'/exp OR (native:ab,ti AND (papilla:ab,ti OR papillae:ab,ti))) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR

[cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1   MeSH descriptor: [Ampulla of Vater] explode all trees
#2   native papilla:ti,ab,kw (Word variations have been searched)
#3   #1 or #2
#4   MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#5   ERCP: ti,ab,kw (Word variations have been searched)
#6   #5 or #6
#7   CBD or bile duct:ti,ab,kw (Word variations have been searched)
#8   MeSH descriptor: [Common Bile Duct] explode all trees
#9   #7 or #8
#10   stone or calculus: ti,ab,kw (Word variations have been searched)
#11   #9 and #10
#12   Choledocholithiasis: ti,ab,kw (Word variations have been searched)
#13   MeSH descriptor: [Choledocholithiasis] explode all trees
#14   #11 or #12 or #13
#15   Any MeSH descriptor with qualifier(s): [Surgery - SU]
#16   extraction or removal: ti,ab,kw (Word variations have been searched)
#17   #15or #16
#21   #3 and #6 and #17 and #14 Publication Year from 2000 to 2015

Results

Results of the bibliographic searches
After removing duplicates, 167 articles (2 reviews and 165 primary studies) were found. 18 primary studies were considered potentially relevant and acquired in full text and another one was suggested by experts(See flow chart).
Because few studies potentially relevant were found, also conference proceeding were considered.
A sample size of 50 patients was used as a cut off for inclusion.

Excluded studies
17 studies were excluded: 7 because size of stones were not reported (Baron 2004, Daradkeh 2000, Kim 2009, Schreurs 2002, Tham 2004,Vitale 2016, Xiu 2013); 5 because stones were greater than 1 cm (Garcia-Cano 2009, Draganov 2009, Kalogeropoulos 2014, Itokawa 2013, Paspatis 2013); 1 because size of stone ranged from 2 to 25 mm and no separate data for stone < 1 cm were provided (Tsujino 2008); 1 because size of stone ranged from 1 to 35 mm and no separate data for stone < 1 cm were provided (Takezawa 2004); 1 because no intervention of interest (Mattila 2014) , 1 because no outcome of interest was reported (Li 2013), 1 because only for a minority of cases (n:24) ERCP was used (Chiappalone 2000).

Included studies
Two studies were finally included (Kuo 2012, Oppong 2012).

Study	N and characteristic of patients undergoing ERCP for stone extraction	Years of recruitments Setting	Intervention	stone extraction rate
Kuo 2012	222 consecutive patients with stones ≤ 1 cm	from December 2004 through the end of November 2008. Department of Internal Medicine, Division of Hepato-Gastroenterology Taiwan	Endoscopic papillary balloon dilation	201/222 (94.6%)
Oppong 2012	4371 ERCPs with attempts of >1 cm stone extraction in patients with native papillas	tertiary and secondary care units in the UK and USA, May 2011	UK attempts: 900 USA attempts: 3471	UK: 96% USA: 99% P<0.001

Conclusions

No definite conclusions can be drawn because only two studies were retrieved addressing this question. In these studies stone extraction rate ranged between 94% and 99%.
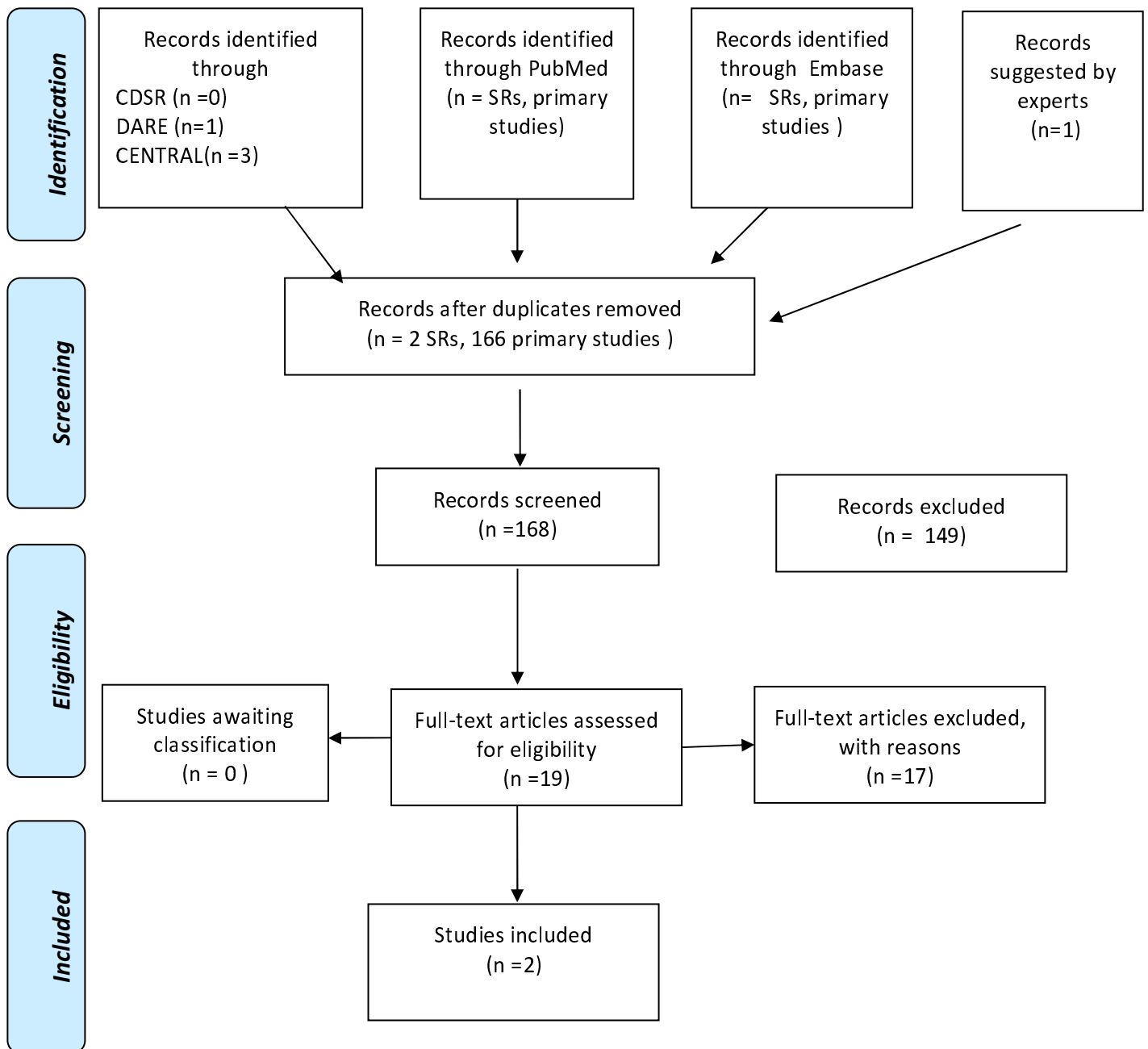
References

Included studies

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2. Oppong K.W., Romagnuolo J., Cotton P.B.Research: The ERCP quality network benchmarking project: A preliminary comparison of practice in UK and USA. Frontline Gastroenterology 2012 3:3 (157-161)

Excluded studies

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6. Itokawa, F.; Itoi, T.; Sofuni, A.; Tsuchiya, T.; Ikeuchi, N., and Tanaka, R. Safety and effectiveness of endoscopic sphincterotmy plus large balloon dilation: Single center mid-term outcome. Gastrointest. Endosc. 2013; 77(5):AB314
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PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n =0)
DARE (n=1)
CENTRAL(n =3)

Records identified through PubMed (n = SRs, primary studies)

Records identified through Embase (n= SRs, primary studies)

Records suggested by experts (n=1)

Screening

Records after duplicates removed
(n = 2 SRs, 166 primary studies)

Records screened
(n =168)

Records excluded
(n = 149)

Eligibility

Studies awaiting classification
(n = 0)

Full-text articles assessed for eligibility
(n =19)

Full-text articles excluded, with reasons
(n =17)

Included

Studies included
(n =2)

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SUCCESS RATE OF STENT PLACEMENT

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1.19. Frequency with which stent placement in patients with native major papillae without surgically altered anatomy undergoing ERCP for stent placement in cases of biliary obstruction below the bifurcation is achieved.

Population
patients with native major papillae without surgically altered anatomy undergoing ERCP for stent placement in cases of biliary obstruction below the bifurcation

Intervention
stent placement

Control
None

Outcome
achieved stent placement rate

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 29/6/2016 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) **AND** ("Stents"[Mesh] OR stent[Title/Abstract] OR stents[Title/Abstract]) **AND** ((("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct"[Title/Abstract] OR biliary[Title/Abstract] OR pancreatic[Title/Abstract]) AND (obstruct*[Title/Abstract] OR occlu*[Title/Abstract] OR stricture[Text Word] OR stenosis[Text Word] OR stone*[Text Word] OR calculi[Text Word] OR

calculus[Text Word] OR cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign* [Title/Abstract] OR tumor [Title/Abstract] OR tumour [Title/Abstract] OR tumors [Title/Abstract] OR tumours [Title/Abstract]   OR carcinom* [Title/Abstract])) OR ((obstruct*[Text Word] OR occlu*[Text Word]) AND benign[Title/Abstract]) OR "Cholangitis"[Mesh] OR Cholangitis[Title/Abstract] OR pancreatitis[Title/Abstract] OR "Pancreatitis"[Mesh] OR sclerosing papillitis[Title/Abstract] OR "Biliary Tract Neoplasms"[Mesh] OR "Pancreatic Neoplasms"[Mesh]) **AND** ("Ampulla of Vater"[Mesh] OR (native[Title/Abstract] AND (papilla[Title/Abstract] OR papillae[Title/Abstract]))) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) **AND** ((('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti) AND (obstruct*:ab,ti OR occlu*:ab,ti OR stricture:ab,ti OR 'stenosis'/exp OR stenosis:ab,ti cancer OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti)) OR ((obstruct*:ab,ti OR occlu*:ab,ti) AND benign:ab,ti) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR pancreatitis:ab,ti OR Cholangitis:ab,ti OR 'cholangitis'/exp OR 'pancreatitis'/exp OR 'sclerosing papillitis':ab,ti) **AND** ('biliary stent'/exp OR stent:ab,ti OR stents:ab,ti) **AND** ('Vater papilla'/exp OR (native:ab,ti AND (papilla:ab,ti OR papillae:ab,ti))) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)
#1   MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#2   ERCP:ti,ab,kw (Word variations have been searched)
#3   #8 or #7
#4   MeSH descriptor: [Stents] explode all trees
#5   stent:ti,ab,kw (Word variations have been searched)
#6   #4 or #5
#7   MeSH descriptor: [Ampulla of Vater] explode all trees
#8   native papilla:ti,ab,kw (Word variations have been searched)
#9   #8 or #7
#10   MeSH descriptor: [Common Bile Duct] explode all trees
#11   CBD or biliary or bile duct:ti,ab,kw (Word variations have been searched)
#12   obstruction or occlusion:ti,ab,kw (Word variations have been searched)
#13   cancer or neoplasm or malign or tumor or carcinoma or stricture or stenosis:ti,ab,kw (Word variations have been searched)
#14   #10 or #11
#15   #12 or #13
#16   #14 and #15
#17   benign:ti,ab,kw (Word variations have been searched)
#18   #12 and #17
#19   cholangitis or pancreatitis or sclerosing papillitis:ti,ab,kw (Word variations have been searched)
#20   MeSH descriptor: [Cholangitis] explode all trees
#21   MeSH descriptor: [Pancreatitis] explode all trees
#22   MeSH descriptor: [Biliary Tract Neoplasms] explode all trees
#23   MeSH descriptor: [Pancreatic Neoplasms] explode all trees

#24 #16 or #18 or #19 or #20 or #21 or #22 or #23
#25 #3 and #6 and #19 and #24 Publication Year from 2000 to 2016

Primary studies

PubMed
("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) **AND** ("Stents"[Mesh] OR stent[Title/Abstract] OR stents[Title/Abstract]) **AND** ((("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct"[Title/Abstract] OR biliary[Title/Abstract] OR pancreatic[Title/Abstract]) AND (obstruct*[Title/Abstract] OR occlu*[Title/Abstract] OR stricture[Text Word] OR stenosis[Text Word] OR stone*[Text Word] OR calculi[Text Word] OR calculus[Text Word] OR cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign* [Title/Abstract] OR tumor [Title/Abstract] OR tumour [Title/Abstract] OR tumors [Title/Abstract] OR tumours [Title/Abstract] OR carcinom* [Title/Abstract])) OR ((obstruct*[Text Word] OR occlu*[Text Word]) AND benign[Title/Abstract]) OR "Cholangitis"[Mesh] OR Cholangitis[Title/Abstract] OR pancreatitis[Title/Abstract] OR "Pancreatitis"[Mesh] OR sclerosing papillitis[Title/Abstract] OR "Biliary Tract Neoplasms"[Mesh] OR "Pancreatic Neoplasms"[Mesh]) **AND** ("Ampulla of Vater"[Mesh] OR (native[Title/Abstract] AND (papilla[Title/Abstract] OR papillae[Title/Abstract]))) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase
('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) **AND** ((('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti) AND (obstruct*:ab,ti OR occlu*:ab,ti OR stricture:ab,ti OR 'stenosis'/exp OR stenosis:ab,ti cancer OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti)) OR ((obstruct*:ab,ti OR occlu*:ab,ti) AND benign:ab,ti) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR pancreatitis:ab,ti OR Cholangitis:ab,ti OR 'cholangitis'/exp OR 'pancreatitis'/exp OR 'sclerosing papillitis':ab,ti) **AND** ('biliary stent'/exp OR stent:ab,ti OR stents:ab,ti) **AND** ('Vater papilla'/exp OR (native:ab,ti AND (papilla:ab,ti OR papillae:ab,ti))) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1 MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#2 ERCP:ti,ab,kw (Word variations have been searched)
#3 #8 or #7
#4 MeSH descriptor: [Stents] explode all trees
#5 stent:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
#7 MeSH descriptor: [Ampulla of Vater] explode all trees
#8 native papilla:ti,ab,kw (Word variations have been searched)
#9 #8 or #7
#10 MeSH descriptor: [Common Bile Duct] explode all trees
#11 CBD or biliary or bile duct:ti,ab,kw (Word variations have been searched)
#12 obstruction or occlusion:ti,ab,kw (Word variations have been searched)

#13   cancer or neoplasm or malign or tumor or carcinoma or stricture or stenosis:ti,ab,kw (Word variations have been searched)
#14   #10 or #11
#15   #12 or #13
#16   #14 and #15
#17   benign:ti,ab,kw (Word variations have been searched)
#18   #12 and #17
#19   cholangitis or pancreatitis or sclerosing papillitis:ti,ab,kw (Word variations have been searched)
#20   MeSH descriptor: [Cholangitis] explode all trees
#21   MeSH descriptor: [Pancreatitis] explode all trees
#22   MeSH descriptor: [Biliary Tract Neoplasms] explode all trees
#23   MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#24   #16 or #18 or #19 or #20 or #21 or #22 or #23
#25   #3 and #6 and #19 and #24 Publication Year from 2000 to 2016

Results

Results of the bibliographic searches
After removing duplicates, 178 articles (1 review and 177 primary studies) were found. 31 primary studies were considered potentially relevant and acquired in full text. (See flow chart).
A sample size of 50 patients was used as a cut off for inclusion.

Excluded studies
25 articles were excluded: 13 because conference abstracts (Anderloni 2016, Ansstas 2009, Cote 2010, Georgopoulos 2013 , Hu 2013 , Hu 2013 b, Hu 2012, Itoh 2012, Moon 2010, Taunk 2015, Lee 2014,Wilcox 2009, Xiu 2013); 4 because no outcome of interest (Ueda 2016, Chang 2014, Cote 2010, Wilcox 2010), one because included patients with altered anatomy (Sandha 2004); 7 because included less than 50 patients (Akin 2015, De Palma 2015, Katsinelos 2006, Jun 2015, Moon 2010, Nakahara 2015, Uchida 2005) .

Included studies
Six studies were finally included (Kim 2013, Kubota 2013, Freeman 2004, Miao 2004, van Berkel 2004, Varadarajulu 2005) with a total of 632 participants.

Conclusions

Successful stent placement rate ranged from 95% and 100% (median: 99%).

Study	N and characteristic of patients undergoing ERCP for stent placement	Years of recruitments Setting	Intervention	stent placement rate
Kim 2013	72 patients with ampullary adenoma < 25 mm diameter and no invasion into the bile or pancreatic duct	September 2005 – March 2012 Digestive and disease center and Research Institute Korea	endoscopic excision (en bloc resection in 3% and piecemeal in 17%) of the adenoma, followed by immediate insertion of a panceratic stent over the guide wire that have been previously placed in the pancreatic duct, and was positioned across the pancreatic duct orifice	72/72 (100%)
Kubota 2013	98 patients who underwent needle-knife sphincterotomy (NKS)	between May 2004 and July 2011 two-centers (university and Medical Center), Japan	Needle-knife precut papillotomy with a small incision using a layer-by-layer method over a pancreatic stent that would represent a good landmark for precut (NKPP-SIPS) (n: 98 patients)	93/98 (95%)
Freeman 2004	225 patients in whom pancreatic stent placement via the major papilla was intended. .	1998 (conventional technique) and 2000 modified technique tertiary referral center for pancreaticobiliary endoscopy USA	Conventional technique: deep passage to at least the genu of the pancreatic duct of a 0.018-in guide-wire or a 0.025- to 0.035-in ''hybrid'' floppy-tip guide-wire. Modified short-wire technique for small or tortuous ducts. The Roadrunner guide-wire was used. If the guide-wire could not be passed beyond the first turn in the pancreatic duct , the tip of the guide-wire was passed a short distance beyond the pancreatic sphincter (at least 1-2 cm), just enough to allow insertion of a short (2 or 3 cm) small diameter (3F, 4F, or 5F) stent. If the duct was of sufficient diameter, the soft tip of the guide wire was knuckled and curled inside the main duct below the sharp turn to provide a better anchor. If the duct was diminutive, the straight tip of the guide-wire was impacted into the first turn in the duct and a small diameter (3F or 4F) stent was inserted	222/225 (99%)

Miao 2004	80 patients with benign biliary strictures or malignant biliary strictures	From June 2001 to October 2002 Department of gastroenterology China	plastic stent: (n:52) gold stent (n: 28) Through papilla of duodenum, contrast medium was injected and location of stricture of bile duct was revealed. A catheter was introduced into the dilated bile duct via the introducer. A guide wire was inserted through the occlusive part of biliary duct. The occlusive part of biliary duct was dilated with a balloon catheter. A stent was inserted into the occlusive bile duct under fluoroscopic control or endoscopy.	80/80 (100%)
van Berkel 2004	60 patients with distal malignant bile duct obstruction.	February 1998 and September 1998 Department of gastroenterology The Netherland	Tannenbaum design stent with a stainless steel mesh and an inner Teflon coating (TTC). (n:30) conventional polyethylene (PE) stent (n:30)	60/60 (100%)
Varadarajulu 2005	97 consecutive patients with pancreatic duct (PD) disruption due to chronic pancreatitis (47), acute pancreatitis (44), operative injury (4), and trauma (2).	from 1995 to 2002 single institution; no more information provided USA	Upon identification of the PD disruption as extravasation of contrast into the PFC, a 0.035-inch guide-wire was inserted into the PD and a Geenen pancreatic stent with an internal flap was inserted. When a 3F stent was placed, a small cut was made on the stent to create an internal flap. The PD was cannulated with a 0.018-inch guide-wire when there was an extremely narrow PD stricture or when a 3F stent was placed. The choice of stent was based on specific ductal anatomic features. Strictures were dilated with a 3-4-5F; a 5-7-10F, step-wise dilator; or a rigid, biliary dilating balloon.	92 /97 (95%)

.

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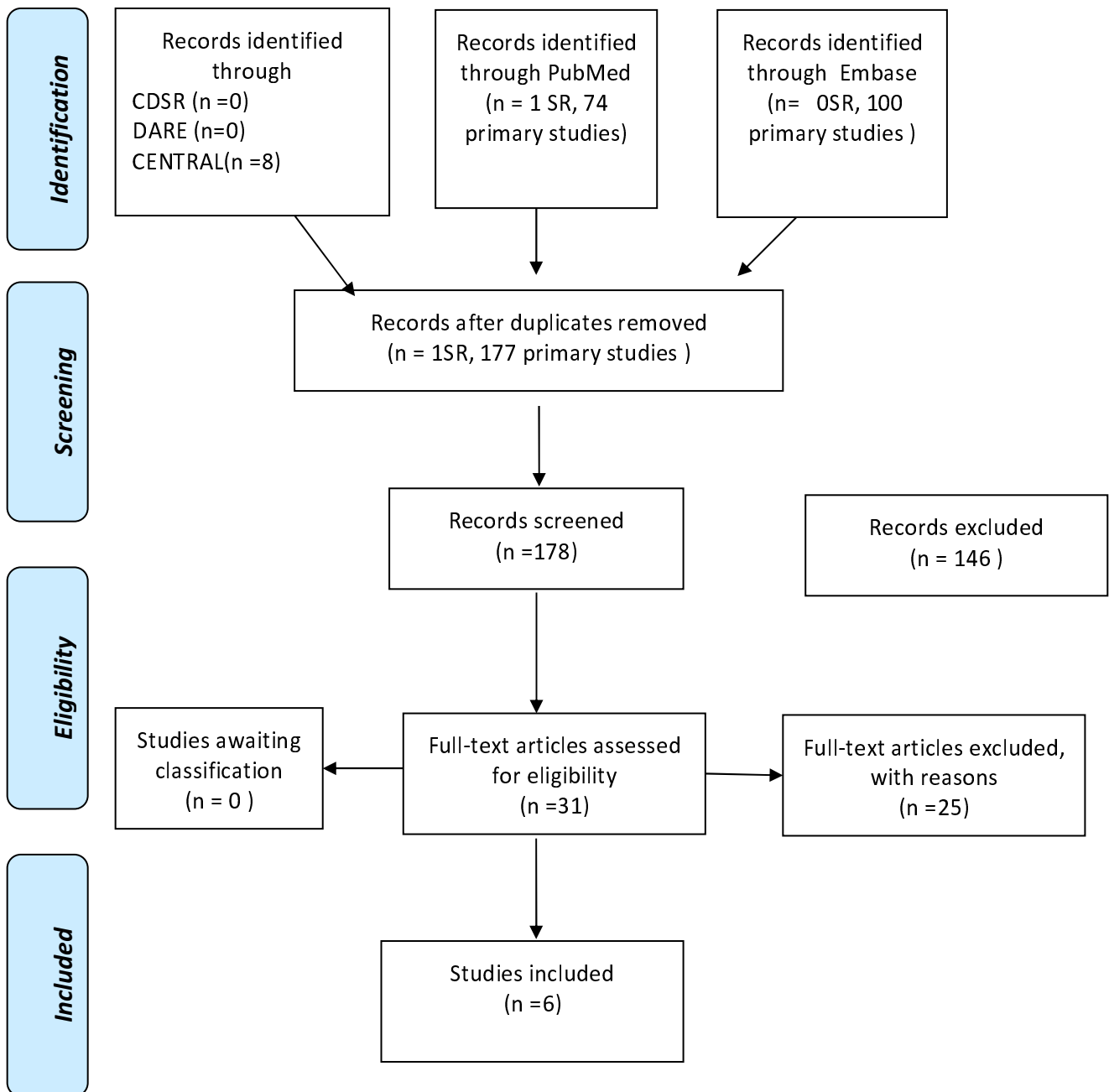

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PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n =0)
DARE (n=0)
CENTRAL(n =8)

Records identified through PubMed
(n = 1 SR, 74 primary studies)

Records identified through Embase
(n= 0SR, 100 primary studies)

Screening

Records after duplicates removed
(n = 1SR, 177 primary studies)

Records screened
(n =178)

Records excluded
(n = 146)

Eligibility

Studies awaiting classification
(n = 0)

Full-text articles assessed for eligibility
(n =31)

Full-text articles excluded, with reasons
(n =25)

Included

Studies included
(n =6)

S.C. Epidemiologia screening, registro tumori –
CPO Piemonte

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MANAGEMENT OF PATIENTS UNDERGOING EUS-FNA

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Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

1.20. Frequency with which EUS-FNP would change patients' management in patients with distant metastasis, ascites, and lymphadenopathy who undergo tissue sampling of both the primary tumor and lesion outside of the primary field.

Population
patients with distant metastasis, ascites, and lymphadenopathy undergoing EUS-guided FNA who have tissue sampling of both the primary tumour and lesions outside of the primary field

Intervention
EUS fine needle biopsy

Control
none

Outcome
percentage of patients in which EUS-FNA changed patients' management

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 29/6/2016 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Endosonography"[Mesh] OR "Biopsy, Fine-Needle"[Mesh] OR ("endoscopic ultrasound" [Title/Abstract] AND fine[Title/Abstract] AND needle[Title/Abstract]) OR (EUS[Title/Abstract] AND FNA[Title/Abstract])) **AND** ("Patient Care Management"[Mesh] OR management[Title/Abstract] OR impact[Title/Abstract]) **AND** ("Ascites"[Mesh] OR lymphadenopathy[Text Word] OR "Lymphatic Metastasis"[Mesh] OR metastas*[Title/Abstract]

OR ascites[Title/Abstract] OR ascite[Title/Abstract] OR lymphadenopaties[Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) **AND** ('patient care'/exp OR management:ab,ti OR impact:ab,ti) **AND** ('ascites'/exp OR 'lymphadenopathy'/exp OR 'lymph node metastasis'/exp OR metastas*:ab,ti OR ascites:ab,ti OR ascite:ab,ti OR lymphadenopaties:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and **Database of Abstracts of Reviews of Effects (DARE)**
#1   MeSH descriptor: [Endosonography] explode all trees
#2   MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#3   endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#4   EUS and FNA:ti,ab,kw (Word variations have been searched)
#5   #1 or #2 or #3 or #4
#6   MeSH descriptor: [Patient Care Management] explode all trees
#7   patient management or impact:ti,ab,kw (Word variations have been searched)
#8   #6 or #7
#9   MeSH descriptor: [Ascites] explode all trees
#10   MeSH descriptor: [Lymphatic Metastasis] explode all trees
#11   lymphadenopathy or metastasis or ascites:ti,ab,kw (Word variations have been searched)
#12   #9 or #10 or #11
#13   #5 and #8 and #12 Publication Year from 2000 to 2016

Primary studies

PubMed
("Endosonography"[Mesh] OR "Biopsy, Fine-Needle"[Mesh] OR ("endoscopic ultrasound"[Title/Abstract] AND fine[Title/Abstract] AND needle[Title/Abstract]) OR (EUS[Title/Abstract] AND FNA[Title/Abstract])) **AND** ("Patient Care Management"[Mesh] OR management[Title/Abstract] OR impact[Title/Abstract]) **AND** ("Ascites"[Mesh] OR lymphadenopathy[Text Word] OR "Lymphatic Metastasis"[Mesh] OR metastas*[Title/Abstract] OR ascites[Title/Abstract] OR ascite[Title/Abstract] OR lymphadenopaties[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase
('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) **AND** ('patient care'/exp OR management:ab,ti OR impact:ab,ti) **AND** ('ascites'/exp OR

'lymphadenopathy'/exp OR 'lymph node metastasis'/exp OR metastas*:ab,ti OR ascites:ab,ti OR ascite:ab,ti OR lymphadenopaties:ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1   MeSH descriptor: [Endosonography] explode all trees
#2   MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#3   endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#4   EUS and FNA:ti,ab,kw (Word variations have been searched)
#5   #1 or #2 or #3 or #4
#6   MeSH descriptor: [Patient Care Management] explode all trees
#7   patient management or impact:ti,ab,kw (Word variations have been searched)
#8   #6 or #7
#9   MeSH descriptor: [Ascites] explode all trees
#10   MeSH descriptor: [Lymphatic Metastasis] explode all trees
#11   lymphadenopathy or metastasis or ascites:ti,ab,kw (Word variations have been searched)
#12   #9 or #10 or #11
#13   #5 and #8 and #12 Publication Year from 2000 to 2016

Results

Results of the bibliographic searches
After removing duplicates, 246 articles (5 reviews and 241 primary studies) were found. 27 primary studies were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies
18 studies were excluded: 12 studies because conference abstracts (Chin 2013, Gara 2016, Kurita 2015, Levy 2014, Issa 2014, Giovannini 2012,Rao 2011, Lankarani 2011, El Hajj 2011, Majmundar 2009, Hassan 2009, Coppola 2013); 2 studies because no intervention of interest (Ferrero 2013, Mui 2014); 3 studies because no outcome of interest (Del Vecchio Blanco 2015, Gleeson 2011, Will 2010), 1 study (Hirdes 2010) because patients were not in the inclusion criteria: more than half of the samples were patients without an established diagnosis of primary cancer.

Included studies
7 studies were finally included (Annema 2005, Araujo 2013, Bodtger 2009, Hassan 2010, Levy 2015, Singh 2007, Talebian 2010).
Four studies (Annema 2005, Bostger 2009, Singh 2007, Talebian 2010) included patients with lung cancer, two studies included patients with gastric carcinoma (Araujio 2013, Hassan 2010) and one study (Levy 2015) included patients with peritoneal anomaly suspected for peritoneal carcinomatosis.

Studies awaiting assessment
For two studies (Kliment 2013, Morris, 2009), it was impossible to retrieve the full text.

Study	N and characteristic of patients	Years of recruitments Country	Intervention	Patients in which EUS-FNA changed patients' management
Annema 2005	242 patients with suspected (n 142) or proven (n 100) lung cancer and enlarged (> 1 cm) mediastinal LNs scheduled for mediastinoscopy/tomy (94%) or exploratory thoracotomy (6%).)	recruitment period not reported the Netherlands	EUS-FNA of mediastinal mass before surgery	70%
Araujo 2013	36 patients with gastro-oesophageal junction (GEJ) adenocarcinoma suspected distant LN metastases	January 2009 - August 2012 France	EUS-FNA of distant lymphnodes	54.2%
Bodtger 2009	40 patients referred to EUS for known or suspected lung cancer with enlarged left adrenal gland	2000-2006 Denmark	EUS-FNA of an enlarged left adrenal gland (LAG)	48% (avoided surgery: 18% gained surgery: 30%)
Hassan 2010	81 consecutive patients with gastric carcinoma and suspected distant metastases (tumour, nodes, metastasis) or suspicious lesions in distant organs	2001-2007 Denmark	EUS-FNA 81/ 234 underwent EUS-FNA because of suspected distant metastasis (35%).	41.9%
Levy 2015	98 patients who underwent EUS- FNA of a peritoneal anomaly. And with available criterion standard that incorporated cyto-histologic, radiologic, and clinical data.	June 2006-November 2013 USA	EUS-FNA of a peritoneal anomaly	21.4%
Singh 2007	93 consecutive patients with a newly detected lung mass suspicious of lung cancer or with a recent tissue diagnosis of non–small cell lung cancer (NSCLC).	March 2004 - July 2005 USA	EUS- FNA for diagnosis of lung cancer and metastasis	8.6%
Talebian 2010	152 consecutive patients with (suspected) NSCLC who were medically fit to undergo surgical resection of the lung tumour	August 2003 - February 2007 the Netherlands	EUS-FNA of mediastinal mass before surgical staging	39%

Quality of evidence

Clinical question 1: patency vs no patency
Factors that can lower quality
Study limitations (risk of bias): yes (case series)
Inconsistency of results: yes
Indirectness of evidence: no
Imprecision: no
Publication bias: undetected
Overall quality of evidence: overall quality of evidence was judged as very low for study limitation and indirectness
Factors that can higher quality
large magnitude of effect: no
opposing plausible residual bias or confounding: no
dose-response gradient: no

Conclusions

EUS-FNA seems to have a relevant impact on patients management, changing planned intervention in percentages of patients ranging from 8.6% to 70%. However variability is high. For lung cancer patients percentages ranged from 8.6% to 70%, for gastric cancer patients from 42% to 54.2% (**VERY LOW QUALITY EVIDENCE**).

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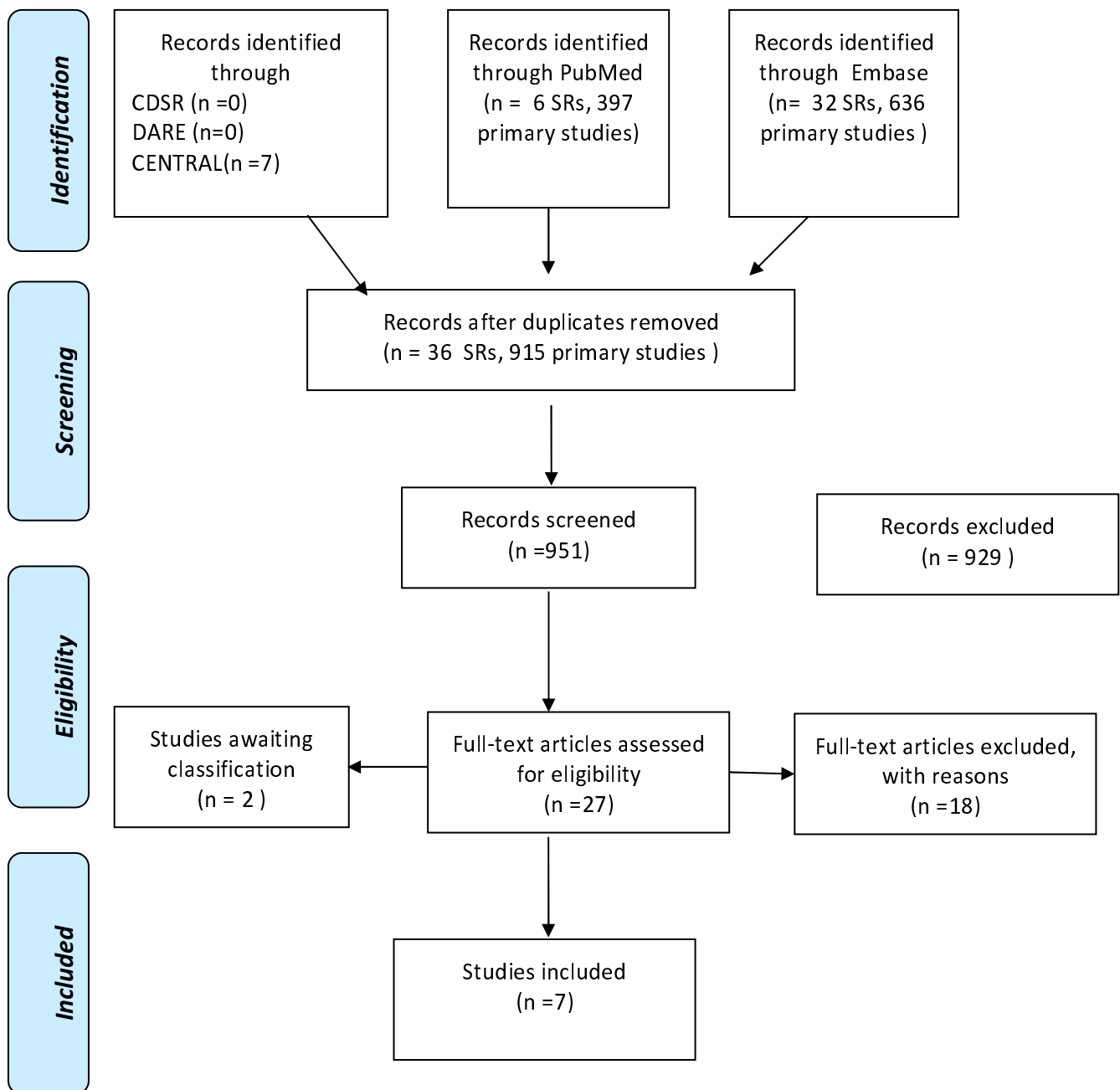
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Studies awaiting assessment
1. Kliment M., Urban O., Loveček M., Straka M., Žiak D., Falt P., Fojtík P., Dvořáčková J. Endosonography-guided fine needle aspiration biopsy of solid pancreatic masses - Accuracy and impact on the treatment of 358 patients.Gastroenterol. Hepatol. 2013; 67(5):431-437

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PRISMA 2009 Flow Diagram

Identification

| Records identified through CDSR (n =0) DARE (n=0) CENTRAL(n =7) | Records identified through PubMed (n = 6 SRs, 397 primary studies) | Records identified through Embase (n= 32 SRs, 636 primary studies) |

Screening

Records after duplicates removed
(n = 36 SRs, 915 primary studies)

Records screened
(n =951)

Records excluded
(n = 929)

Eligibility

Studies awaiting classification
(n = 2)

Full-text articles assessed for eligibility
(n =27)

Full-text articles excluded, with reasons
(n =18)

Included

Studies included
(n =7)

**S.C. Epidemiologia screening, registro tumori –
CPO Piemonte**
Direttore: Dr. Nereo Segnan
via Cavour 31, 10123 Torino
tel. 011.6333881 - fax 011.6333861
www.cpo.it - email: info@cpo.it

Centro di Riferimento per l'Epidemiologia
e la Prevenzione Oncologica in Piemonte

AZIENDA OSPEDALIERO - UNIVERSITARIA
Città della Salute e della Scienza di Torino

DIAGNOSTIC RATE OF ADEQUATE EUS-FNA SAMPLING

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Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

1.21. Frequency of successful diagnostic tissue sampling in patients with solid lesions undergoing EUS-FNA.

Population
patients with solid lesions undergoing EUS-FNA

Intervention
EUS fine needle biopsy

Control
none

Outcome
diagnostic rate of adequate EUS-FNA sampling

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 29/6/2016 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Endosonography"[Mesh] OR "Biopsy, Fine-Needle"[Mesh] OR ("endoscopic ultrasound" [Title/Abstract] AND fine[Title/Abstract] AND needle[Title/Abstract]) OR (EUS[Title/Abstract] AND FNA[Title/Abstract])) **AND** ((sampling[Text Word] OR samplings[Title/Abstract] OR "Specimen Handling"[Mesh] OR specimen [Text Word] OR specimens[Title/Abstract] OR "pathology" [Subheading]) AND (adequate[Title/Abstract] OR satisf*[Title/Abstract] OR suitable[Title/Abstract] OR sufficient[Title/Abstract])) **AND** ((("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct"[Title/Abstract] OR biliary[Title/Abstract] OR

stomach[Title/Abstract] OR mediastinum[Title/Abstract] OR pancreatic[Title/Abstract] OR rectal[Title/Abstract] OR gastric[Title/Abstract] OR esophageal[Title/Abstract] OR oesophageal[Title/Abstract]) AND (cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign* [Title/Abstract] OR tumor [Title/Abstract] OR tumour [Title/Abstract] OR tumors [Title/Abstract] OR tumours [Title/Abstract] OR carcinom* [Title/Abstract] OR "Lymph Nodes"[Mesh] OR "lymph nodes"[Title/Abstract] OR "lymph node"[Title/Abstract] OR lymphnodes[Title/Abstract] OR lymphnode[Title/Abstract]) OR "Biliary Tract Neoplasms"[Mesh] OR "Pancreatic Neoplasms"[Mesh] OR "Gastrointestinal Neoplasms"[Mesh] OR "Rectal Neoplasms"[Mesh] OR "Mediastinal Neoplasms"[Mesh] OR "Stomach Neoplasms"[Mesh]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) **AND** (('laboratory diagnosis'/exp OR sampling:ab,ti OR sampling:ab,ti OR specimens:ab,ti OR specimens:ab,ti) AND (adequate:ab,ti OR satisf*:ab,ti OR suitable:ab,ti OR sufficient:ab,ti)) **AND** ((('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti OR rectal:ab,ti OR gastric:ab,ti OR esophageal:ab,ti OR oesophageal:ab,ti OR stomach:ab,ti OR mediastinum:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR 'lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti)) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR 'rectum cancer'/exp OR 'esophagus cancer'/exp OR 'digestive system cancer'/exp OR 'mediastinum lymph node'/exp OR 'digestive system cancer'/exp) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)
#1   MeSH descriptor: [Endosonography] explode all trees
#1   MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#3   endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#4   EUS and FNA:ti,ab,kw (Word variations have been searched)
#5   #1 or #2 or #3 or #4
#6   Any MeSH descriptor with qualifier(s): [Pathology - PA]
#7   MeSH descriptor: [Specimen Handling] explode all trees
#8   specimen or sampling:ti,ab,kw (Word variations have been searched)
#9   #6 or #7 or #8
#10   adequate or sufficient or suitable:ti,ab,kw (Word variations have been searched)
#11   #9 and #10
#12   CBD or biliary or pancreatic or bile duct or rectal or gastric or esphageal or mediastinum:ti,ab,kw (Word variations have been searched)
#13   cancer or neoplasm or malign or tumor or carcinoma or lymph nodes:ti,ab,kw (Word variations have been searched)
#14   MeSH descriptor: [Lymph Nodes] explode all trees
#15   #13 or #14
#16   #12 and #15
#17   MeSH descriptor: [Gastrointestinal Neoplasms] explode all trees
#18   MeSH descriptor: [Rectal Neoplasms] explode all trees

#19   MeSH descriptor: [Mediastinal Neoplasms] explode all trees
#20   MeSH descriptor: [Stomach Neoplasms] explode all trees
#21   MeSH descriptor: [Biliary Tract Neoplasms] explode all trees
#22   MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#21   #16 or #17 or #18 or #19 or #20 or #211 or #22
#22   #5 and #11 and #21 Publication Year from 2000 to 2016

Primary studies

PubMed
("Endosonography"[Mesh] OR "Biopsy, Fine-Needle"[Mesh] OR ("endoscopic ultrasound" [Title/Abstract] AND fine[Title/Abstract] AND needle[Title/Abstract]) OR (EUS[Title/Abstract] AND FNA[Title/Abstract])) **AND** ((sampling[Text Word] OR samplings[Title/Abstract] OR "Specimen Handling"[Mesh] OR specimen [Text Word] OR specimens[Title/Abstract] OR "pathology" [Subheading]) AND (adequate[Title/Abstract] OR satisf*[Title/Abstract] OR suitable[Title/Abstract] OR sufficient[Title/Abstract])) **AND** ((("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct"[Title/Abstract] OR biliary[Title/Abstract] OR stomach[Title/Abstract] OR mediastinum[Title/Abstract] OR pancreatic[Title/Abstract] OR rectal[Title/Abstract] OR gastric[Title/Abstract] OR esophageal[Title/Abstract] OR oesophageal[Title/Abstract]) AND (cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign* [Title/Abstract] OR tumor [Title/Abstract] OR tumour [Title/Abstract] OR tumors [Title/Abstract] OR tumours [Title/Abstract] OR carcinom* [Title/Abstract] OR "Lymph Nodes"[Mesh] OR "lymph nodes"[Title/Abstract] OR "lymph node"[Title/Abstract] OR lymphnodes[Title/Abstract] OR lymphnode[Title/Abstract])) OR "Biliary Tract Neoplasms"[Mesh] OR "Pancreatic Neoplasms"[Mesh] OR "Gastrointestinal Neoplasms"[Mesh] OR "Rectal Neoplasms"[Mesh] OR "Mediastinal Neoplasms"[Mesh] OR "Stomach Neoplasms"[Mesh]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase
('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) **AND** (('laboratory diagnosis'/exp OR sampling:ab,ti OR sampling:ab,ti OR specimens:ab,ti OR specimens:ab,ti) AND (adequate:ab,ti OR satisf*:ab,ti OR suitable:ab,ti OR sufficient:ab,ti)) **AND** ((('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti OR rectal:ab,ti OR gastric:ab,ti OR esophageal:ab,ti OR oesophageal:ab,ti OR stomach:ab,ti OR mediastinum:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR 'lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti)) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR 'rectum cancer'/exp OR 'esophagus cancer'/exp OR 'digestive system cancer'/exp OR 'mediastinum lymph node'/exp OR 'digestive system cancer'/exp) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1   MeSH descriptor: [Endosonography] explode all trees

#1   MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#3   endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#4   EUS and FNA:ti,ab,kw (Word variations have been searched)
#5   #1 or #2 or #3 or #4
#6   Any MeSH descriptor with qualifier(s): [Pathology - PA]
#7   MeSH descriptor: [Specimen Handling] explode all trees
#8   specimen or sampling:ti,ab,kw (Word variations have been searched)
#9   #6 or #7 or #8
#10   adequate or sufficient or suitable:ti,ab,kw (Word variations have been searched)
#11   #9 and #10
#12   CBD or biliary or pancreatic or bile duct or rectal or gastric or esphageal or mediastinum:ti,ab,kw (Word variations have been searched)
#13   cancer or neoplasm or malign or tumor or carcinoma or lymph nodes:ti,ab,kw (Word variations have been searched)
#14   MeSH descriptor: [Lymph Nodes] explode all trees
#15   #13 or #14
#16   #12 and #15
#17   MeSH descriptor: [Gastrointestinal Neoplasms] explode all trees
#18   MeSH descriptor: [Rectal Neoplasms] explode all trees
#19   MeSH descriptor: [Mediastinal Neoplasms] explode all trees
#20   MeSH descriptor: [Stomach Neoplasms] explode all trees
#21   MeSH descriptor: [Biliary Tract Neoplasms] explode all trees
#22   MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#21   #16 or #17 or #18 or #19 or #20 or #211 or #22
#22   #5 and #11 and #21 Publication Year from 2000 to 2016

Results

Results of the bibliographic searches
After removing duplicates, 612 articles (20 reviews and 592 primary studies) were found. 36 primary studies were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies
Overall 11 studies were excluded.
Pancreas
8 studies were excluded: 3 because no outcome of interest (Chen 2012, Park 2016, Siddiqui 2011); 3 because EUS –FNA was performed only in a subgroup of patients smaller than 100 (Aso 2014, Imaoka 2009, Matsuyama 2013); 2 (Lee 2003, Rocca 2007) because 26% and 30% respectively of patients had cystic lesions and no separate results were reported for solid lesions.
Mediastinal Lymph Nodes
1study was excluded patients were not in the inclusion criteria: clinical diagnosis of mediastinal granulomatous lymphadenitis (Manucha 2013).
Gastric lesions
1 study was excluded because no outcome of interest (Hoda 2009).
All sites
1 study was excluded because no outcome of interest (Sodikoff 2013).

Studies awaiting assessment
4 studies were classified as awaiting assessment because written in German, Japanese, Chinese and we were not able to get the translations (Bohle 2013, Furuhata 2012, Gao 2016, Sudhof 2004).

<u>Included studies</u>
Overall 21 studies were included.
Pancreas: 12 studies (Alatawi 2015 , Ardengh 2008 , Baek 2015, Cleveland 2010, Eloubeidi 2003, Fritscher-Ravens 2001, Hucl 2013, Iglesias-Garcia 2011, Kamata 2016 , Mitsuhashi 2006, Möller 2009, Will 2010).
Mediastinal Lymph Nodes: 1 study (Fritscher-Ravens 2000).
Gastric lesions: 1 study (Mekky 2010).
All sites: 7 studies (Aithal 2007, Mehmood 2015, Paik 2015, Larghi 2011, Wittmann 2006, Jhala 2004, Carrara 2016)

Pancreas

Study	N and characteristic of patients	Setting	Intervention	Diagnostic rate of adequate EUS-FNA sampling
Alatawi 2015 (RCT)	100 consecutive patients with solid pancreatic tumours of at least 2 cm in size showed on CT scanner or MRI	Between 1 April 2012 and 30 March 2013 tertiary referral academic center for bilio-pancreatic pathology France	EUS-FNA with standard 22G Echo-ultra TM needle (n=50) EUS-FNB with 22G Echotip Procore needle (n=50)	EUS FNA: 45/50 (90%) EUS-FNB 50/50 (100%) Overall 95/100 (95%)
Ardengh 2008 (data extracted from abstract because full text not available)	611 patients with pancreatic tumors	From January 1997 to December 2006 setting not reported	cytological smears (n=282) only cell blocks (n=329)	cytological smears + cell blocks: 595/611 (97.4%)
Baek 2015	191 cases of solid pancreatic lesions	Between January 2010 and December 2012 Department of Pathology, Seoul National University Hospital - Korea	Endoscopic ultrasound guided fine needle apiration cytology (EUS-FNAC); details on needle not provided	171/191 (89.5%)
Cleveland 2010	247 solid pancreatic masses 276 lymph nodes	Between 1997 and 2007 tertiary care center USA	EUS-FNA for cytodiagnosis; default needle gauge was 22. Exceptions were noted in the clinical record	pancreatic tumours 240/247 (97%) lymph nodes 252/276 (91%)
Eloubeidi 2003	101 consecutive patients with suspected pancreatic carcinoma based on clinical results and/or other imaging studies	Between July 2000 and August 2001 University of Alabama at Birmingham USA	Endoscopic ultrasound–guided fine-needle aspiration biopsy with a 22-gauge needle (EUS-FNAB)	99/101 (98%)
Fritscher-Ravens 2001	114 patients with focal solid pancreatic masses	recruitment period not reported Department of Interdisciplinary	EUS-FNA with 22-gauge needle for cytodiagnosis	112/114 (98.2%)

		Endoscopy, Institute of Cytopathology, Germany		
Hucl 2013 (RCT)	144 Consecutive patients with a pancreatic mass lesion or peri-intestinal lymphadenopathy	Between March 2011 and July 2012 Institute of Gastroenterology, India	fine needle biopsy with both a newly developed 22G core needle (the FNB needle) (n=145) standard 22G fine needle aspiration (FNA) needle (n=145)	FNB: 125 (86.2 %) FNA: 127 (87.6 %)
Iglesias-Garcia 2011	182 patients with solid pancreatic masses	a 2-year study period (dates not reported) Department of Gastroenterology and Hepatology Spain	EUS-FNA with standard 22-gauge needle with on-site cytopathologist (n: 95) cases without on-site cytopathologist (n: 87) cases	on-site cytopathologist 94/95(98.9%) without on-site cytopathologist:76/87 (87.4%)
Kamata 2016 (RCT)	214 consecutive patients with solid pancreatic masses who presented to	April - September 2013 eight referral centers, Japan	standard 25-gauge needle (n=108) for core biopsy a 25-gauge needle with a core trap (ProCore) for core biopsy (n=106)	standard 25-gauge needle: 81.1 % a 25-gauge needle with a core trap (ProCore): 69.4 %;
Mitsuhashi 2006	267 patients with solid pancreatic masses	Between February 1996 and October 2000 California Irvine Medical Center USA	EUS-FNA for cytodiagnosis with 22-gauge, 10-cm needle	253/267 (95.9%)
Möller 2009	192 patients with solid pancreatic masses	6-year period until the end of 2006 three centers, no more details provided	EUS-FNA with 22-gauge needles for cytological and histological diagnosis	histology: 86.5% cytology: 92.7% cytology + histology: 190/192 (98.9%)

		Germany		
Will 2010	153 consecutive patients with pancreatic tumor lesions revealed by any imaging procedure	Fron January 2000 to march 2003 Department of Gastroenterology, Germany	EUS-FNA with 19 or 22-gauge needles for cytological and patho-histological diagnosis	cytology: 152/153 (99.3%) patho-histology: 96/153 (62.7%)

Mediastinal Lymph Nodes

Study	N and characteristic of patients	Setting	Intervention	Diagnostic rate of adequate EUS-FNA sampling
Fritscher-Ravens 2000	153 patients with Mediastinal lymphadenopathy	Between November 1997 and November 1999 Department of Interdisciplinary Endoscopy Germany	EUS-FNA with 22-gauge Vilmann-Hancke needle or a 22-gauge Wilson-Cook echo tip for cytodiagnosis	150/153 (98%)

Gastric tumours

Study	N and characteristic of patients	Setting	Intervention	Diagnostic rate of adequate EUS-FNA sampling
Mekky 2010	141 consecutive patients with sub-mucosal tumours s of the stomach	Between January 2000 and December 2008 Aichi Cancer Center Hospital Japan	EUS-FNA with 22-gauge needles for cytodiagnosis	117/141(83%)

All sites

Study	N and characteristic of patients	Setting	Intervention	Diagnostic rate of adequate EUS-FNA sampling
Aithal 2007	167 patient with mural and extramural solid masses suitable for both FNA and tru-cut biopsy that could be approached via trans-oesophaeal (n:57) or trans-gastric approach (n: 86); patients that can	period of recruitment not reported three centers UK	dual sampling with both FNA for cytology and tru-cut biopsy for histology (n: 95) sequential sampling(FNA only when tru-	adequacy of samples reported only for tru-cut biopsy dual sampling: tru-cut biopsy 85/95 (89%) sequential sampling: 64/75 (89%)

	be approached via with trans-duodenal (n:24)only when the lesion can be approached with the scope in a relatively straight position		cut biopsy tissue cores were macroscopically inadequate (n: 75)	
Carrara 2016	144 consecutives patients with solid masses : pancreas (n:102), adenopathies (n:21), parietal masses of the GI tract (n:17) other locations (n: 4).	Between August 2013 and October 2014 Endoscopy Unit of the Humanitas Research Hospital Italy	EUS-FNA for cytological diagnosis with 25-G needles (n:72) EUS-FNA with 22-G needles (n:72)	25-G group :58/72 (81%) 22-G group 49/72 (68%); Overall: 107/144 (74.3%)
Jhala 2004	209 consecutive samples from 151 patients pancreas (n:84; solid 76, cystic 8), lymph nodes and spleen (n: 91; lymph nodes :89, spleen 2), gastrointestinal tract (n: 15; esophagus 5, stomach 3, duodenum 7), liver and biliary tract (n:11; liver 7, biliary tract 4), adrenal glands (n: 4), and others (n:4; mediastinum 3, retro-peritoneum 1)	period of recruitment not reported The University of Alabama at Birmingham, USA	EUS-FNAB EUS-guided fine-needle aspiration biopsy with 22-gauge needle for cytological diagnosis	96% (201 of 209).
Larghi 2011	120 consecutive patients: Enlarged lymph nodes (n:37), Abdominal mass (n:26), Sub-epithelial lesion (n:17) , Pancreatic body or tail mass (n:13), Thickened oesophago-gastric wall (n:11) , Mediastinal mass (n:6) , Liver mass (n:5) , Spleen mass (n:2), Left adrenal mass (n:2), Perirectal mass (n:1)	Between January 2007 and December 2008 Tertiary care academic medical center Italy	EUS-guided fine-needle tissue acquisition (EUS-FNTA) with a 19-gauge needle.	116 of the 119 patients (97.5%)
Mehmood 2015	393 patients : mediastinal	Between August 2008 and	EUS-FNA with 22-gauge	369 / 393 (93.9%)

| | lymphadenopathy (n: 181), pancreatic lesions (n: 115) intra-abdominal lymphadenopathy (n:79) miscellaneous lesions (gastric mass, splenic, retroperitoneal, oesophageal, or adrenal lesions) (n: 18). | September 2013.

Departments of Internal Medicine and Pathology at a tertiary care center Pakistan | needles for cytodiagnosis | |
|---|---|---|---|---|
| Paik 2015 | 33 procedures in 125 patients : pancreas (n: 58), Lymph node (n=48), retroperitoneal mass (n=8), Ampulla of Vater (n=2), Gallbladder (n=8), Common bile duct (n=2), Duodenum (n=2), Liver (n=5) | Between October 2011 and March 2013.

Department of gastroenterology, Korea | EUS-guided fine needle biopsy with 22G ProCore needle using capillary sampling (EUS-FNB) | 122/133 (94%) |
| Wittmann 2006 | 159 patients : pancreas (n: 83), mediastinum (n:55), oesophagus (n: 9), stomach (n:7), rectum (n: 2), hepatic hilum (n: 1), hypopharynx (n: 1) third part of duodenum (n:1). | Between May 2002 and April 2005

University College London Hospitals UK | EUS-FNA with 22-gauge needle for cytology (159) EUS-TNB tru-cut needle biopsy with 19-gauge outer cutting needle for histology (n:96) EUS-FNA/TNB (n: 96) | EUS-FNA: 91% EUS-TNB: 88% EUS-FNA/TNB: 97% |

Conclusions

Overall adequate samples ranged from 62.7% to 100% (mean 90.8% , median; 94%).

Pancreatic lesions : adequate samples ranged from 62.7% to 100% (mean 90.4% , median: 95.9%): in the eight studies were EUS-FNA was performed for cytodiagnosis adequate samples ranged from 87.4% to 99.3% (mean 94%, median 94.3%); in the six studies were FNB were performed for histological diagnosis adequate samples ranged from 62.7% to 100% (mean 83.4%, median 86.2%).

Mediastinal Lymph Nodes: adequate sample was obtained in 98% of patients were EUS-FNA was performed for cytological diagnosis (one study).

Gastric lesion : adequate sample was obtained in 83% of patients were EUS-FNA was performed for cytological diagnosis (one study).

All sites: in the studies that included patients with lesions at various sites and reported only overall results adequate samples ranged from 74.3% to 97.5% (median 94%, mean 91.7%): in the four studies were EUS_FNA was performed for cytodiagnosis adequate samples ranged from 74.3% to 96% (mean 88.8%, median 92.4%) ; in the four studies were FNB were performed for histological diagnosis adequate samples ranged from 88% to 97.5% (mean 92.1%, median 91.5%)

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Included studies
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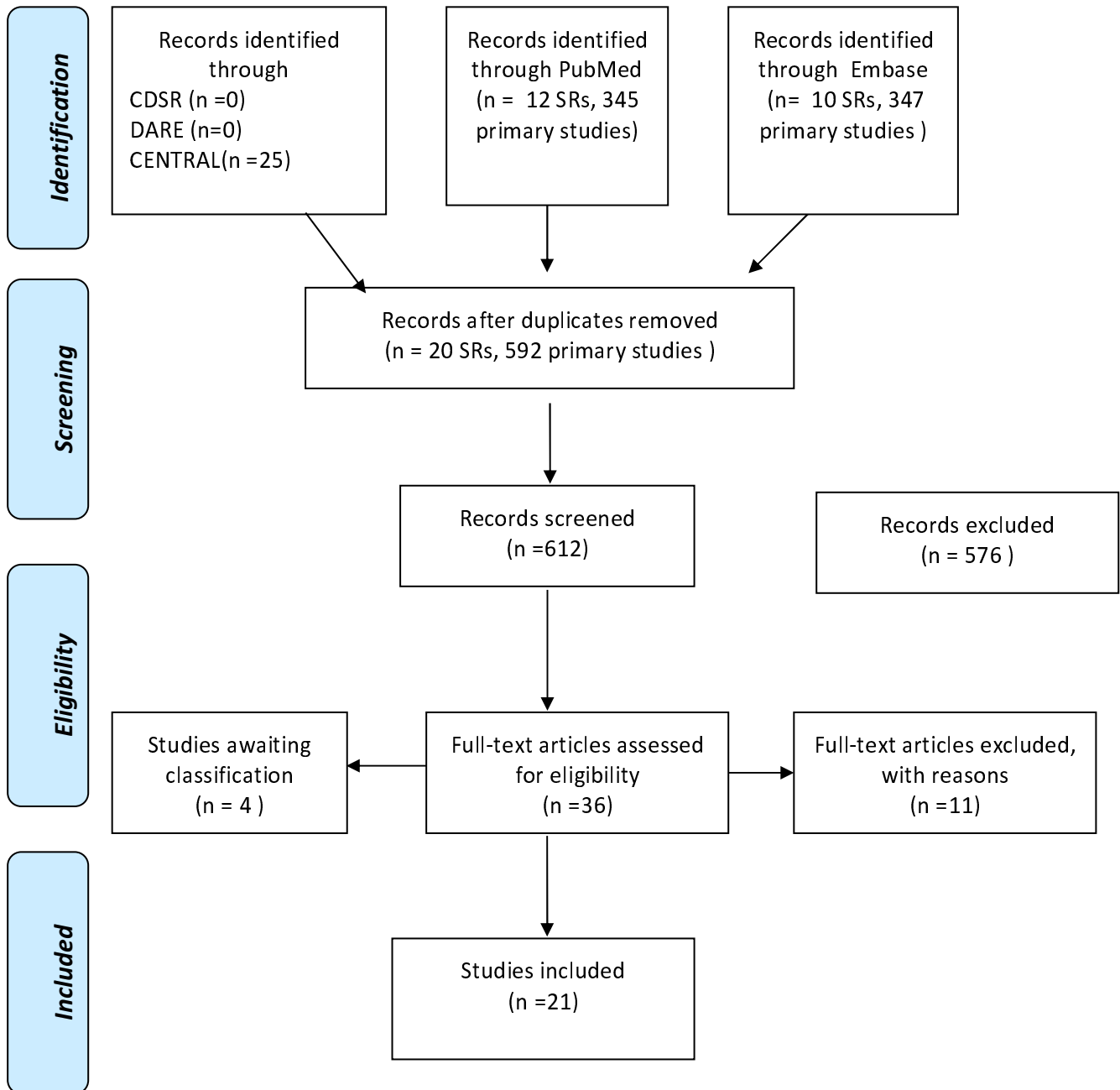
Excluded studies
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Awaiting assessment

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PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n =0)
DARE (n=0)
CENTRAL(n =25)

Records identified through PubMed
(n = 12 SRs, 345 primary studies)

Records identified through Embase
(n= 10 SRs, 347 primary studies)

Screening

Records after duplicates removed
(n = 20 SRs, 592 primary studies)

Records screened
(n =612)

Records excluded
(n = 576)

Eligibility

Studies awaiting classification
(n = 4)

Full-text articles assessed for eligibility
(n =36)

Full-text articles excluded, with reasons
(n =11)

Included

Studies included
(n =21)

S.C. Epidemiologia screening, registro tumori –
CPO Piemonte
Direttore: Dr. Nereo Segnan
via Cavour 31, 10123 Torino
tel. 011.6333881 - fax 011.6333861
www.cpo.it - email: info@cpo.it

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CPO
Centro di Riferimento per l'Epidemiologia
e la Prevenzione Oncologica in Piemonte

B VISUALIZATION OF DEFINED LANDMARKS IN EUS

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Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

2.1 (B I(a)). **Does the visualization of defined landmarks improve the quality of EUS in patients suffering from esophageal cancer?**

Population
Patients suffering from oesophageal cancer undergoing EUS

Intervention
Visualization of the tumour, mediastinum (lymph nodes), gastro-oesophageal junction, celiac axis (lymph nodes) and left lobe of the liver (to rule out metastatic disease)

Control
Not to visualize the above mentioned landmarks

Outcome
Accurate Staging, impact on patients' management

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Endosonography"[Mesh] OR EUS[Title/Abstract]) **AND** ("Neoplasm Staging"[Mesh] OR stag*[Title/Abstract] OR TNM[Title/Abstract] OR "Patient Care Management"[Mesh] OR "clinical management"[Title/Abstract] OR "patient management" [Title/Abstract] OR impact[Title/Abstract]) **AND** (((esophageal[Title/Abstract] OR oesophageal[Title/Abstract]) AND (cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign*[Title/Abstract] OR tumor[Title/Abstract] OR

tumour[Title/Abstract] OR tumors[Title/Abstract] OR tumours[Title/Abstract] OR carcinom*[Title/Abstract] OR mass[Title/Abstract] OR masses[Title/Abstract])) "Esophageal Neoplasms"[Mesh]) **AND** ("Lymph Nodes"[Mesh] OR "lymph node"[Title/Abstract] OR "lymph nodes"[Title/Abstract] OR "lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract] OR "Esophagogastric Junction"[Mesh] OR mediastinum[Title/Abstract] OR "celiac axis"[Title/Abstract] OR (("Liver"[Mesh] OR liver[Title/Abstract]) AND ("right lobe" [Title/Abstract]OR "left lobe" [Title/Abstract]))) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('endoscopic echography'/exp OR EUS:ab,ti) **AND** ('cancer staging'/exp OR stag*:ab,ti OR TNM:ab,ti OR 'patient management':ab,ti OR 'clinical management':ab,ti OR impact:ab,ti) **AND** ((((esophageal:ab,ti OR oesophageal:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti)) OR 'esophagus cancer'/exp) **AND** ('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti OR 'mediastinum lymph node'/exp OR 'celiac axis':ab,ti OR 'lower esophagus sphincter'/exp OR (('liver'/exp OR liver:ab,ti) AND ('left lobe':ab,ti OR 'right lobe':ab,ti))) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)
#1   MeSH descriptor: [Endosonography] explode all trees
#2   EUS:ti,ab,kw (Word variations have been searched)
#3   MeSH descriptor: [Neoplasm Staging] explode all trees
#4   MeSH descriptor: [Patient Care Management] explode all trees
#5   staging or TNM or impact or clinical management or patient management:ti,ab,kw (Word variations have been searched)
#6   #1 or #2
#7   #3 or #4 or #5
#8   MeSH descriptor: [Esophageal Neoplasms] explode all trees
#9   esophageal:ti,ab,kw (Word variations have been searched)
#10   Cancer or tumor or mass or malignant or carcinoma or neoplasm:ti,ab,kw (Word variations have been searched)
#11   #9 and #10
#12   #11 or #8
#13   MeSH descriptor: [Lymph Nodes] explode all trees
#14   MeSH descriptor: [Esophagogastric Junction] explode all trees
#15   lymph nodes:ti,ab,kw (Word variations have been searched)
#16   mediastinum:ti,ab,kw (Word variations have been searched)
#17   celiac axis:ti,ab,kw (Word variations have been searched)
#18   MeSH descriptor: [Liver] explode all trees
#19   liver:ti,ab,kw (Word variations have been searched)
#20   "right lobe" or "left lobe'":ti,ab,kw (Word variations have been searched)
#21   #18 or #19
#22   #21 and #20
#23   #22 or #13 or #14 or #15 or #16 or #17
#24   #6 and #7 and #12 and #23 Publication Year from 2000 to 2015

Primary studies

PubMed
("Endosonography"[Mesh] OR EUS[Title/Abstract]) **AND** ("Neoplasm Staging"[Mesh] OR stag*[Title/Abstract] OR TNM[Title/Abstract] OR "Patient Care Management"[Mesh] OR "clinical management"[Title/Abstract] OR "patient management" [Title/Abstract] OR impact[Title/Abstract]) **AND** (((esophageal[Title/Abstract] OR oesophageal[Title/Abstract]) AND (cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign*[Title/Abstract] OR tumor[Title/Abstract] OR tumour[Title/Abstract] OR tumors[Title/Abstract] OR tumours[Title/Abstract] OR carcinom*[Title/Abstract] OR mass[Title/Abstract] OR masses[Title/Abstract])) "Esophageal Neoplasms"[Mesh]) **AND** ("Lymph Nodes"[Mesh] OR "lymph node"[Title/Abstract] OR "lymph nodes"[Title/Abstract] OR "lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract] OR "Esophagogastric Junction"[Mesh] OR mediastinum[Title/Abstract] OR "celiac axis"[Title/Abstract] OR (("Liver"[Mesh] OR liver[Title/Abstract]) AND ("right lobe" [Title/Abstract]OR "left lobe" [Title/Abstract]))) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase
('endoscopic echography'/exp OR EUS:ab,ti) **AND** ('cancer staging'/exp OR stag*:ab,ti OR TNM:ab,ti OR 'patient management':ab,ti OR 'clinical management':ab,ti OR impact:ab,ti) **AND** ((((esophageal:ab,ti OR oesophageal:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti)) OR 'esophagus cancer'/exp) **AND** ('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti OR 'mediastinum lymph node'/exp OR 'celiac axis':ab,ti OR 'lower esophagus sphincter'/exp OR (('liver'/exp OR liver:ab,ti) AND ('left lobe':ab,ti OR 'right lobe':ab,ti))) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1   MeSH descriptor: [Endosonography] explode all trees
#2   EUS:ti,ab,kw (Word variations have been searched)
#3   MeSH descriptor: [Neoplasm Staging] explode all trees
#4   MeSH descriptor: [Patient Care Management] explode all trees
#5   staging or TNM or impact or clinical management or patient management:ti,ab,kw (Word variations have been searched)
#6   #1 or #2
#7   #3 or #4 or #5
#8   MeSH descriptor: [Esophageal Neoplasms] explode all trees
#9   esophageal:ti,ab,kw (Word variations have been searched)
#10   Cancer or tumor or mass or malignant or carcinoma or neoplasm:ti,ab,kw (Word variations have been searched)
#11   #9 and #10
#12   #11 or #8
#13   MeSH descriptor: [Lymph Nodes] explode all trees
#14   MeSH descriptor: [Esophagogastric Junction] explode all trees

#15   lymph nodes:ti,ab,kw (Word variations have been searched)
#16   mediastinum:ti,ab,kw (Word variations have been searched)
#17   celiac axis:ti,ab,kw (Word variations have been searched)
#18   MeSH descriptor: [Liver] explode all trees
#19   liver:ti,ab,kw (Word variations have been searched)
#20   "right lobe" or "left lobe'":ti,ab,kw (Word variations have been searched)
#21   #18 or #19
#22   #21 and #20
#23   #22 or #13 or #14 or #15 or #16 or #17
#24   #6 and #7 and #12 and #23 Publication Year from 2000 to 2015

Results

Results of the bibliographic searches
After removing duplicates, 500 articles (33 reviews and 467 primary studies) were found. 7 systematic reviews and 29 primary studies were found as potentially relevant and acquired in full text for more proof evaluation. 2 further potentially relevant articles were retrieved in the references of the retrieved studies. (See flow chart).
In first instance systematic reviews were considered. All assessed only the accurate staging outcome and the most updated review included primary studies published up to June 2010. So we selected primary studies which assessed accurate staging only if published since July 2010 and primary studies which assessed the impact on patients management published within 2000 and August 2015.

Excluded studies
21 studies were excluded: one because no intervention of interest (EUS combined with endoscopy) (Grotenhuis 2013); one because written in Chinese language (Li 2011), 17 because they were conference abstract (Canipe 2014, Choi 2012, De Nucci 2015, Fernández-Sordo 2011, Giever 2015, Hatta 2012, Hrdlicka 2011, Mansfield 2015, Meister 2012 Am. J. Gastroenterol, Meister 2012 Ultraschall Med, Pathiraja 2012, Peck 2013 , Puli 2009, Singh 2013 S518, Singh 2013 S516-S517, Thosani 2011, Thota 2014), because lacked of a reliable reference standard (Shami 2006), one because did not provide separate results for different sites of upper gastrointestinal tract (Mortensen 2007).

Included studies
17 studies were included: five systematic reviews (Kelly 2001, Puli 2008, Sgourakis 2011, Thosani 2012, Van Vliet 2008) and 12 primary studies (Bergeron 2014, Bulsiewicz 2014, Dhupar 2015, Gheorghe 2006, Lee 2014, Meister 2013, Pouw 2011, Preston 2003, Shah 2004, Shumaker 2002, Subasinghe 2010, Walker 2011).

Accurate staging
None of the included studies exactly matched the review question, i.e. whether the quality of EUS influenced the accurate staging.
We found 5 systematic reviews (Kelly 2001, Puli 2008, Sgourakis 2011, Thosani 2012, Van Vliet 2008) and 4 primary studies (Bergeron 2014, Dhupar 2015, Lee 2014, Meister 2013) assessing the diagnostic accuracy of EUS. All the studies used histopathology as reference standard. Because the overlapping of primary studies included in the systematic reviews was low (less than 50%) we extracted data from all the SRs.

Two SRs (Kelly 2001, Thosani 2012) assessed the accuracy of EUS for T staging, the other three reviews assessed the accuracy of EUS for N staging (Puli 2008, Sgourakis 2011, Van Vliet 2008). Three primary studies assessed accuracy of EUS both for T and N stage for esophageal cancer (Lee 2014, Bergeron 2014, Meister 2013), one study (Dhupar 2015) assessed the accuracy of EUS for T stage of the gastro-esophageal junction cancer. For T stage the studies used different cut off to measure sensitivity, specificity and overall accuracy. N stage was measured for regional and celiac lymph nodes.

Overall accuracy for T stage ranged from 48% to 86.7%. Accuracy for T1 stage ranged from 83% to 86.7%; for T2 ranged from 75% to 86.7%; for T3 ranged from 79% to 93.3%; for T4 it was of 95% in one study. One SR assessed the sensitivity and specificity of EUS in distinguishing T1,T2 vs T3,T4 and they ranged from 71-100 and 66.7-100 respectively. Sensitivity and specificity of EUS in staging T1a ranged from 41.6% to 85% and from 81.3% to 87% respectively. Sensitivity and specificity of EUS in staging T1b ranged from 58% to 86% and from 49% to 86% respectively. Sensitivity and specificity of EUS for N1 stage of regional lymph nodes ranged from 76% to 80% and 70% to 72% respectively. Sensitivity and specificity of EUS for N1 stage of celiac lymph nodes ranged from 67% to 85% and 95% to 98% respectively.

Impact on patients' management
None of the included studies exactly matched the review question, i.e. whether the quality of EUS influenced the impact on patient management.

We found eight studies (Shah 2004, Bulsiewicz 2014, Walker 2011, Subasinghe 2010, Gheorghe 2006, Preston 2003, Pouw 2011, Shumaker 2002) that assessed the impact of EUS results on management plans. The studies differed substantially for the measures used to assess the impact on patients' management. Outcomes, results and authors conclusions are reported in the table below.

Overlapping of primary studies between systematic reviews

	Thosani 2012	van Vliet 2008	Puli 2008	Kelly 2001
Arima 2004	X			
Binmoeller 1995		X	X	X
Botet 1991		X		X
Bowrey 1999		X	X	
Buskens 2004	X			
Catalano 1994				X
Catalano 1999		X	X	
Chemaly 2008	X			
Choi 2000		X		
DeWitt 2005		X	X	
Dittler and Siewert 1993		X		X
Eloubeidi 2001			X	
Eloubeidi 2001		X	X	
Fok 1992			X	
Fukuda 2000	X			
Giovannini 1999			X	

Greenberg 1994		X		
Grimm 1993		X	X	X
Hasegawa 1996		X		
Heintz 1991				X
Heeren 2004				
Hunerbein 1996		X		X
Kallimanis 1995			X	
Kawano 2003	X			
Kouzu 1992	X			
Krasna 1999			X	
Larghi 2005	X			
Lowe 2005		X		
Manzoni 1993				X
May 2004	X			
Murata 1988	X			X
Murata 1993				X
Murata 1996	X			
Natsugoe 1996		X	X	
Nesje 2000		X		
Nishimaki 1999		X	X	
Parmar 2002		X		
Pech 2006	X			
Pedrazzani 2005		X		
Peters 1994				X
Pham 1998		X		
Rampado 2008	X			
Rasanen 2003				
reed 1998			X	
Rice 1991		X		
Richards 2000		X		
Salminen 1999		X	X	
Scotiniotis 2001	X			
Shimizu 1997			X	
Shinkai 2000	X	X		
Sihvo 2004		X		
Simizu 1995	X			
Takemoto 1986				X
Tio 1986			X	
Tio 1989			X	
tio 1990		X	X	
Tio 1989			X	
tio 1990			X	
Toh 1993	X			

Vazquez-Sequeiros 2001		X	X	
Vazquez-Sequeiros 2003		X		
Vickers 1998		X	X	
Wallace 2000			X	
Williams 1999			X	
Wu 2003		X		
Yanai 1996	X			
Yanai 2003	X			
Yoshikane 1994	X	X		
Ziegler 1991		X		X

(the overlapping of the studies included in Sgourakis 2011 could not be assessed because the review did not provide the references of the included studies)

Accurate staging

Study	N patients	T staging	N staging	M staging	Cases over staged by EUS	Cases under staged by EUS
Thosani 2012 Systematic review and meta-analysis	19 studies with 1019 patients with superficial EC (SEC)	Mucosal invasion (T1a) Sensitivity(95% CI): 0.85 (0.82-0.88) Specificity (95% CI): 0.87 (0.84-0.90) PLR (95% CI): 6.62 (3.61-12.12) NLR (95% CI): 0.20 (0.14-0.30) Submucosal invasion (T1b) Sensitivity (95% CI): 0.86 (0.82-0.89) Specificity (95% CI): 0.86 (0.83-0.89) PLR (95% CI): 5.13 (3.36-7.82) NLR (95% CI): 0.17 (0.09-0.30)				

Van Vliet 2008

Systematic review and meta-analysis | 1963 patients with oesophageal cancer who performing EUS

31 studies on EUS for regional lymph node metastases with 1841 participants

5 studies on EUS for celiac lymph node metastases with 339 participants | | Regional lymph node metastases

Sensitivity (95% CI) = 0.80 (0.75 –0.84)

Specificity (95% CI) = 0.70 (0.65 –0.75)

Celiac lymph node metastases

Sensitivity (95% CI) = 0.85 (0.72 –0.99)

Specificity (95% CI) = 0.96 (0.92 –1.00) | | | |
| Puli 2008

Systematic review and meta-analysis | 25 studies including 2029 participants | | Celiac axis lymph node metastasis

Sensitivity (95% CI) = 0.67 (0.62-0.71)

Specificity (95% CI) = 0.98 (0.97-0.99)

PLR (95% CI) = 14.96 (11.17-20.03)

NLR (95% CI) = 0.34 (0.30-0.39) | distal metastasis

Sensitivity = 0.67 (0.63-0.72)

Specificity = 0.98 (0.97-0.99)

PLR= 14.56 (10.97-19.33) | | |

				NLR= 0.34 (0.29-0.39)		
Kelly 2001

Systematic review | 13 studies for staging oesophageal carcinoma; n. of participants not reported | Ranges of sensitivity to correctly stage T1/T2 and not over stage cancers as T3/T4: 71.4–100

Ranges of specificity to correctly stage T3/T4 and not under stage cancers as T1/T2 66.7–100 | | | | |
| Sgourakis 2011

Systematic review and meta-analysis | 39 studies for regional lymph node metastases

8 on EUS for celiac lymph node metastases | | Regional lymph node

Sensitivity = 0.76 (0.74-0.79)

Specificity = 0.72 (0.69-0.75)

Celiac lymph node metastases

Sensitivity = 0.81 (0.72-0.88)

Specificity = 0.95 (0.92-0.98) | | | |

					T 29%	T 23%
Dhupar 2015	181 patients (median age 66 years) with GE junction oesophageal cancer	Sensitivity: T0 6% (1/18); T1a 56% (23/41); T1b 58% (41/71); T2 10% (2 / 21); T3 70% (21 / 30) Overall accuracy T stage: 48/181(48%)				
Lee 2014	15 patients (mean age=68.1 ± 7 y) newly diagnosed with oesophageal cancer	Accuracy for distinguishing T1 lesions= 86.7% Accuracy for distinguishing T2 lesions= 86.7% Accuracy for distinguishing T3 lesions= 93.3% Overall accuracy: 86.7%	Accuracy: 75%			
Bergeron 2014	107 patients mean age :66 years (range, 39-91 years with oesophageal high-grade dysplasia, carcinoma in situ, or T1 oesophageal cancer	cT1a lamina propria tumour invasion Sensitivity: 41.6% Specificity : 81.35%. invasion superficial to the submucosa (<cT1b) Sensitivity = 72% Specificity= 48.7%	Sensitivity 0% none of the patients with EUS predicted to have lymph node involvement actually had pathologically positive lymph nodes. Specificity: 90% (likely due to the large number of patients (89/107) with pN0)			

Meister 2013	143 patients (mean age 63.8 ± 10.7) with oesophageal cancer	**T1** Sensitivity (95 % CI) = 0.68 (0.58–0.79) Specificity (95 % CI) = 0.97 (0.96–1) Accuracy (95 % CI)= 0.83 (0.77–0.89) **T2** Sensitivity (95 % CI) = 0.39 (0.23–0.56) Specificity (95 % CI) = 0.84 (0.75–0.89) Accuracy (95 % CI)= 0.75 (0.65–0.79) **T3** Sensitivity (95 % CI) = 0.72 (0.56–0.89) Specificity (95 % CI) = 0.81 (0.7–0.86) Accuracy (95 % CI)= 0.79 (0.70–0.84) **T4** Sensitivity (95 % CI) = 0.13 (0–0.35)	**N1** Sensitivity (95 % CI) = 0.76 (0.65–0.89) Specificity (95 % CI) = 0.71 (0.56–0.84) Accuracy (95 % CI)= 0.74 (0.65–0.83)		11%	11%

| | | Specificity (95 % CI) = 0.97 (0.95–1.0)

Accuracy (95 % CI)= 0.93 (0.89–0.97)

Overall accuracy T stage: 60%

<u>Considering only tumours of the GE junction (n = 38)</u>

<u>T1</u>
Sensitivity (95 % CI) = 0.7 (0.42–0.98)

Specificity (95 % CI) = 0.1 (0–1)

Accuracy (95 % CI)= 0.92 (0.84–1)
<u>T2</u>
Sensitivity (95 % CI) = 0.27 (0.04–0.49)

Specificity (95 % CI) = 0.82 (0.67–0.98)

Accuracy (95 % CI)= 0.61 (0.45–0.76)

<u>T3</u>
Sensitivity (95 % CI) = 0.83 (0.62–1) | | | | |

		Specificity (95 % CI) = 0.58 (0.39–0.77) Accuracy (95 % CI)= 0.66 (0.51–0.81) T4 Sensitivity (95 % CI) = Not calculable due to only one case Specificity (95 % CI) = 0.97 (0.92–1) Accuracy (95 % CI)= 0.94 (0.88–1)				

Q*: the value of TPR where TPR=(1−FPR) with 95%CI
This value was obtained from the intercept of the SROC curve and a line plotting sensitivity equals specificity. Due to the dichotomy chosen for cancer staging, T1 or T2 is analogous to a positive diagnosis in a conventional 2´2 table, and therefore T3 or T4 is analogous to a negative diagnosis. This implies that sensitivity is a measure of the ability of EUS to correctly stage T1/T2 and not over-stage cancers as T3/T4, and conversely specificity is a measure of the ability of EUS to correctly stage T3/T4 and not understage cancers as T1/T2. Neither understaging nor overstaging can be assumed to have more or less impact than the other: understaging cancer will result in surgical operations which are unnecessary and overstaging will result in palliative or non-surgical treatments when resection may have been possible. The most appropriate threshold is one which minimises both understaging and overstaging

Impact on patients' management

Study	N patients	Outcome	Results	Conclusions
Shah 2004	22 patients with known or suspected esophageal cancer	Change in management plan on the basis of EUS results	**Management plan changes post-EUS**: 12/22 (56%) Toward more complex : 5/12 (42%) Toward less complex: 7/12 (58%)	Based on EUS examination findings, clinicians requesting EUS alter patient management in one half of cases, and more often pursue a less-complicated approach. EUS substantially impacts clinical care
Bulsiewicz 2014	135 patients (median age 65 years) with Barrett's oesophagus (BE) and HGD (n=106, 79%) or IMC (n=29, 21%) had staging by EUS (79 non-nodular, 56 nodular).	Frequency of patients excluded from endoscopic therapy based on EUS findings EUS abnormal: no endoscopic therapy EUS normal and nodular disease: EMR	Non nodular disease=0/79; none underwent EMR, all received endoscopic therapy Nodular disease: At EUS, 8 had endo-sonographic evidence of sub-mucosal invasion (14%). EMR provided more useful information than did EUS. In six cases, if EMR had not been performed, EUS would have understaged the disease.	EUS did not alter management in patients with non-nodular HGD or IMC. Because the diagnostic utility of EUS in subjects with non-nodular BE is low, the value of performing EUS in this setting is questionable. For patients with nodular neoplasia, resection of the nodule with histologic examination had greater utility than staging by EUS.
Walker 2011	81 patients (mean age=63.5 (±11.6) years) with biopsy proven oesophageal cancer diagnosed from May 2004 to December 2007	Change in management plan following EUS results All included patients initially considered surgical candidates. Change in management if:	EUS re-directed patient care to neo-adjuvant therapy prior to surgical resection= 26/69 (37.7%) Among these 26 patients = 6 had nodal involvement or loco-regional disease on PET/CT. Thus EUS improved the ability to provide loco-	EUS and integrated PET/CT appear to independently affect treatment decisions, indicating complimentary and necessary roles in the staging of ECA

		locally advanced disease (T3 N0 or T1–3 N1) at EUS: change to neo-adjuvant therapy with chemo-radiation followed by surgery -presence of distant metastases or invasion into local structures at EUS: change to no surgery	regional staging in an additional 20 patients as compared to PET/CT.	
Subasinghe 2010	30 patients (mean age= 58.2 years ,range, 45–84 years) with histologically proven carcinoma of the oesophagus	Change in management plan previously stated on the basis of CT findings, after EUS results	According to CT scan findings, 17 (56.6%) patients were candidates for curative surgery, but after EUS staging (as more advanced stage of oesophageal carcinoma was revealed). Preoperative EUS changed the decision of primary oesophagectomy in 12 (40%) patients and allowed primary oesophagectomy only in 5 (16.6%)	EUS staging revealed a more advanced stage of cancer in the majority of patients. It appears to be far more superior in detecting lymph node involvement compared with CT. Therefore, EUS may have a significant impact on deciding the treatment modality of a patient with oesophageal carcinoma.
Gheorghe 2006	41 patients with oesophageal cancer	change in management plan assuming that without preoperative staging by EUS, all patients in the study group would have been offered surgical treatment	Preoperative EUS staging changed the decision for surgery in 18 of 41 patients (44%) (p<0.0001)	esophageal EUS offers useful information to clinicians who treat patients with esophageal cancer, impacts clinical decision making, and should be used in appropriate settings to plan therapeutic strategy
Preston 2003	100 patients (median age 68, range 33–88	Concordance in management plans	EUS deemed useful by surgeons in making management	The addition of EUS data did not significantly affect the mean number

years), with carcinoma of the oesophagus or oesophagogastric junction	between surgeons with and without EUS results Usefulness of EUS according to surgeons	decisions: in 87.0% 65% and 63.% of patients by the 3 surgeons <u>Number of concordant management plans,</u> without EUS :56% with EUS=62%	of concordant results for management by radical surgery alone, non-surgical therapy with curative intent and neoadjuvant therapy plus surgery There was, however, an increase in the mean number of patients for whom non-surgical palliation was planned, from 18.5 to 24.
Pouw 2011	131 patients (mean age 66± 12.6 years) with early oesophageal or cardia neoplasia who were considered for endoscopic treatment	Number of patients excluded from diagnostic ER and directly referring the patient for surgery based on EUS results only. To investigate the relative contribution of EUS over the preceding endoscopic examination, cases were separated into 2 groups: abnormal EUS and normal endoscopy and abnormal EUS and abnormal endoscopy.	Patients referred for diagnostic ER: <u>Normal EUS:</u> 105/131(80%) <u>Abnormal EUS</u>. 26/ 131 (20%) <u>abnormal EUS and normal endoscopy</u>= 14/26 (54%) in 7 of these 14 patients (50%) no sub-mucosal invasion or other risk factors for lymph node metastasis were found on diagnostic ER <u>abnormal EUS and abnormal endoscopy</u> :12/26 (46%)	the additional value of EUS during the workup including ER and follow-up was very limited. In none of the patients did EUS alone change the treatment policy. In addition, the results of this study strengthen the role of diagnostic ER as a final step in the workup for endoscopic treatment
Shumaker 2002	180 patients (mean age 66.5 ears) referred for preoperative staging of uesophageal cancer by EUS	Proportions of EUS stage 1 and 4 tumours that would not be treated with combined modality therapy: Stage I esophageal cancer are not offered neoadjuvant Chemoradiotherapy Stage IV: unresectable	Stage I: 23/180 (14%) Stage IV: 19/180 (12%)	Preoperative staging of esophageal cancer with EUS identifies a significant proportion of patients (26% in this series) with stage I and IV tumors who may be spared combined modality therapy

Quality of evidence

Accurate staging
Study limitations (risk of bias): no.
Inconsistency of results: yes
Indirectness of evidence: yes (none of the retrieved studies exactly matched the review question, i.e. whether the quality of EUS influenced the accurate staging)
Imprecision: no,
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judges as low because of indirectness and inconsistency

Impact on patients management
Study limitations (risk of bias): no
Inconsistency of results: yes
Indirectness of evidence: yes (none of the retrieved studies exactly matched the review question, i.e. whether the quality of EUS impact patients management)
Imprecision: no
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judges as low because of inconsistency and indirectness.

Conclusions

Overall accuracy for T stage ranged from 48% to 86.7%. Sensitivity and specificity of EUS in distinguishing T1,T2 vs T3,T4 and they ranged from 71-100 and 66.7-100 respectively. Sensitivity and specificity of EUS for N1 stage of regional lymph nodes ranged from 76% to 80% and 70% to 72% respectively. Sensitivity and specificity of EUS for N1 stage of celiac lymph nodes ranged from 67% to 85% and 95% to 98% respectively
(**LOW QUALITY OF EVIDENCE**).

No conclusion can be drawn on the impact of EUS results on changes in patients managements, three studies concluding that EUS was not useful or did not have a significant impact and five concluding that EUS significant impacted on patients management.
(**LOW QUALITY OF EVIDENCE).**

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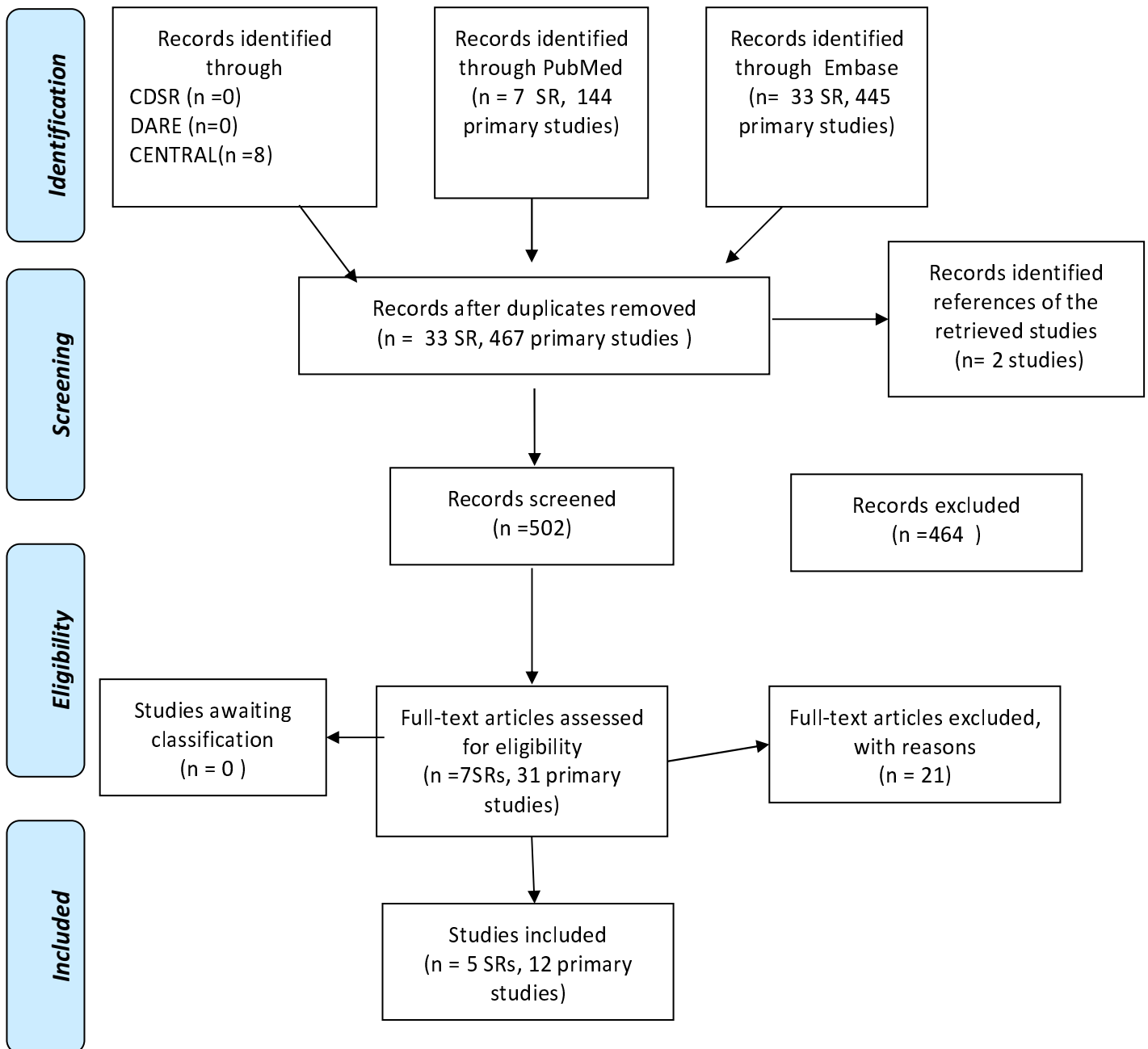
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PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n =0)
DARE (n=0)
CENTRAL(n =8)

Records identified through PubMed
(n = 7 SR, 144 primary studies)

Records identified through Embase
(n= 33 SR, 445 primary studies)

Screening

Records after duplicates removed
(n = 33 SR, 467 primary studies)

Records identified references of the retrieved studies
(n= 2 studies)

Records screened
(n =502)

Records excluded
(n =464)

Eligibility

Studies awaiting classification
(n = 0)

Full-text articles assessed for eligibility
(n =7SRs, 31 primary studies)

Full-text articles excluded, with reasons
(n = 21)

Included

Studies included
(n = 5 SRs, 12 primary studies)

**S.C. Epidemiologia screening, registro tumori –
CPO Piemonte**
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B VISUALIZATION OF DEFINED LANDMARKS IN EUS

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Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

2.2 (B I(b)). **Does the visualization of defined landmarks improve the quality of EUS in patients suffering from pancreatic cancer?**

Population
Patients suffering from pancreatic cancer undergoing EUS

Intervention
Visualization of the entire pancreas, pancreatic mass (tumour, cancer), local lymph nodes (peri-pancreatic), celiac axis (lymph nodes) and left lobe of the liver and visible parts of the right lobe (to rule out metastatic disease), vascular infiltration: mesenteric artery, mesenteric vene, portal vein; infiltration of other peri-pancreatic organs.

Control
Not to visualize the above mentioned landmarks

Outcome
Accurate Staging, impact on patients' management

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Endosonography"[Mesh] OR EUS[Title/Abstract]) **AND** ("Neoplasm Staging"[Mesh] OR stag*[Title/Abstract] OR TNM[Title/Abstract] OR "Patient Care Management"[Mesh] OR "clinical management"[Title/Abstract] OR "patient management" [Title/Abstract] OR impact[Title/Abstract]) **AND** ((pancreatic[Title/Abstract] AND (cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR

malign*[Title/Abstract] OR tumor[Title/Abstract] OR tumour[Title/Abstract] OR tumors[Title/Abstract] OR tumours[Title/Abstract] OR carcinom*[Title/Abstract] OR mass[Title/Abstract] OR masses[Title/Abstract])) OR "Pancreatic Neoplasms"[Mesh]) **AND** ("Lymph Nodes"[Mesh] OR "lymph node"[Title/Abstract] OR "lymph nodes"[Title/Abstract] OR "lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract] OR "celiac axis"[Title/Abstract] OR "Mesenteric Arteries"[Mesh] OR "Mesenteric Veins"[Mesh] OR (mesenteric[Title/Abstract] AND (veins[Title/Abstract] OR vein[Title/Abstract] OR artery[Title/Abstract] OR arteries[Title/Abstract])) OR "vascular infiltration"[Text Word] OR (infiltration[Title/Abstract] AND ("peripancreatic organ"[Title/Abstract] OR "peripancreatic organs"[Title/Abstract]))) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase

('endoscopic echography'/exp OR EUS:ab,ti) **AND** ('cancer staging'/exp OR stag*:ab,ti OR TNM:ab,ti OR 'patient management':ab,ti OR 'clinical management':ab,ti OR impact:ab,ti) **AND** ((pancreatic:ab,ti AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti)) OR 'pancreas tumor'/exp) **AND** ('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti OR 'mediastinum lymph node'/exp OR 'celiac axis':ab,ti OR 'mesenteric artery'/exp OR 'mesenteric vein'/exp OR (mesenteric:ab,ti AND (veins:ab,ti OR vein:ab,ti OR artery:ab,ti OR arteries:ab,ti)) OR 'vascular infiltration':ab,ti OR (infiltration:ab,ti AND ('peripancreatic organ':ab,ti OR 'peripancreatic organs':ab,ti))) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)

#1   MeSH descriptor: [Endosonography] explode all trees
#2   EUS:ti,ab,kw (Word variations have been searched)
#3   MeSH descriptor: [Neoplasm Staging] explode all trees
#4   MeSH descriptor: [Patient Care Management] explode all trees
#5   staging or TNM or impact or clinical management or patient management:ti,ab,kw (Word variations have been searched)
#6   #1 or #2
#7   #3 or #4 or #5
#8   MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#9   pancreatic:ti,ab,kw (Word variations have been searched)
#10   Cancer or tumor or mass or malignant or carcinoma or neoplasm:ti,ab,kw (Word variations have been searched)
#11   #9 and #10
#12   #11 or #8
#13   MeSH descriptor: [Lymph Nodes] explode all trees
#14   lymph nodes:ti,ab,kw (Word variations have been searched)
#15   celiac axis:ti,ab,kw (Word variations have been searched)
#16   MeSH descriptor: [Mesenteric Arteries] explode all trees
#17   MeSH descriptor: [Mesenteric Veins] explode all trees
#18   mesenteric and (artery or vein):ti,ab,kw (Word variations have been searched)
#19   vascular infiltration:ti,ab,kw (Word variations have been searched)
#20   peripancreatic organ and infiltration:ti,ab,kw (Word variations have been searched)

#21   #13 or #15 or #17 or #14 or #16 or #18 or #19or #20
#22   #6 and #7 and #12 and #21 Publication Year from 2000 to 2015

Primary studies

PubMed
("Endosonography"[Mesh] OR EUS[Title/Abstract]) **AND** ("Neoplasm Staging"[Mesh] OR stag*[Title/Abstract] OR TNM[Title/Abstract] OR "Patient Care Management"[Mesh] OR "clinical management"[Title/Abstract] OR "patient management" [Title/Abstract] OR impact[Title/Abstract]) **AND** ((pancreatic[Title/Abstract] AND (cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign*[Title/Abstract] OR tumor[Title/Abstract] OR tumour[Title/Abstract] OR tumors[Title/Abstract] OR tumours[Title/Abstract] OR carcinom*[Title/Abstract] OR mass[Title/Abstract] OR masses[Title/Abstract])) OR **"Pancreatic Neoplasms"[Mesh]) AND** ("Lymph Nodes"[Mesh] OR "lymph node"[Title/Abstract] OR "lymph nodes"[Title/Abstract] OR "lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract] OR "celiac axis"[Title/Abstract] OR "Mesenteric Arteries"[Mesh] OR "Mesenteric Veins"[Mesh] OR (mesenteric[Title/Abstract] AND (veins[Title/Abstract] OR vein[Title/Abstract] OR artery[Title/Abstract] OR arteries[Title/Abstract])) OR "vascular infiltration"[Text Word] OR (infiltration[Title/Abstract] AND ("peripancreatic organ"[Title/Abstract] OR "peripancreatic organs"[Title/Abstract]))) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase
('endoscopic echography'/exp OR EUS:ab,ti) **AND** ('cancer staging'/exp OR stag*:ab,ti OR TNM:ab,ti OR 'patient management':ab,ti OR 'clinical management':ab,ti OR impact:ab,ti) **AND** ((pancreatic:ab,ti AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti)) OR 'pancreas tumor'/exp) **AND** ('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti OR 'mediastinum lymph node'/exp OR 'celiac axis':ab,ti OR 'mesenteric artery'/exp OR 'mesenteric vein'/exp OR (mesenteric:ab,ti AND (veins:ab,ti OR vein:ab,ti OR artery:ab,ti OR arteries:ab,ti)) OR 'vascular infiltration':ab,ti OR (infiltration:ab,ti AND ('peripancreatic organ':ab,ti OR 'peripancreatic organs':ab,ti))) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1   MeSH descriptor: [Endosonography] explode all trees
#2   EUS:ti,ab,kw (Word variations have been searched)
#3   MeSH descriptor: [Neoplasm Staging] explode all trees
#4   MeSH descriptor: [Patient Care Management] explode all trees
#5   staging or TNM or impact or clinical management or patient management:ti,ab,kw (Word variations have been searched)
#6   #1 or #2
#7   #3 or #4 or #5
#8   MeSH descriptor: [Pancreatic Neoplasms] explode all trees

#9   pancreatic:ti,ab,kw (Word variations have been searched)
#10   Cancer or tumor or mass or malignant or carcinoma or neoplasm:ti,ab,kw (Word variations have been searched)
#11   #9 and #10
#12   #11 or #8
#13   MeSH descriptor: [Lymph Nodes] explode all trees
#14   lymph nodes:ti,ab,kw (Word variations have been searched)
#15   celiac axis:ti,ab,kw (Word variations have been searched)
#16   MeSH descriptor: [Mesenteric Arteries] explode all trees
#17   MeSH descriptor: [Mesenteric Veins] explode all trees
#18   mesenteric and (artery or vein):ti,ab,kw (Word variations have been searched)
#19   vascular infiltration:ti,ab,kw (Word variations have been searched)
#20   peripancreatic organ and infiltration:ti,ab,kw (Word variations have been searched)
#21   #13 or #15 or #17 or #14 or #16 or #18 or #19or #20
#22   #6 and #7 and #12 and #21 Publication Year from 2000 to 2015

Results

Results of the bibliographic searches
After removing duplicates, 282 articles (9 reviews and 273 primary studies) were found. 2 systematic reviews and 6 primary studies were found as potentially relevant and acquired in full text for more proof evaluation. 1 further potentially relevant article was retrieved in the references of the retrieved studies. (See flow chart).

Excluded studies
Five studies were excluded: one because did not assess no outcome of interest (Vukobrat-Bijedic 2014), one because written in Chinese language (Tian 2008) and three because they were conference abstract (Iglesias-Garcia 2010, Nawaz 2010, Wong 2010).

Included studies
4 studies were finally included (Kala 2007, Li 2014, Shah 2004, Soriano 2004).
None of the included studies exactly matched the review question, i.e. whether the quality of EUS influenced the accurate staging or impact on patients' management.

Accurate staging
We found one systematic review (Li 2014) assessing the diagnostic accuracy of EUS in TN staging and evaluation of vascular invasion in Pancreatic Cancer. The review included 20 studies including 726 patients.
For the T1–2 staging, the overall sensitivity, specificity, PLR, NLR, were 0.72 (95% CI, 0.65–0.79), 0.90 (95% CI, 0.87–0.93), 6.27 (95% CI, 3.23–12.14), 0.28 (95% CI, 0.12–0.64), respectively.
For the T3–4 staging, the overall sensitivity, specificity, PLR, NLR were 0.90 (95% CI, 0.87–0.93), 0.72 (95% CI, 0.65–0.79), 3.58 (95% CI, 1.57–8.19), 0.16 (95% CI, 0.08–0.31), respectively.
For N staging the overall sensitivity, specificity, PLR, NLR were 0.62 (0.56–0.68), 0.74 (0.68–0.80), 2.54 (1.73–3.75), 0.51(0.38–0.68), and 6.67 (3.29–13.51), respectively.
For vascular invasion the overall sensitivity, specificity, PLR, NLR were 0.87 (0.80–0.92), 0.92 (0.86–0.96), 7.16 (3.61–14.19), 0.20 (0.14–0.30), and 56.19 (24.46–129.08), respectively.

Impact on patients' management

We found two primary studies (Kala 2007, Soriano 2004) that assessed the ability of EUS in predicting tumor resectability, that we considered as a proxy of impact on patient management.

In Kala 2007, 41 patients with pancreatic cancer underwent EUS and laparotomy. In 53% of patients cancer was judged non- resectable at EUS and at laparotomy 51% were found actually non-resectables.

In 34% of patients cancer was judged resectable at EUS and at laparotomy 32% were found actually resectables. In 17% of patients EUS did not allow even judge about resectability before surgery. In conclusion in 83% of patients resectability and non-resectability were well predicted by EUS.

In Soriano 2004, 52 patients received EUS followed by surgical procedure. EUS has a sensitivity, specificity and overall accuracy in predicting resectability of 23%, 100% and 67% respectively.

Finally we found a study that assessed the impact of EUS results on management of known or suspected malignancies (Shah 2004). In this study the physicians requesting EUS were contacted before the EUS examination and were asked: "How would you manage this patient if EUS were not available?" After the examination the referring clinicians were recontacted within 1 week of the procedure, informed of the EUS findings, and asked: (1) "What management plan will you recommend to this patient given the EUS findings?" and if the management strategy differed compared with the pre-EUS response, (2) "Is the recommended change in the management plan directly the result of the EUS findings?" 43 patients were included for which EUS was requested to evaluate solid pancreatic masses (n 19), cystic lesions (n 6), and suspected pancreatic masses (n 8). Requesting physicians changed management strategies in 49% of patients after pancreatic EUS procedures. This most often involved a less-complex approach (71%), and included 32% of patients in whom surgery was no longer recommended.

Quality of evidence

Accurate staging
Study limitations (risk of bias): no.
Inconsistency of results: no
Indirectness of evidence: yes (none of the retrieved studies exactly matched the review question, i.e. whether the quality of EUS influenced the accurate staging)
Imprecision: no
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judges as moderate because of indirectness for accurate staging.

Impact on patients' management
Study limitations (risk of bias): no.
Inconsistency of results: no
Indirectness of evidence: yes (none of the retrieved studies exactly matched the review question, i.e. whether the quality of EUS influenced the patients' management)
Imprecision: yes (only 3 studies with 133 patients)
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judges as low because of imprecision and indirectness.

Conclusions

No direct conclusions can be drawn about the impact of quality of EUS on accurate staging or impact on patient management.
For the T1–2 staging, the overall sensitivity and specificity were 0.72 and 0.90. For the T3–4 staging, the overall sensitivity and specificity were 0.90 and 0.72.
For N staging the overall sensitivity and specificity were 0.62 and 0.74
For vascular invasion the overall sensitivity and specificity were 0.87 and 0.92
(**MODERATE QUALITY OF EVIDENCE**)

Tumour resectability was correctly predicted by EUS in 67%- 83% of patients
Treatment plan was altered in 49% of patients after pancreatic EUS results.
(**LOW QUALITY OF EVIDENCE).**

References

Included studies
1. Kala, Z.; Valek, V.; Hlavsa, J.; Hana, K., and Vanova, A. The role of CT and endoscopic ultrasound in pre-operative staging of pancreatic cancer. Eur J Radiol. 2007 May; 62(2):166-9.
2. Li J.-H.; He R.; Li Y.-M.; Cao G.; Ma Q.-Y., and Yang W.-B. Endoscopic ultrasonography for tumor node staging and vascular invasion in pancreatic cancer: a meta-analysis. Dig Surg. 2014; 31(4-5):297-305;
3. Shah JN, Ahmad NA, Beilstein MC et al. Clinical impact of endoscopic ultrasonography on the management of malignancies. Clin Gastroenterol Hepatol 2004; 2: 1069-1073
4. Soriano A, Castells A, Ayuso C, Ayuso JR, de Caralt MT, Ginès MA, Real MI, Gilabert R, Quintó L, Trilla A, Feu F, Montanyà X, Fernández-Cruz L, Navarro S. Preoperative Staging and Tumor Resectability Assessment of Pancreatic Cancer: Prospective Study Comparing Endoscopic Ultrasonography, Helical Computed Tomography, Magnetic Resonance Imaging, and Angiography. Am. J. Gastroenterol. 2004; 99(3):492-501;

Excluded studies
1. Iglesias-Garcia J.; Alvarez-Castro A.; Iglesias-Canle J.; Larino-Noia J.; Pazos G.; Forteza J.; Varo E., and Dominguez-Munoz E. Endoscopic ultrasound (EUS) vs helical CT scan for TN staging and evaluation of resectability of pancreatic cancer: A prospective, comparative study using histology of surgical specimens as gold-standard. Gastroenterology. 2010; 138(5):S11;
2. Nawaz H.; Chen Y.-F.; Khalid A.; Sanders M.; Moser J.; Landsittel D., and Papachristou G. Comparison of endoscopic ultrasound (EUS) and computed tomography (CT) in assessing loco-regional lymph node involvement, vascular invasion, and resectability of pancreatic cancer: A meta-analysis. Am. J. Gastroenterol. 2010; 105S59;
3. Tian Y.-T.; Wang C.-F.; Shan Y.; Zhao D.-B.; Wang G.-Q.; Zhao X.-M.; Ouyang H.; Hao Y.-Z.; Sun Y.-M.; Qu H., and Zhao P. Prospective evaluation of ultrasonography, multi-slice spiral CT, endoscopic ultrasonography, and magnetic resonance imaging in assessment of TNM staging and assessment of resectibility in pancreatic carcinoma. Nat. Med. J. China. 2008; 88(40):2829-2832;

4. Vukobrat-Bijedic Z.; Husic-Selimovic A.; Bijedic N.; Gornjakovic S.; Sofic A.; Gogov B.; Bjelogrlic I.; Mehmedovic A., and Glavas S. Sensitivity of EUS and ERCP endoscopic procedures in the detection of pancreatic cancer during preoperative staging correlated with CT and CT angiography imaging methods. Acta Inform. Med. 2014; 22(3):160-163;

5. Wong R.; Binmoeller K.F.; Hassoun A., and Shah J.N. Electronic curvilinear EUS for assessing resectability of pancreatic cancer. Gastrointest. Endosc. 2010; 71(5):AB291-AB292;

PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n =0)
DARE (n=0)
CENTRAL(n =4)

Records identified through PubMed
(n = 1 SR, 130 primary studies)

Records identified through Embase
(n= 9 SR, 238 primary studies)

Screening

Records after duplicates removed
(n = 9 SR, 273 primary studies)

Records identified references of the retrieved studies
(n= 1 study)

Records screened
(n =283)

Records excluded
(n = 274)

Eligibility

Studies awaiting classification
(n =0)

Full-text articles assessed for eligibility
(n =9)

Full-text articles excluded, with reasons
(n = 5)

Included

Studies included
(n =4)

S.C. Epidemiologia screening, registro tumori –
CPO Piemonte
Direttore: Dr. Nereo Segnan
via Cavour 31, 10123 Torino
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www.cpo.it - email: info@cpo.it

B VISUALIZATION OF DEFINED LANDMARKS IN EUS

Silvia Minozzi, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

2.3 (B I(c)). **Does the visualization of defined landmarks improve the quality of EUS in patients suffering from rectal cancer?**

Population
Patients suffering from rectal cancer undergoing EUS

Intervention
Visualization of the tumor (location, extention, infiltration of surrounding structures). Visualization of surrounding structures: genitourinary structures, iliac vessels, sphincter apparatus, lymph nodes.

Control
Not to visualize the above mentioned landmarks

Outcome
Accurate Staging, impact on patients' management

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Endosonography"[Mesh] OR EUS[Title/Abstract]) **AND** ("Neoplasm Staging"[Mesh] OR stag*[Title/Abstract] OR TNM[Title/Abstract] OR "Patient Care Management"[Mesh] OR "clinical management"[Title/Abstract] OR "patient management" [Title/Abstract] OR impact[Title/Abstract]) **AND** ((rectal[Title/Abstract] AND (cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign*[Title/Abstract] OR tumor[Title/Abstract] OR tumour[Title/Abstract] OR tumors[Title/Abstract] OR tumours[Title/Abstract] OR carcinom*[Title/Abstract] OR mass[Title/Abstract] OR masses[Title/Abstract])) OR "Rectal Neoplasms"[Mesh]) **AND** ("Lymph Nodes"[Mesh] OR "lymph node"[Title/Abstract] OR "lymph nodes"[Title/Abstract] OR

"lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract] OR extention[Title/Abstract] OR location[Title/Abstract] OR (sphincter[Title/Abstract] AND apparatus[Title/Abstract]) OR (iliac[Title/Abstract] AND (vessel [Title/Abstract] OR vessels[Title/Abstract])) OR (genitourinary[Title/Abstract] AND (structures[Title/Abstract] OR structure[Title/Abstract]))) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('endoscopic echography'/exp OR EUS:ab,ti) **AND** ('cancer staging'/exp OR stag*:ab,ti OR TNM:ab,ti OR 'patient management':ab,ti OR 'clinical management':ab,ti OR impact:ab,ti) **AND** ((rectal:ab,ti AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti)) OR 'rectum cancer'/exp) **AND** ('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti OR extention:ab,ti OR location:ab,ti OR (sphincter:ab,ti AND apparatus:ab,ti) OR (iliac:ab,ti AND (vessel:ab,ti OR vessels:ab,ti)) OR (genitourinary:ab,ti AND (structures:ab,ti OR structure:ab,ti))) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)
#1	MeSH descriptor: [Endosonography] explode all trees
#2	EUS:ti,ab,kw (Word variations have been searched)
#3	MeSH descriptor: [Neoplasm Staging] explode all trees
#4	MeSH descriptor: [Patient Care Management] explode all trees
#5	staging or TNM or impact or clinical management or patient management:ti,ab,kw (Word variations have been searched)
#6	#1 or #2
#7	#3 or #4 or #5
#8	MeSH descriptor: [Rectal Neoplasms] explode all trees
#9	rectal:ti,ab,kw (Word variations have been searched)
#10	Cancer or tumor or mass or malignant or carcinoma or neoplasm:ti,ab,kw (Word variations have been searched)
#11	#9 and #10
#12	#11 or #8
#13	MeSH descriptor: [Lymph Nodes] explode all trees
#14	lymph nodes:ti,ab,kw (Word variations have been searched)
#15	extention:ti,ab,kw (Word variations have been searched)
#16	location:ti,ab,kw (Word variations have been searched)
#17	sphincter and apparatus:ti,ab,kw (Word variations have been searched)
#18	iliac vessel:ti,ab,kw (Word variations have been searched)
#19	genitourinary structures:ti,ab,kw (Word variations have been searched)
#20	#13 or #15 or #14 or #16 or #17 or #18 or #19
#21	#6 and #7 and #12 and #20 Publication Year from 2000 to 2015

Primary studies

PubMed
("Endosonography"[Mesh] OR EUS[Title/Abstract]) **AND** ("Neoplasm Staging"[Mesh] OR stag*[Title/Abstract] OR TNM[Title/Abstract] OR "Patient Care Management"[Mesh] OR "clinical management"[Title/Abstract] OR "patient management" [Title/Abstract] OR impact[Title/Abstract]) **AND** ((rectal[Title/Abstract] AND (cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign*[Title/Abstract] OR tumor[Title/Abstract] OR tumour[Title/Abstract] OR tumors[Title/Abstract] OR tumours[Title/Abstract] OR carcinom*[Title/Abstract] OR mass[Title/Abstract] OR masses[Title/Abstract])) OR "Rectal Neoplasms"[Mesh]) **AND** ("Lymph Nodes"[Mesh] OR "lymph node"[Title/Abstract] OR "lymph nodes"[Title/Abstract] OR "lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract] OR extention[Title/Abstract] OR location[Title/Abstract] OR (sphincter[Title/Abstract] AND apparatus[Title/Abstract]) OR (iliac[Title/Abstract] AND (vessel [Title/Abstract] OR vessels[Title/Abstract])) OR (genitourinary[Title/Abstract] AND (structures[Title/Abstract] OR structure[Title/Abstract]))) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase
('endoscopic echography'/exp OR EUS:ab,ti) **AND** ('cancer staging'/exp OR stag*:ab,ti OR TNM:ab,ti OR 'patient management':ab,ti OR 'clinical management':ab,ti OR impact:ab,ti) **AND** ((rectal:ab,ti AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti)) OR 'rectum cancer'/exp) **AND** ('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti OR extention:ab,ti OR location:ab,ti OR (sphincter:ab,ti AND apparatus:ab,ti) OR (iliac:ab,ti AND (vessel:ab,ti OR vessels:ab,ti)) OR (genitourinary:ab,ti AND (structures:ab,ti OR structure:ab,ti))) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)

#1   MeSH descriptor: [Endosonography] explode all trees
#2   EUS:ti,ab,kw (Word variations have been searched)
#3   MeSH descriptor: [Neoplasm Staging] explode all trees
#4   MeSH descriptor: [Patient Care Management] explode all trees
#5   staging or TNM or impact or clinical management or patient management:ti,ab,kw (Word variations have been searched)
#6   #1 or #2
#7   #3 or #4 or #5
#8   MeSH descriptor: [Rectal Neoplasms] explode all trees
#9   rectal:ti,ab,kw (Word variations have been searched)
#10   Cancer or tumor or mass or malignant or carcinoma or neoplasm:ti,ab,kw (Word variations have been searched)
#11   #9 and #10
#12   #11 or #8
#13   MeSH descriptor: [Lymph Nodes] explode all trees

#14   lymph nodes:ti,ab,kw (Word variations have been searched)
#15   extention:ti,ab,kw (Word variations have been searched)
#16   location:ti,ab,kw (Word variations have been searched)
#17   sphincter and apparatus:ti,ab,kw (Word variations have been searched)
#18   iliac vessel:ti,ab,kw (Word variations have been searched)
#19   genitourinary structures:ti,ab,kw (Word variations have been searched)
#20   #13 or #15 or #14 or #16 or #17 or #18 or #19
#21   #6 and #7 and #12 and #20 Publication Year from 2000 to 2015

Results

Results of the bibliographic searches
After removing duplicates, 229 articles (10 reviews and 219 primary studies) were found. 1 systematic reviews and 42 primary studies were found as potentially relevant and acquired in full text for more proof evaluation. 1 further potentially relevant article was found in the references of the retrieved studies. (See flow chart).

Excluded studies
25 studies were excluded: 1 because no comparison of interest: comparison of frontal probe with radial probe (Beer-Gabel 2009); 4 because written in Chinese language (Guo 2014, Ju 2006, Zhang 2009, Zhu 2013); 1 because written in Hungarian language (Bor 2013); 1 because written in Serbian language (Radovanovic 2008); 1 because written in Greek (Kalantzis 2004); 7 because conference abstracts (Azzam 2010, Cote 2010, Gleeson 2015, Kim 2014, Kim 2013, Silon 2014, Senturk 2013); 5 because patients not in the inclusion criteria (Fuchsjager 2003, Hunerbein Surg Endosc 2000, Hunerbein Ann Surg 2000, Kim 2006, Santoro 2007); 3 because a narrative reviews (Frascio 2001, Frascio 2001b, Pessaux, 2001); one because study design not in the inclusion criteria: accuracy measured in case control design including patients with known rectal cancer and patients with known other diseases (Joksimovic 2005); one (Bianchi 2006) because the 18% of the sample underwent preoperative chemoradiotherpy) .

Included studies
19 studies were included (Ahuja 2015, Bali 2004, Can 2000, Genna 2000, Halefoglu 2008, Ju 2009, Kalantzis 2002, Kim 2014, Kocaman 2014, Kolev 2014, Kuran 2014, Mukae 2015, Palacios Fanlo 2000, Puli 2009, Ravizza 2011, Shah 2004, Shami 2004, Surace 2014, Unsal 2012).

Accurate staging
We didn't find studies exactly matching the review question, i.e. whether the quality of EUS influenced the accurate staging.
We found one systematic review and 16 primary studies assessing the diagnostic accuracy of EUS. Because we found one systematic review assessing the accuracy of N staging updated up to Juanuary 2008, primary studies assessing diagnostic accuracy for N staging were considered only since 2008. For T staging all the studies published since 2000 were considered. All the studies used histopathology as reference standard.

<u>N staging</u>
The systematic review included 35 studies with 2732 participants with rectal cancer and reported the following values of diagnostic accuracy of EUS for nodal invasion of rectal cancer:
Sensitivity =73.2% (95% CI 70.6–75.6), Specificity = 75.8% (95% CI 73.5–78.0), Positive likelihood ratio=2.84 (95% CI 2.16–3.72) and Negative likelihood ratio = 0.42 (95% CI 0.33–0.52). Overall accuracy ranged from 63.2% to 84.3% in the six primary studies which reported this value. In the seven primary studies which reported the values, sensitivity and specificity of EUS ranged from 45.4% to 95.5% and from 71.1% to 95.5% respectively.

<u>T staging</u>
Overall accuracy reported in 10 primary studies ranged from 73.7% to 91.3%. In the five primary studies which reported the values, sensitivity and specificity of EUS ranged from 70.59% to 93.8% and from 80% to 99.2% respectively. Over-staging ranged from 2.75% to 17.6%. Downstage ranged from 2.5% to 20%.

Study	N patients	T staging	N staging	Cases overstaged by EUS	Cases understaged by EUS
Puli 2009 Systematic review and meta-analysis	35 studies with 2732 participants with rectal cancer		**Sensitivity** =73.2% (95% CI 70.6–75.6) **Specificity** = 75.8% (95% CI 73.5–78.0) **Positive likelihood ratio** = 2.84 (95% CI 2.16–3.72) **Negative likelihood ratio** = 0.42 (95% CI 0.33–0.52).		
Ahuja 2015	86 patients with rectal cancer initially staged as T2N0 by EUS mean age= 62.5 years (range, 29-86)	**NPV** for tumor depth amenable to primary resection= 83.7 %(95% CI, 74.2–90.8).	**NPV** = 87.2% (95% CI, 78.3–93.4).	**T:** 16.3% (T2 instead of T1)	**T:** 16.3% (T3 instead of T2) **N:** 12.8% **TN:** 23.3%
Bali 2004	31 patients with biopsy-proven rectal cancer underwent evaluation of the invasion of the rectal wall, the mesorectal lymph nodes status and the pelvic organs using EUS mean age= 70 years (range 46–89 years)	**T staged correctly** T2 =50% T3=84% **Overall accuracy**= 79%		**T** = 10.3%	**T** = 10.3%

Can 2000	27 patients in whom rectal carcinoma was pathologically pre-diagnosed Median age=56.3 years (range 32-84 years)	Rectal wall invasion **Accuracy=** 81% **Specificity**=80% **Sensitivity**=85.7%			
Halefoglu 2008	34 consecutive patients who had biopsy proven rectal carcinoma underwent both MRI and ERUS examinations before surgery mean age= 58.7 (range 29- 75 years)	**Accuracy=** 85.29% (24 / 34). **sensitivity** = 70.59% **specificity** = 90.20%. discriminating between pT1-pT2 and pT3-pT4 tumors **accuracy** = 76.47% **sensitivity**=87.5% **specificity**= 50%. **PPV**=80.77% **NPV** =62.50%		**T** =17.6%	**T** =11.7%
Genna 2000	42 patients with a preoperative histological diagnosis of adenocarcinoma localised in the rectal segment, extending up to 10cm from the dentate line, undergoing radical surgical	**Overall accuracy =**81% **Sensitivity** T1=67% T2=60% T3=92% T4=67% **Specificity** T1=100% T2=94% T3=67% T4=100%			

	Mean age=not reported	**PPV** T1=100% T2=75% T3=80% T4=100% **NPV** T1=98% T2=90% T3=86% T4=98%			
Ju 2009	78 patients with rectal Carcinoma mean age of 61 years (range 32 - 78).	**Accuracy** T1=100% T2=84.0% T3=81.8% T4=84.6% Overall=84.6%	**Sensitivity** =54.5% **Specificity** =71.1% **Overall accuracy** = 64.1%		
Kalantzis 2002	80 patients with histologically proven colorectal cancer. Prior to surgery all patients underwent colonoscopy and biopsy, double-contrast barium enema, ultrasound and lower and upper andomen computed tomography Mean age=69.8±11 years	**Sensitivity** T1=100% T2=100% T3=92.5% T4= Overall=93.8% **Specificity** T1=100% T2=97.1% T3=100% T4=100% Overall=99.2%		**T** =3.75%	**T** =2.5%

Kocaman 2014	50 patients with rectal carcinoma mean age =60±12 years	**Specificity**: T2=73% T3=100% T4=90% **Sensitivity**: T2=100% T3=82% T4=100% **PPV, %** T2=100% T3=81% T4=100% **NPV:** T2=89% T3=100% T4=97% **Accuracy**: T2=92% T3=90% T4=98%	**Sensitivity**:72% **Specificity**:92% **PPV**:81% **NPV**:88% **Accuracy**=84%	**Overall T**=12% T2=33.3% T3=4.5%	**Overall T**=20% T2=6.6% T3=18.1% T4=45.4%
Kolev 2014	71 patients with rectal cancer	**Accuracy** T1=97.1% T2=94.3% T3 =95.7% T4= 98.5% **Sensitivity** T1= 92.8% T2=93.1% T3 =91.6% T4= 100% **Specificity** T1=98.2% T2=95.4% T3 =97.8%	**Sensitivity**: 79.1% **Specificity**: 91.4% **Overall accuracy**: 84.3%	T1=7.6% T2=3.4% **Overall T**=2.75%	T2=3.4% T3=4.1% T4=20% **Overall T**=6.87%

		T4= 98.5% **PPV** T1=92.8% T2=93.1% T3 =95.8% T4= 80% **NPV** T1= 98.2% T2=95.4% T3 =95.7% T4= 100%			
Kuran 2014	38 patients diagnosed with rectal cancer mean age= 57.6 ± 11.3 years	Stenotic lesion= 13 Non-stenotic lesions= 25 **accuracy** 73.7% By stenotic lesion= 68% Non stenotic lesion= 84.6% assessment of internal sphincter involvement **Sensitivity**=100% **Specificity**=100% **Accuracy**=100% assessment of external sphincter involvement **Sensitivity**=100% **Specificity**=96.3% **Accuracy**=96.8%	**Sensitivity**=41.2% **Specificity**=81.0% **Accuracy**=63.2%		
Mukae 2015	705 patients (714 lesions) with early CRC undergoing EUS to estimate the depth of tumor invasion.	**sensitivity for pTis or pT1a** (endoscopic resection indicated)=90%			

	Mean age=64.0 years	**Specificity for pT1b** (colectomy indicated)**=** 87% **Overall accuracy**= 89%			
Palacios Fanlo 2000	120 patients with rectal cancer Mean age=70 years (range 39-85 years)	**Sensitivity** T1: 100% T2: 44.4% T3: 96.4% T4: 100% **Overall accuracy**: 90%		**T**:5.8%	**T**: 4.2%
Ravizza 2011	92 patients with rectal neoplasia (adenomas and primary adenocarcinomas located within 15 cm from the anal verge) Median age= 64.5 years (range 40–85)	**Accuracy** =91.3% **sensitivity**=86% **specificity**=95.9% **PPV**=94.9% **NPV** =88.7%	**Accuracy** =83% **sensitivity**=45.4% **specificity**=95.5% **PPV**=76.9% **NPV** =84.0%	6.5%_(from T2 to T1 in 5 cases from T3 to pT0–1)	
Shami 2004	60 consecutive patients diagnosed with rectal carcinoma referred for endoscopic ultrasound staging Mean age=not reported	**Sensitivity** =82% **Specificity** =96% **accuracy** = 89%	**Sensitivity** =95% **Specificity** =79% **accuracy** = 85%		
Surace 2014	77 reports ultrasound with the final diagnosis of rectal cancer Mean age=not reported	**Sensitivity, [95%I.C]** pT0= 95.8 %[69.9-99.6] pT is=90% [46.3-98.9] pT1=77.8% [45.3 -93.7]	**Sensitivity**: 95.5% **Specificity**: 91.4%	**overstaging risk** pT0= 0% [0.51-52.18] pT is= 42.11% [23.06 -63.95]	**understaging risk** pT0= 0% [0.51-52.18] pT is= 0% [0.51-52.18]

		pT2=83.3% [55.2 -95.3] pT3=71.4% [45.4 -88.3] pT4=83.3% [31 - -98.2] **Specificity, [95%I.C]** pT0= 86.9% [76.6 -93.1] pT is= 99.3% [93.7 99.9] pT1= 88.2% [78.5 -93.9] pT2= 0.908% [0.813 -0.957] pT3= 95.2% [86.9 -98.4] pT4= 99.3% [93.9 -99.9]		pT1= 47.06% [26.02 -69.24] pT2= 33.03% [16.29 -56.55] pT3= 17.65% [16.29 -41.42] pT4= 0% [0.51-52.18]	pT1= 11.76% [3.58 -34.71] pT2= 11.11% [3.38 -33.14] pT3= 23.53 % [9.69 -47.64] pT4= 0% [0.51-52.18]
Unsal 2012	31 consecutive patients with resectable rectal carcinoma Mean age= 3.7±11.5 ye- ars	T1 **Sensitivity=**100% **Specificity=**96% **PPV=**80% **NPV =**100% **Accuracy=**96% T2 **Sensitivity=**73% **Specificity=**100% **PPV=**100% **NPV=**70% **Accuracy=**70% T3	Presence of lymph nodes **Sensitivity=**70% **Specificity=**86% **PPV=**80% **NPV=**100% **Accuracy=**83% characteristics lymph nodes (malignant) **Sensitivity=**100% **Specificity=**22% **PPV =**74%**NPV=**100% **Accuracy=**76%		

		Sensitivity=100% **Specificity=**88% **PPV=**66% **NPV=**100% **Accuracy=**84% <u>T4</u> **Sensitivity=**100% **Specificity=**96% **PPV=**66% **NPV=**100% **Accuracy=**96% <u>Overall T</u>**:** **Sensitivity**: 93.4% **Specificity**: 96.5% **Accuracy:** 80.6%			

Impact on patients' management

We didn't find studies that directly assess the review question (i.e. whether the quality of US impact patient management). We found 3 primary studies (Kim 2014, Shah 2004, Shami 2004) assessing the impact of EUS results on patients' management. One study (Kim 2014) assessed the utility of EUS for assessing the risk of invasion or metastasis of NETs less than 10mm in diameter and found that its necessity is questionable because rectal NETs smaller than 10 mm have a very low possibility of invasion to the proper muscle layer and a low risk of adjacent lymph node metastasis. The two other studies the impact of EUS results on changes of patients' management and found that in 38%- to 50% of cases clinicians changed management plans.

Study	N patients	Outcomes	Results	Conclusions
Kim 2014	76 patients with rectal neuroendocrine tumors (NETs) less than 10 mm in diameter Mean age=53.6 years (range, 29-78 years)	Utility of EUS for assessing the risk of invasion or metastasis of NETs less than 10mm in diameter	7 lesions were located in the mucosa and 69 lesions were located in the submucosa. This finding was consistent with histologic results	Although EUS is a useful method for evaluating the depth of invasion, its necessity is questionable in cases of rectal NETs ≤10 mm in size. As shown in this study, rectal NETs smaller than 10 mm have a very low possibility of invasion to the proper muscle layer and a low risk of adjacent lymph node metastasis. The number of rectal NETs included in this study is too small to conclude that rectal NETs less than 10 mm in diameter have an extremely low possibility of invasion to the proper muscle or risk of metastasis and further studies including a larger number of rectal NETs less than 10 mm in size are needed to verify our findings.
Shah 2004	10 patients with known or suspected rectal malignancies	Changes in management plan	**Management plan changes post-EUS=** 4/10 (40%) More complex= 2/4 (50%)	Based on EUS examination findings, clinicians requesting EUS alter patient management in one half of cases, and more

				often pursue a less-complicated approach. EUS substantially impacts clinical care, and should be used in appropriate settings to guide patient management.
			Surgery alone to neoadjuvant therapy and surgery =2 Less complex= 2/4 (50%) Surgery to chemotherapy=1 Neoadjuvant therapy and surgery to surgery alone =1	
Shami 2004	60 consecutive patients diagnosed with rectal carcinoma referred for endoscopic ultrasound staging	Changes in management plan	**Impact on patients' management** the additional staging information provided by EUS (more than CT alone) effected a change in management in 18 of 48 (38 percent) patients. All of these cases involved identification of lymph nodes by EUS not detected by CT, therefore, upstaging the cancer and identifying a group of patients who would undergo preoperative neoadjuvant therapy	Preoperative staging with endoscopic ultrasound resulted in a change of management in 38 percent of patients

Quality of evidence

Accurate staging
Study limitations (risk of bias): no
Inconsistency of results: yes
Indirectness of evidence: yes (none of the retrieved studies exactly matched the review question, i.e. whether the quality of EUS influenced the accurate staging)
Imprecision: no
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as low because of indirectness and inconsistency for accurate staging.

Impact on patient management
Study limitations (risk of bias): yes
Inconsistency of results: no
Indirectness of evidence: yes (none of the retrieved studies exactly matched the review question, i.e. whether the quality of EUS influenced the patients' management)
Imprecision: yes (only 3 studies with a total of 146 participants)
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as very low because of study limitation, imprecision and indirectness.

Conclusions

Accurate staging
No direct conclusions can be drawn about the impact of quality of EUS on accurate staging or impact on patient management.
For N staging the systematic review reported a pooled sensitivity of 73.2% (95% CI 70.6–75.6), and a pooled specificity = 75.8% (95% CI 73.5–78.0). Overall accuracy ranged from 63.2% to 84.3.% in the six primary studies which reported this value. In the seven primary studies which reported these values, sensitivity and specificity of EUS ranged from 45.4% to 95.5% and from 71.1% to 95.5% respectively.
For T staging the overall accuracy reported in 10 primary studies ranged from 73.7% to 91.3%. In the five primary studies which reported these values, sensitivity and specificity of EUS ranged from 70.59% to 93.8% and from 80% to 99.2% respectively. Overstage ranged from 2.75% to 17.6%. Downstage ranged from 2.5% to 20%
(**LOW QUALITY EVIDENCE**)

Impact on patient management
In 38%- to 50% of cases clinicians changed management plans on the basis of EUS results
(**VERY LOW QUALITY EVIDENCE**).

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PRISMA 2009 Flow Diagram
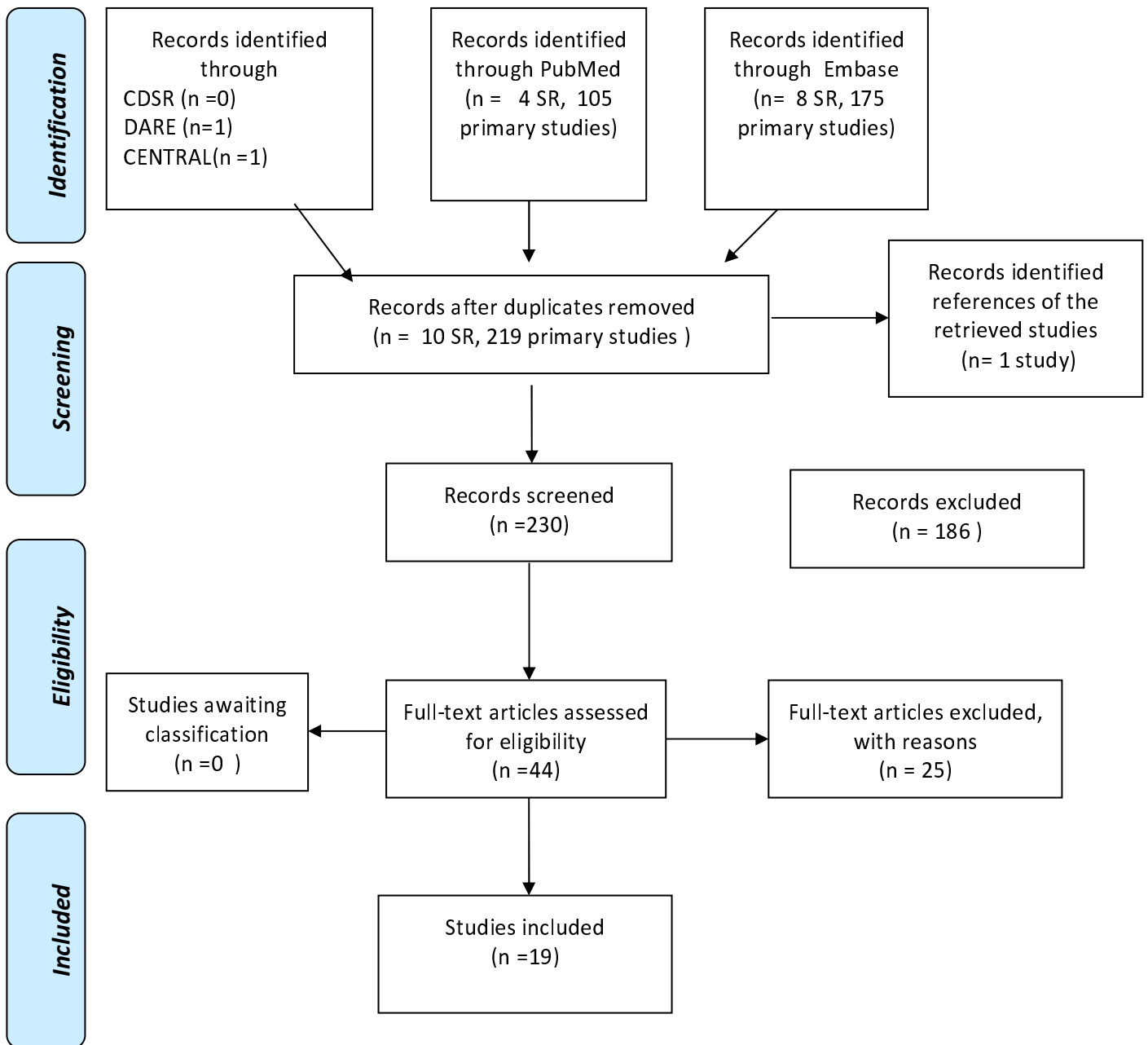
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B VISUALIZATION OF DEFINED LANDMARKS IN EUS

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2.4 (B I(d)). **Does the visualization of defined landmarks improve the quality of EUS in patients with subepithelial gastric masses (synonym: submucosaltumor)?**

Population
Patients with subepithelial gastric masses (synonym: submucosaltumor)

Intervention
Visualization of the mass (tumor) including the exact location within the gastric wall layer, differentiation of the wall layers, signs of infiltration, lymph nodes.

Control
Not to visualize the above mentioned landmarks

Outcome
Accurate Staging, impact on patients' management

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Endosonography"[Mesh] OR EUS[Title/Abstract]) **AND** ("Neoplasm Staging"[Mesh] OR stag*[Title/Abstract] OR TNM[Title/Abstract] OR "Patient Care Management"[Mesh] OR "clinical management"[Title/Abstract] OR "patient management" [Title/Abstract] OR impact[Title/Abstract]) **AND** (((gastric[Title/Abstract] OR stomach[Title/Abstract]) AND (cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign*[Title/Abstract] OR tumor[Title/Abstract] OR tumour[Title/Abstract] OR tumors[Title/Abstract] OR tumours[Title/Abstract] OR carcinom*[Title/Abstract] OR mass[Title/Abstract] OR masses[Title/Abstract])) "Stomach Neoplasms"[Mesh]) **AND** ("Lymph Nodes"[Mesh] OR "lymph node"[Title/Abstract] OR "lymph nodes"[Title/Abstract] OR "lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract] OR "vascular infiltration"[Text Word] OR location[Title/Abstract] OR "wall layer"[Title/Abstract] OR "wall layers"[Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('endoscopic echography'/exp OR EUS:ab,ti) **AND** ('cancer staging'/exp OR stag*:ab,ti OR TNM:ab,ti OR 'patient management':ab,ti OR 'clinical management':ab,ti OR impact:ab,ti) **AND** (((gastric:ab,ti OR stomach:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti)) OR 'stomach cancer'/exp) **AND** ('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti OR 'vascular infiltration':ab,ti OR location:ab,ti OR 'wall layer':ab,ti OR 'wall layers':ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and **Database of Abstracts of Reviews of Effects (DARE)**
#1   MeSH descriptor: [Endosonography] explode all trees
#2   EUS:ti,ab,kw (Word variations have been searched)
#3   MeSH descriptor: [Neoplasm Staging] explode all trees
#4   MeSH descriptor: [Patient Care Management] explode all trees
#5   staging or TNM or impact or clinical management or patient management:ti,ab,kw (Word variations have been searched)
#6   #1 or #2
#7   #3 or #4 or #5
#8   MeSH descriptor: [Stomach Neoplasms] explode all trees
#9   gastric or stomach:ti,ab,kw (Word variations have been searched)
#10   Cancer or tumor or mass or malignant or carcinoma or neoplasm:ti,ab,kw (Word variations have been searched)
#11   #9 and #10

#12   #11 or #8
#13   MeSH descriptor: [Lymph Nodes] explode all trees
#14   lymph nodes:ti,ab,kw (Word variations have been searched)
#15   location:ti,ab,kw (Word variations have been searched)
#16   vascular infiltration:ti,ab,kw (Word variations have been searched)
#17   wall layer:ti,ab,kw (Word variations have been searched)
#18   #13 or #15 or #14 or #15 or #16
#19   #6 and #7 and #12 and #18Publication Year from 2000 to 2015

Primary studies

PubMed
("Endosonography"[Mesh] OR EUS[Title/Abstract]) **AND** ("Neoplasm Staging"[Mesh] OR stag*[Title/Abstract] OR TNM[Title/Abstract] OR "Patient Care Management"[Mesh] OR "clinical management"[Title/Abstract] OR "patient management" [Title/Abstract] OR impact[Title/Abstract]) **AND** (((gastric[Title/Abstract] OR stomach[Title/Abstract]) AND (cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign*[Title/Abstract] OR tumor[Title/Abstract] OR tumour[Title/Abstract] OR tumors[Title/Abstract] OR tumours[Title/Abstract] OR carcinom*[Title/Abstract] OR mass[Title/Abstract] OR masses[Title/Abstract])) **"Stomach Neoplasms"[Mesh]) AND** ("Lymph Nodes"[Mesh] OR "lymph node"[Title/Abstract] OR "lymph nodes"[Title/Abstract] OR "lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract] OR "vascular infiltration"[Text Word] OR location[Title/Abstract] OR "wall layer"[Title/Abstract] OR "wall layers"[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase
('endoscopic echography'/exp OR EUS:ab,ti) **AND** ('cancer staging'/exp OR stag*:ab,ti OR TNM:ab,ti OR 'patient management':ab,ti OR 'clinical management':ab,ti OR impact:ab,ti) **AND** (((gastric:ab,ti OR stomach:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti)) OR 'stomach cancer'/exp) **AND** ('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti OR 'vascular infiltration':ab,ti OR location:ab,ti OR 'wall layer':ab,ti OR 'wall layers':ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1   MeSH descriptor: [Endosonography] explode all trees
#2   EUS:ti,ab,kw (Word variations have been searched)
#3   MeSH descriptor: [Neoplasm Staging] explode all trees
#4   MeSH descriptor: [Patient Care Management] explode all trees
#5   staging or TNM or impact or clinical management or patient management:ti,ab,kw (Word variations have been searched)
#6   #1 or #2
#7   #3 or #4 or #5
#8   MeSH descriptor: [Stomach Neoplasms] explode all trees
#9   gastric or stomach:ti,ab,kw (Word variations have been searched)

#10   Cancer or tumor or mass or malignant or carcinoma or neoplasm:ti,ab,kw (Word variations have been searched)
#11   #9 and #10
#12   #11 or #8
#13   MeSH descriptor: [Lymph Nodes] explode all trees
#14   lymph nodes:ti,ab,kw (Word variations have been searched)
#15   location:ti,ab,kw (Word variations have been searched)
#16   vascular infiltration:ti,ab,kw (Word variations have been searched)
#17   wall layer:ti,ab,kw (Word variations have been searched)
#18   #13 or #15 or #14 or #15 or #16
#19   #6 and #7 and #12 and #18Publication Year from 2000 to 2015

Results

Results of the bibliographic searches
After removing duplicates, 309 articles (10 reviews and 299 primary studies) were found.
4 systematic reviews were considered potentially relevant and acquired in full text (See flow chart).
In first instance systematic reviews were considered. All assessed only the accurate staging outcome and the most updated review included primary studies published up to January 2015. So we selected primary studies which assessed accurate staging only if published between January and August 2015 and primary studies which assessed the impact on patients management published within 2000 and August 2015. Seven primary studies were acquired in full text as potentially relevant. 1 further potentially relevant article was retrieved in the references of the retrieved studies.

Excluded studies
Three studies were excluded: one because it was conference abstract (Antonini 2013) and one because it did not assess our outcomes of interest (Vukobrat-Bijedic 2013), one because did not assess intervention of interest (Hassan 2010).

Included studies
4 reviews (Kelly 2001, Kwee 2009, Mocellin 2015, Mocellin 2011) and 5 primary studies (Ganpathi 2006, Kutup 2012, Shah 2004, Willis 2000, Yamamoto 2012) were finally included .
The overlapping of primary studies included in the four systematic reviews was near total, i.e. all but two of the studies included in the other SRs were also included in Mocellin 2015, which was also of high methodological quality, the most updated and included the largest number of studies; we therefore extracted data only from Mocellin 2015 .

Overlapping of primary studies between systematic reviews

	Mocellin 2015	Mocellin 2011	Kelly 2001	Kwee 2009
Ahn 2009	X	X		
Akahoshi 1991	X	X	X	
Akahoshi 1998	X	X		X
Akashi 2006	X	X		
Ang 2006	X	X		X
Arocena 2006	X	X		X
Barbour 2007	X	X		
Bentrem 2007	X	X		X
Bhandari 2004	X	X		X
Blackshaw 2008	X	X		
Bohle 2011	X			
Botet 1991	X	X	X	X
Caletti 1993	X	X	X	
Cerizzi 1991	X			
Chen 2002	X	X		X
Choi 2010	X	X		
De Manzoni 1999	X			
Dittler 1993	X	X	X	X
François 1996	X	X		X
Furukawa 2011	X			
Ganpathi 2006	X	X		X
Garlipp 2011	X			
Grimm 1993	X	X	X	X
Habermann 2004	X	X		X
Hamada 1997	X	X		X
Heye 2009	X	X		
Hizawa 2002	X	X		
Hünerbein 1996			X	X
Hünerbein 1998	X	X		X
Hünerbein 2004	X	X		
Hwang 2010	X	X		
Javaid 2004	X	X		X
Kim 2007	X			
Kim 2010	X	X		
Kutup 2012	X			
Lok 2008	X	X		X
Mancino 2000	X	X		X
Massari 1996	X	X	X	
Mouri 2009	X	X		
Murata 1988	X	X	X	
Nakamura 1999a	X	X		
Nomura 1999	X			
Ohashi 1999	X			
Okada 2011	X			
Okamura 1999	X	X		

Park 2008	X	X		
Pedrazzani 2005	X	X		
Perng 1996	X	X	X	X
Polkowski 2004	X	X		X
Potrc 2006	X	X		X
Repiso 2010	X	X		
Saito 1991	X	X	X	
Shimizu 1994	X	X	X	
Smith 1993				X
Shimoyama 2004	X	X		
Tan 2007	X	X		X
Tio 1989	X	X	X	X
Tsendsuren 2006	X	X		X
Tseng 2000	X	X		X
Wang 1998	X	X		X
Willis 2000	X	X		X
Xi 2003	X	X		X
Yamamoto 2012	X			
Yanai 1997	X	X		
Yanai 1999	X	X		
Yoshida 2005	X	X		
Zheng 2011	X			
Ziegler 1993	X	X	X	X

Accurate staging

Only one (Yamamoto 2012) of the included studies exactly matched the review question, i.e. whether the quality of EUS influenced the accurate staging.

The study included 75 patients suspected of having early gastric cancer who received EUS. EUS examination were evaluated for quality according to the following criteria: quality of the EUS images: according to: (1) repeatability of detection (presence [1] or absence [0]), (2) appropriate placement of the probe (ensuring the proper spacing between the probe and the lesion [1]) or impingement of the probe (probe was positioned too close to the lesion; [0]), and (3) clarity of the five layers of the gastric wall including the lesion (clear [1] or unclear [0]). The scores were summed (total ranged from 0 to 3) to calculate the quality of the EUS image of each lesion. The study found that the quality of the EUS influence the accuracy of diagnosis (N (%) of correct diagnosis by EUS image quality

Low (score 0,1) quality EUS allowed only 35.7% of correct diagnosis, whereas High (score 2, 3 allowed 93.4% of correct diagnosis

We found one systematic review (Mocellin 2015) assessing the diagnostic accuracy of EUS in TN staging of gastric carcinoma. The review included 66 studies including 7747 patients.

For T1 - T2 versus T3 - T4 staging, the overall sensitivity and specificity were 0.86(95% CI: 0.81-0.90) and 0.90 (95% CI: 0.87 to 0.93), respectively.

For N staging the overall sensitivity and specificity were: 0.83 (95% CI: 0.79 to 0.87) and 0.67 (95% CI: 0.61 to 0.72), respectively.

Impact on patient management

We didn't find studies that directly assess the review question. We found four primary studies assessing the impact of EUS results on patients' management.

We found three primary studies (Ganpathi 2006, Kutup 2012, Willis 2000) that assessed the ability of EUS in predicting tumor resectability, that we considered as a proxy of impact on patient's management.

In Ganpathi 2006, 109 patients with gastric cancer underwent EUS and surgical exploration. 89% of the patients actually underwent the proposed treatment on the basis of EUS. 7% were down staged by EUS, i.e proposed for gastrectomy and found inoperable (n:3), received palliative gastrectomy (n:3) received bypass (n:2). 3.7% were over staged by EUS: deemed as inoperable received radical gastrectomy (n:1) and extended resection (n:1); proposed for bypass and received extended resection(1).

In Willis 2000 116 patients received EUS followed by surgical procedure. EUS has a sensitivity in correctly predicting curative surgery by standardized gastrectomy with radical lymphadenectomy of of 94% and a specificity in correctly excluding this therapy of 83%. Overall accuracy was of 91.4%.

In Kutup 2012, 123 patients received EUS in order to assess whether they should receive surgery (if T1 /2N0) or neoadjuvant or perioperative chemotherapy (if T3/4, or any N +).

Cases correctly classified by EUS were 51.3% of cases with histopathological T1/2N0 and 91.8% of cases with histopathological T3/4, or any N +. Overall EUS correctly predicted further management in 79.7% of patients.

A fourth study assessed the impact of EUS results on management of known or suspected malignancies (Shah 2004). In these studies the physicians requesting EUS were contacted before the EUS examination and were asked: "How would you manage this patient if EUS were not available?" After the examination the referring clinicians were recontacted within 1 week of the procedure, informed of the EUS findings, and asked: (1) "What management plan will you recommend to this patient given the EUS findings?" and if the management strategy differed compared with the pre-EUS response, (2) "Is the recommended change in the management plan directly the result of the EUS findings?" 15 patients were included for which EUS was requested to evaluate known or suspected cancers (n 5) and submucosal masses (n =10).

Requesting physicians altered patient management in 60% of patients after gastric EUS. A less-complex management strategy was involved in the majority (78%), and included 2 of 5 patients in whom surgery was no longer considered.

Quality of evidence

Accurate staging
Study limitations (risk of bias): no
Inconsistency of results: no
Indirectness of evidence: no
Imprecision: yes only one study with 75 patients
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as low because of imprecision

<u>Impact on patient management</u>
Study limitations (risk of bias): no
Inconsistency of results: no
Indirectness of evidence: yes
Imprecision: yes only three studies with 240 patients
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as low because of imprecision and indirectness.

Conclusions

High-quality EUS images increased the diagnostic accuracy of EGC invasion depth. Lower-quality EUS images may lead to an inaccurate diagnosis
(**LOW QUALITY OF EVIDENCE**)

No direct conclusions can be drawn about the impact of quality of EUS on impact on patient management.
Tumor resectability /unresectability was correctly predicted by EUS in 79.7% - 91% of patients
Treatment plan was altered in 60% of patients after pancreatic EUS results
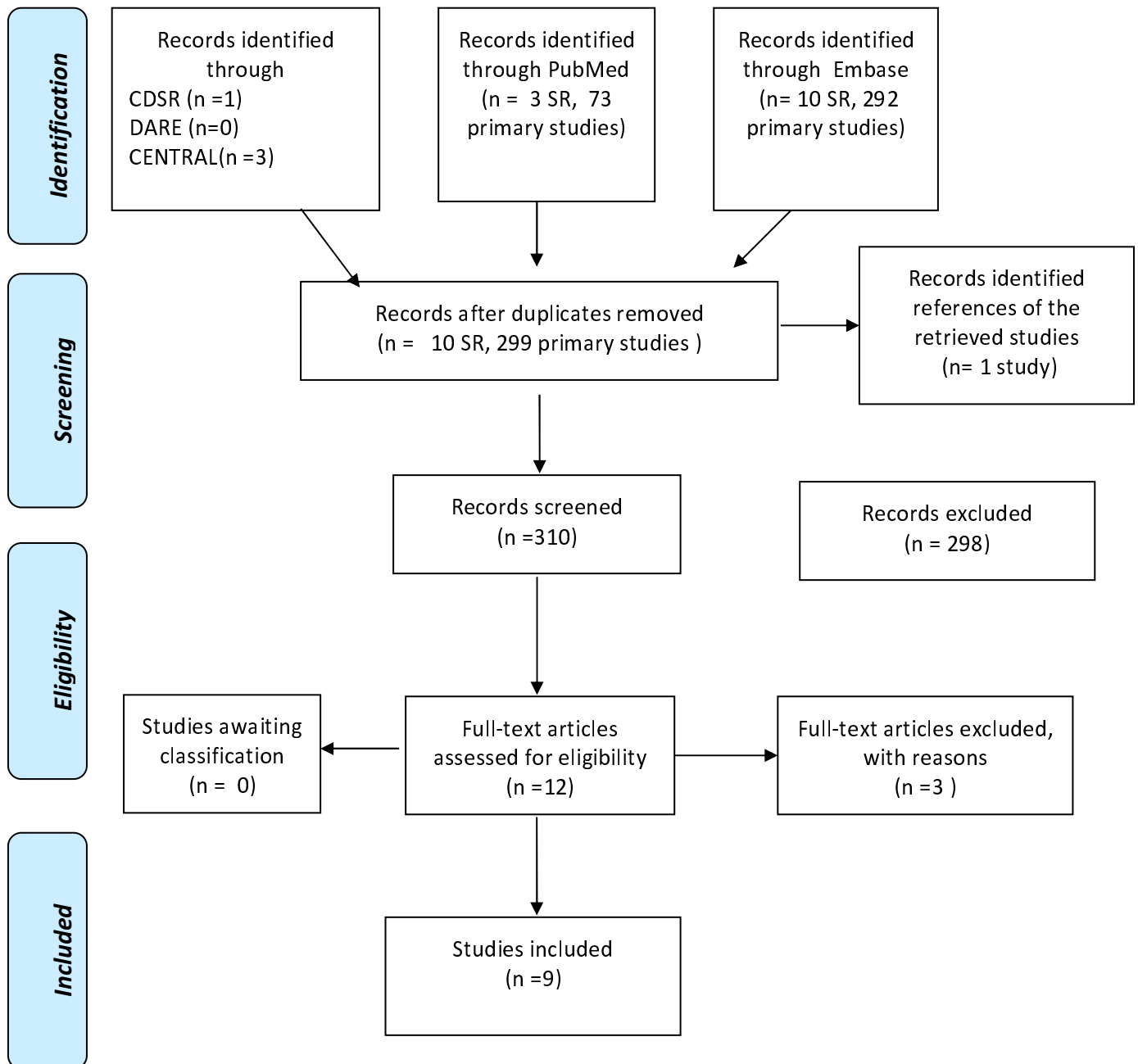(**LOW QUALITY OF EVIDENCE).**

References

Included studies
1. Ganpathi I.S.; So J.B.-Y., and Ho K.-Y. Endoscopic ultrasonography for gastric cancer: Does it influence treatment? Surg. Endosc. Interv. Tech. 2006; 20(4):559-562;
2. Kelly S.; Harris K.M.; Berry E.; Hutton J.; Roderick P.; Cullingworth J.; Gathercole L., and Smith M.A. A systematic review of the staging performance of endoscopic ultrasound in gastro-oesophageal carcinoma. Gut. 2001; 49(4):534-539;
3. Kutup A.; Vashist Y.K.; Groth S.; Vettorazzi E.; Yekebas E.F.; Soehendra N., and Izbicki J.R. Endoscopic ultrasound staging in gastric cancer: Does it help management decisions in the era of neoadjuvant treatment? Endoscopy. 2012; 44(6):572-576;
4. Kwee, R. M. and Kwee, T. C. Imaging in assessing lymph node status in gastric cancer. Gastric Cancer. 2009; 12(1):6-22.
5. Mocellin S. and Pasquali S. Diagnostic accuracy of endoscopic ultrasonography (EUS) for the preoperative locoregional staging of primary gastric cancer. Cochrane Database Syst Rev. 2015; 2CD009944;
6. Mocellin, S.; Marchet, A., and Nitti, D. EUS for the staging of gastric cancer: a meta-analysis. Gastrointest Endosc. 2011 Jun; 73(6):1122-34.
7. Shah JN, Ahmad NA, Beilstein MC et al. Clinical impact of endoscopic ultrasonography on the management of malignancies. Clin Gastroenterol Hepatol 2004; 2: 1069-1073
8. Willis S.; Truong S.; Gribnitz S.; Fass J., and Schumpelick V. Endoscopic ultrasonography in the preoperative staging of gastric cancer: Accuracy and impact on surgical therapy. Surg. Endosc. 2000; 14(10):951-954;
9. Yamamoto S.; Nishida T.; Kato M.; Inoue T.; Hayashi Y.; Kondo J.; Akasaka T.; Yamada T.; Shinzaki S.; Iijima H.; Tsujii M., and Takehara T. Evaluation of endoscopic ultrasound image quality is necessary in endosonographic assessment of early gastric cancer invasion depth. Gastroenterol. Res. Pract. 2012;

Excluded studies
1. Antonini F.; Siquini W.; Piergallini S.; Belfiori V.; Marraccini B.; Lo Cascio M.; Manfredi C., and Macarri G. Diagnostic value of eus in the selection of patients with gastric cancer eligible for a neoadjuvant chemotherapy. Dig. Liver Dis. 2013; 45S198
2. Hassan H.; Vilmann P., and Sharma V. Impact of EUS-guided FNA on management of gastric carcinoma. Gastrointest. Endosc. 2010; 71(3):500-504;
3. Vukobrat-Bijedic Z.; Husic-Selimovic A.; Sofic A.; Bijedic N.; Gogov B.; Mehmedovic A.; Saray A.; Glavas S., and Bjelogrlic I. Comparability of diagnostic methods: Proximal endoscopy, CT and EUS in determining stomach tumor localization and their importance in the preoperative analysis of process progression. Acta Inform. Med. 2013; 21(4):246-249;

PRISMA 2009 Flow Diagram

Identification

Records identified through CDSR (n =1) DARE (n=0) CENTRAL(n =3)	Records identified through PubMed (n = 3 SR, 73 primary studies)	Records identified through Embase (n= 10 SR, 292 primary studies)

Screening

Records after duplicates removed
(n = 10 SR, 299 primary studies)

Records identified references of the retrieved studies
(n= 1 study)

Records screened
(n =310)

Records excluded
(n = 298)

Eligibility

Studies awaiting classification
(n = 0)

Full-text articles assessed for eligibility
(n =12)

Full-text articles excluded, with reasons
(n =3)

Included

Studies included
(n =9)

S.C. Epidemiologia screening, registro tumori –
CPO Piemonte
Direttore: Dr. Nereo Segnan
via Cavour 31, 10123 Torino
tel. 011.6333881 - fax 011.6333861
www.cpo.it - email: info@cpo.it

ADMINISTRATION OF ANTIBIOTICS IN PATIENTS UNDERGOING ERCP

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Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

3.1 (C I(a))**. Administration of antibiotics in patients undergoing ERCP**

Population
Patients undergoing ERCP suffering from either
- cholangitis
- primary sclerosing cholangitis
- biliary obstruction without cholangitis, successful placement of drainage/stent
- biliary obstruction without cholangitis, unsuccessful placement of drainage/stent
- pancreatic cyst / pseudocyst communicating with pancreatic duct

Intervention
Administration of antibiotics

Control
No administration of antibiotics

Outcome
Preventing an inflammation

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and randomized controlled trials using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Anti-Bacterial Agents"[Mesh] OR antibiotic[Text Word] OR antibiotics [Title/Abstract]) **AND** ("Cholangitis"[Mesh] OR Cholangitis[Title/Abstract] OR (("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct"[Title/Abstract] OR biliary[Title/Abstract] OR pancreatic[Title/Abstract]) AND (obstruct*[Title/Abstract] OR occlu*[Title/Abstract] OR stone*[Text Word] OR calculi[Text Word] OR calculus[Text Word] OR cyst[Text Word]))) **AND** ("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('antibiotic agent'/exp OR antibiotic:ab,ti OR antibiotics:ab,ti) **AND** ((('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti) AND (obstruct*:ab,ti OR occlu*:ab,ti OR stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti OR cyst:ab,ti)) OR Cholangitis:ab,ti OR 'cholangitis'/exp) **AND** ('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and **Database of Abstracts of Reviews of Effects (DARE)**
#1   MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#2   antibiotic:ti,ab,kw (Word variations have been searched)
#3   #1 or #2
#4   MeSH descriptor: [Common Bile Duct] explode all trees   4
#5   CBD or biliary or pancreatic or bile duct:ti,ab,kw (Word variations have been searched
#6   #4 or #5
#7   obstruction or occlusion:ti,ab,kw (Word variations have been searched)
#8   stone or calculus or cyst:ti,ab,kw (Word variations have been searched)
#9   #8 or #7
#10   #6 and #9
#11   MeSH descriptor: [Cholangitis] explode all trees
#12   Cholangitis:ti,ab,kw (Word variations have been searched)
#13   #10 or #11 or #12
#14   MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#15   ERCP:ti,ab,kw (Word variations have been searched)
#16   #14 or #15
#17   #16 and #13 and #3 Publication Year from 2000 to 2015

Randomized controlled trials

PubMed
("Anti-Bacterial Agents"[Mesh] OR antibiotic[Text Word] OR antibiotics [Title/Abstract]) **AND** ("Cholangitis"[Mesh] OR Cholangitis[Title/Abstract] OR (("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct"[Title/Abstract] OR biliary[Title/Abstract] OR pancreatic[Title/Abstract]) AND (obstruct*[Title/Abstract] OR occlu*[Title/Abstract] OR stone*[Text Word] OR calculi[Text Word] OR calculus[Text Word] OR cyst[Text Word]))) **AND** ("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) **AND** ((Randomized Controlled Trial[ptyp] OR Controlled Clinical Trial[ptyp] OR randomized[Title/Abstract] OR placebo[Title/Abstract] OR "drug therapy" [Subheading] OR randomly [Title/Abstract] OR trial[Title/Abstract] OR group[Title/Abstract]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]))

Embase
('antibiotic agent'/exp OR antibiotic:ab,ti OR antibiotics:ab,ti) **AND** ((('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti) AND (obstruct*:ab,ti OR occlu*:ab,ti OR stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti OR cyst:ab,ti)) OR Cholangitis:ab,ti OR 'cholangitis'/exp) **AND** ('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) **AND** ('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR 'controlled clinical trial'/exp OR 'clinical trial'/exp OR placebo:ab,ti OR 'double blind':ab,ti OR 'single blind':ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*:ab,ti OR random*:ab,ti OR factorial*:ab,ti OR crossover:ab,ti OR (cross:ab,ti AND over:ab,ti))

Cochrane Central Register of Controlled Trials (CENTRAL)
#1   MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#2   antibiotic:ti,ab,kw (Word variations have been searched)
#3   #1 or #2
#4   MeSH descriptor: [Common Bile Duct] explode all trees   4
#5   CBD or biliary or pancreatic or bile duct:ti,ab,kw (Word variations have been searched)
#6   #4 or #5
#7   obstruction or occlusion:ti,ab,kw (Word variations have been searched)
#8   stone or calculus or cyst:ti,ab,kw (Word variations have been searched)
#9   #8 or #7
#10   #6 and #9
#11   MeSH descriptor: [Cholangitis] explode all trees
#12   Cholangitis:ti,ab,kw (Word variations have been searched)
#13   #10 or #11 or #12
#14   MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#15   ERCP:ti,ab,kw (Word variations have been searched)
#16   #14 or #15
#17   #16 and #13 and #3 Publication Year from 2000 to 2015

Results

Results of the bibliographic searches

After removing duplicates, 177 articles (26 reviews and 151 primary studies) were found. Three potentially relevant systematic reviews were found and acquired in full text. All of these were pertinent and so we screened only RCTs published after March 2010 (data of search update of the latest systematic reviews included available in full text).One potentially relevant primary study was acquired in full text for more evaluation (Minami 2014)(See flow chart).

Excluded studies

The primary study published after March 2010 was excluded because it was not an RCT and did not assess the outcome of interest (Minami 2014)

Included studies

Three studies were finally included: all were systematic reviews (Bai 2009, Brand 2010); for one only conference abstract was available (Romana 2015).

Overlapping of primary studies included in the systematic reviews.

	SR	
Studies included	**Brand 2010**	**Bai 2009**
Brandes 1981	X	
Byl 1995	X	
Finkelstein 1996		X
Llach 2006	X	X
Lorenz 1996	X	X
Niederau 1994	X	X
Räty 2001	X	X
Sauter 1990	X	X
Spicak 2001	X	
Van Den Hazel 1996	X	X

	N studies included	**N participants included**	**Post ERCP cholangitis**	**Pancreatitis**	**other infective complications**
Romana 2015	10 RCTs	1705 ERCPs	antibiotic group=3.8% placebo group=5.8% OR = 0.63; 95%CI: 0.40 - 0.98; p = 0.04; I^2 = 25%	OR = 0.37; CI: 0.15 - 0.89; p= 0.03; I^2 = 0%	OR = 0.64; 95%CI: 0.41 - 1.01; p = 0.06; I^2 = 3.7%
Brand 2010	9 RCTS	1573 patients	**Acute cholangitis** (all studies) N studies included=8 N of participants=1474 Antibiotics= 2.97% (21/706) Control=5.21% (40/768) Risk Ratio (M-H, Fixed, 95% CI) = 0.57 [0.34, 0.94] only including patients with biliary obstruction relieved at first ERCP N studies included=3 N of participants=309 Antibiotics= 4.08%(6/147) Control= 4.32%(7/162) Risk Ratio (M-H, Fixed, 95% CI) 0.98 [0.35, 2.69]	N studies included=4 N of participants=698 Antibiotics= 4.36%(14/321) Control= 7.69%(29/377) Risk Ratio (M-H, Fixed, 95% CI)= 0.54 [0.29, 1.00]	**Septicaemia** N studies included=6 N of participants=973 Antibiotics= 1.04%(5/480) Control=4.26% (21/493) Risk Ratio (M-H, Fixed, 95% CI)= 0.28 [0.12, 0.68]
Bai 2009	7 RCTs	1389 patients	Control=5.8% (41/705) Antibiotics=3.4% (23/684), RR=0.58; 95% CI:0.22-1.55 only trials (n=2) mainly targeted		

| | | | at patients with suspicious biliary obstruction:

Antibiotics=2.8% (12/425)
Control= 5.4%(24/441)
RR=0.33;
95% CI:0.03-3.32 | | |
|---|---|---|---|---|---|

Quality of evidence

Study limitations (risk of bias): no (for Romana 2015 methodological quality could not be fully assessed because only a conference abstract was available)
Inconsistency of results: yes for cholangitis
Indirectness of evidence: no (all but one study did not specify whether all patients were with native papilla
Imprecision: no (included more than 1700 ERCP)
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as high for pancreatitis, moderate for cholangitis because of inconsistency

Conclusions

Prophylactic antibiotics seem to reduce cholangitis
(**MODERATE QUALITY OF EVIDENCE**),
septicaemia, and pancreatitis. in patients undergoing elective ERCP
(**HIGH QUALITY OF EVIDENCE**).

References

Included studies
1. Bai Y.; Gao F.; Gao J.; Zou D.-W., and Li Z.-S. Prophylactic antibiotics cannot prevent endoscopic retrograde cholangio-pancreatography-induced cholangitis: A meta-analysis. Pancreas. 2009; 38(2):126-130;
2. **Brand M, Bizos D, O'Farrell PJR.** Antibiotic prophylaxis for patients undergoing elective endoscopic retrograde cholangio-pancreatography. Cochrane Database of Systematic Reviews 2010, Issue 10. Art. No.: CD007345. DOI:10.1002/14651858.CD007345.pub2.
3. Romana B.S.; Siddique S.; Yandrapu H.; Vennalaganti P.; Vennelaganti S.; Uhlich R.M.; Parasa S.; Rai T.; Kanakadandi V.; Bansal A.; Sharma P., and Choudhary A. Is there need for more randomized controlled trails to evaluate the role of prophylactic antibiotics before ERCP? A meta-analysis of randomized controlled trials. Gastrointest. Endosc. 2015; 81(5):AB417;

Excluded studies
1. Minami, T.; Sasaki, T.; Serikawa, M.; Ishigaki, T.; Murakami, Y., and Chayama, K. Antibiotic prophylaxis for endoscopic retrograde chlangiopancreatography increases the detection rate of drug-resistant bacteria in bile. J Hepatobiliary Pancreat Sci. 2014 Sep; 21(9):712-8.

PRISMA 2009 Flow Diagram

Identification	**Records identified through** CDSR (n =2) DARE (n=1) CENTRAL(n =15)

Records identified through PubMed (n = 3 SR, 55 RCTs)

Records identified through Embase (n= 25 SR, 110 RCTs)

Screening

Records after duplicates removed (n = 26 SR, 151 RCTs)

Records screened (n =177)

Records excluded (n = 173)

Eligibility

Studies awaiting classification (n = 0)

Full-text articles assessed for eligibility (n =4)

Full-text articles excluded, with reasons (n = 1)

Included

Studies included (n =3)

ADMINISTRATION OF ANTIBIOTICS IN PATIENTS UNDERGOING EUS

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3.2 (C I(b)). Administration of antibiotics in patients undergoing EUS

Population
Patients undergoing EUS including EUS-FNA suffering from either
- EUS-FNA of solid masses in the upper GI-tract
- EUS-FNA of solid masses in the lower GI-tract
- EUS-FNA of cystic lesions

Intervention
Administration of antibiotics

Control
No administration of antibiotics

Outcome
Preventing an inflammation

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and randomized controlled trials using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Anti-Bacterial Agents"[Mesh] OR antibiotic[Text Word] OR antibiotics [Title/Abstract]) **AND** ("Endosonography"[Mesh] OR "Biopsy, Fine-Needle"[Mesh] OR ("endoscopic ultrasound" [Title/Abstract] AND fine[Title/Abstract] AND needle[Title/Abstract]) OR (EUS[Title/Abstract] AND FNA[Title/Abstract])) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('antibiotic agent'/exp OR antibiotic:ab,ti OR antibiotics:ab,ti) **AND** ('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)
#1   MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#2   antibiotic:ti,ab,kw (Word variations have been searched)
#3   #1 or #2
#4   MeSH descriptor: [Endosonography] explode all trees
#5   MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#6   endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#7   EUS and FNA:ti,ab,kw (Word variations have been searched)
#8   #4 or #5 or #6 or #7
#9   #3 and #8 Publication Year from 2000 to 2015

Randomized controlled trials

PubMed
("Anti-Bacterial Agents"[Mesh] OR antibiotic[Text Word] OR antibiotics [Title/Abstract]) **AND** ("Endosonography"[Mesh] OR "Biopsy, Fine-Needle"[Mesh] OR ("endoscopic ultrasound" [Title/Abstract] AND fine[Title/Abstract] AND needle[Title/Abstract]) OR (EUS[Title/Abstract] AND FNA[Title/Abstract])) **AND** ((Randomized Controlled Trial[ptyp] OR Controlled Clinical Trial[ptyp] OR randomized[Title/Abstract] OR placebo[Title/Abstract] OR "drug therapy" [Subheading] OR randomly [Title/Abstract] OR trial[Title/Abstract] OR group[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]))

Embase
('antibiotic agent'/exp OR antibiotic:ab,ti OR antibiotics:ab,ti) **AND** ('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) **AND** ('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR 'controlled clinical trial'/exp OR 'clinical trial'/exp OR placebo:ab,ti OR 'double blind':ab,ti OR 'single blind':ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*:ab,ti OR random*:ab,ti OR factorial*:ab,ti OR crossover:ab,ti OR (cross:ab,ti AND over:ab,ti))

Cochrane Central Register of Controlled Trials (CENTRAL)
#1   MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#2   antibiotic:ti,ab,kw (Word variations have been searched)
#3   #1 or #2
#4   MeSH descriptor: [Endosonography] explode all trees
#5   MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#6   endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#7   EUS and FNA:ti,ab,kw (Word variations have been searched)
#8   #4 or #5 or #6 or #7
#9   #3 and #8 Publication Year from 2000 to 2015

Results

Results of the bibliographic searches

After removing duplicates, 421 articles (45 reviews and 376 primary studies) were found. No potentially relevant systematic reviews were found; 6 RCTs studies were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies

All the studies were excluded: three studies because the comparison was not in the inclusion criteria: two regimens of antibiotics were compared (Kehinde 2013, Kwok 2015, Luong 2015); two because they were not RCT (Guarner-Argente 2011, Rivera 2010).

Awaiting assessment

One study was awaiting assessment because it written in Chinese (Yang 2001).

Included studies

No studies fulfilled our inclusion criteria

Conclusion

No conclusion can be drawn because no studies fulfilling our inclusion criteria were found.

References

Excluded studies
1. Guarner-Argente C.; Shah P.; Buchner A.; Ahmad N.A.; Kochman M.L., and Ginsberg G.G. Use of antimicrobials for EUS-guided FNA of pancreatic cysts: A retrospective, comparative analysis. Gastrointest. Endosc. 2011; 74(1):81-86;
2. Kehinde, E. O.; Al-Maghrebi, M.; Sheikh, M., and Anim, J. T. Combined ciprofloxacin and amikacin prophylaxis in the prevention of septicemia after transrectal ultrasound guided biopsy of the prostate. The Journal of Urology. 2013; 189(3):911-5;
3. Kwok K.; Chang J.C.; Lim B.S.; Kao K.T.; Giap A.Q., and Wu B.U. A pilot study on the use of prophylactic antibiotics for EUS-guided pancreatic cyst aspiration. Gastrointest. Endosc. 2015; 81(5):AB207
4. Luong, B.; Danforth, T.; Visnjevac, O.; Suraf, M.; Duff, M., and Chevli, K. K. Reduction in hospital admissions with the addition of prophylactic intramuscular ceftriaxone before transrectal ultrasonography-guided prostate biopsies. Urology. 2015 Mar; 85(3):511-6.
5. Rivera R.; Ray A., and Zacharia G. Endoscopic ultrasound-guided fine needle aspiration of pancreatic cysts with and without antibiotic prophylaxis: A retrospective analysis of infectious complications. Am. J. Gastroenterol. 2010; 105S49;

Awaiting assessment
1. Yang L.; Hu J.; Wei H.; Wang L., and Zhong H. Clinical significance of antibiotic prophylaxis for transrectal prostate biopsy. Zhonghua Wai Ke Za Zhi. 2001; 39(12):940-942;

PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n =0)
DARE (n=0)
CENTRAL(n =8)

Records identified
through PubMed
(n = 1 SR, 204
RCTs)

Records identified
through Embase
(n= 44 SR, 176
RCTs)

Screening

Records after duplicates removed
(n = 45 SR, 376 RCts)

Records screened
(n =421)

Records excluded
(n =415)

Eligibility

Studies awaiting
classification
(n = 1)

Full-text articles assessed
for eligibility
(n =6)

Full-text articles excluded,
with reasons
(n =5)

Included

Studies included
(n =0)

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ANTIBIOTICS TO CONTRAST MEDIA FOR PREVENTION OF CHOLANGITIS

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3.3 (C I(c)). **Adding antibiotics to contrast media for prevention of cholangitis**

Population
Patients undergoing ERCP suffering from either

- cholangitis
- primary sclerosing cholangitis
- biliary obstruction without cholangitis, successful placement of drainage/stent
- biliary obstruction without cholangitis, unsuccessful placement of drainage/stent
- pancreatic cyst / pseudocyst communicating with pancreatic duct

- Independent of the indication for ERCP

Intervention
Adding antibiotics to contrast media

Control
No administration of antibiotics to contrast media

Outcome
Preventing an inflammation

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Anti-Bacterial Agents"[Mesh] OR antibiotic[Text Word] OR antibiotics [Title/Abstract]) **AND** ("Contrast Media"[Mesh] OR "contrast media"[Title/Abstract] OR "contrast medium"[Title/Abstract]) **AND** ("Cholangitis"[Mesh] OR Cholangitis[Title/Abstract] OR (("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct"[Title/Abstract] OR biliary[Title/Abstract] OR pancreatic[Title/Abstract]) AND (obstruct*[Title/Abstract] OR occlu*[Title/Abstract] OR stone*[Text Word] OR calculi[Text Word] OR calculus[Text Word] OR cyst[Text Word]))) **AND** ("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('antibiotic agent'/exp OR antibiotic:ab,ti OR antibiotics:ab,ti) **AND** ('contrast medium'/exp OR 'contrast media':ab,ti OR 'contrast medium':ab,ti) **AND** ((('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti) AND (obstruct*:ab,ti OR occlu*:ab,ti OR stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti OR cyst:ab,ti)) OR Cholangitis:ab,ti OR 'cholangitis'/exp) **AND** ('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and **Database of Abstracts of Reviews of Effects (DARE)**
#1	MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#2	antibiotic:ti,ab,kw (Word variations have been searched)
#3	#1 or #2
#4	MeSH descriptor: [Common Bile Duct] explode all trees
#5	CBD or biliary or pancreatic or bile duct:ti,ab,kw (Word variations have been searched
#6	#4 or #5
#7	obstruction or occlusion:ti,ab,kw (Word variations have been searched)
#8	stone or calculus or cyst:ti,ab,kw (Word variations have been searched)
#9	#8 or #7
#10	#6 and #9
#11	MeSH descriptor: [Cholangitis] explode all trees
#12	Cholangitis:ti,ab,kw (Word variations have been searched)
#13	#10 or #11 or #12
#14	MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#15	ERCP:ti,ab,kw (Word variations have been searched)
#16	#14 or #15
#17	MeSH descriptor: [Contrast Media] explode all trees
#18	contrast media:ti,ab,kw (Word variations have been searched)
#19	#113 or #114
#20	#16 and #13 and #3 and #19 Publication Year from 2000 to 2015

Primary studies

PubMed
("Anti-Bacterial Agents"[Mesh] OR antibiotic[Text Word] OR antibiotics [Title/Abstract]) **AND** ("Contrast Media"[Mesh] OR "contrast media"[Title/Abstract] OR "contrast medium"[Title/Abstract]) **AND** ("Cholangitis"[Mesh] OR Cholangitis[Title/Abstract] OR (("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct"[Title/Abstract] OR biliary[Title/Abstract] OR pancreatic[Title/Abstract]) AND (obstruct*[Title/Abstract] OR occlu*[Title/Abstract] OR stone*[Text Word] OR calculi[Text Word] OR calculus[Text Word] OR cyst[Text Word]))) **AND** ("Cholangiopancreatography, Endoscopic Retrograde"[Mesh] OR ERCP[Title/Abstract]) AND ((Randomized Controlled Trial[ptyp] OR Controlled Clinical Trial[ptyp] OR randomized[Title/Abstract] OR placebo[Title/Abstract] OR "drug therapy" [Subheading] OR randomly [Title/Abstract] OR trial[Title/Abstract] OR group[Title/Abstract]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]))

Embase
('antibiotic agent'/exp OR antibiotic:ab,ti OR antibiotics:ab,ti) **AND** ('contrast medium'/exp OR 'contrast media':ab,ti OR 'contrast medium':ab,ti) **AND** ((('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti) AND (obstruct*:ab,ti OR occlu*:ab,ti OR stone*:ab,ti OR calculi:ab,ti OR calculus:ab,ti OR cyst:ab,ti)) OR Cholangitis:ab,ti OR 'cholangitis'/exp) **AND** ('endoscopic retrograde cholangiopancreatography'/exp OR ERCP:ab,ti) **AND** ('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR 'controlled clinical trial'/exp OR 'clinical trial'/exp OR placebo:ab,ti OR 'double blind':ab,ti OR 'single blind':ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*:ab,ti OR random*:ab,ti OR factorial*:ab,ti OR crossover:ab,ti OR (cross:ab,ti AND over:ab,ti))

Cochrane Central Register of Controlled Trials (CENTRAL)
#1   MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#2   antibiotic:ti,ab,kw (Word variations have been searched)
#3   #1 or #2
#4   MeSH descriptor: [Common Bile Duct] explode all trees
#5   CBD or biliary or pancreatic or bile duct:ti,ab,kw (Word variations have been searched
#6   #4 or #5
#7   obstruction or occlusion:ti,ab,kw (Word variations have been searched)
#8   stone or calculus or cyst:ti,ab,kw (Word variations have been searched)
#9   #8 or #7
#10   #6 and #9
#11   MeSH descriptor: [Cholangitis] explode all trees
#12   Cholangitis:ti,ab,kw (Word variations have been searched)
#13   #10 or #11 or #12
#14   MeSH descriptor: [Cholangiopancreatography, Endoscopic Retrograde] explode all trees
#15   ERCP:ti,ab,kw (Word variations have been searched)
#16   #14 or #15
#17   MeSH descriptor: [Contrast Media] explode all trees
#18   contrast media:ti,ab,kw (Word variations have been searched)
#19   #113 or #114
#20   #16 and #13 and #3 and #19 Publication Year from 2000 to 2015

Results

Results of the bibliographic searches
After removing duplicates, 33 articles (1 review and 32 primary studies) were found. No potentially relevant systematic reviews were found; 1 randomized controlled trials was considered potentially relevant and acquired in full text; moreover 4 primary studies were suggested by authors. (See flow chart)

Excluded studies
Two studies were excluded because they were laboratory studies without the outcome of interest (Jendrzejewski 1980, Ramirez 2010).

Included studies
Three studies were finally included (Collen 1980, Norouzi 2013, Pugliese 1986). All assessed the effectiveness of adding gentamicin to contrast media

Study	Patients	Intervention	Control	Post-ERCP complications
Collen 1980	61 Patients undergoing ERCP for standard diagnostic indications	80 mg of gentamicin added to each 60 cc of contrast media (n=29)	placebo (n=32)	<u>post-ERCP septic complication</u> Placebo group: 1/32 (3%) one patient developed a febrile episode with subsequent blood cultures growing Escherichia coli. Gentamicin group: 1/29 (3%) one patient developed a febrile episode with no subsequent blood cultures growing
Norouzi 2013	114 patients with non-calculous obstructive jaundice who underwent endoscopic biliary stenting	10 mg (2 mL) gentamicin (n=57) 2 g ceftriaxone intravenously 30 min before ERCP and daily for 3 days.	distilled water (n=57) 2 g ceftriaxone intravenously 30 min before ERCP and daily for 3 days.	<u>post-ERCP cholangitis</u> Intervention group: 5/57 Placebo group: 5/57
Pugliese 1986	330 consecutive patients undergoing ERCP (with absence of fever, normal white blood cell count and no rises in serum and urine amylase levels)	Gentamicin 1,6mg/ml (n=168)	without gentamicin (n=162)	**Increase of white blood cells** gentamicin: 13/168 (7.74%) no gentamicin : 5/162 (3.09%) RR: 2.51 [95%CI 0.91, 6.87] with a trend in favor of no gentamicin **Fever +/- white blood cells** gentamicin: 16/168 (9.52%) no gentamicin: 6/162 (3.70%) RR: 2.57 [95%CI 1.03, 6.41] in favor of no gentamicin **Acute Pancreatitis** gentamicin: 1/168 (0.59%) no gentamicin: 0/162 (0%) **Acute cholangitis** gentamicin: 0/168 (0%) no gentamicin: 0/162 (0%)

Quality of evidence

Study limitations (risk of bias): no (RCTs; two studies at unclear risk of bias for all items but attrition bias, for which they were at low risk).
Inconsistency of results: no
Indirectness of evidence: no
Imprecision: no (three studies with 505 patients overall)
Publication bias: not assessed

Overall quality of evidence
The overall quality of evidence was judged as high

Conclusions

The incidence of post-ERCP complications is not modified by the addition of gentamicin to the contrast media.
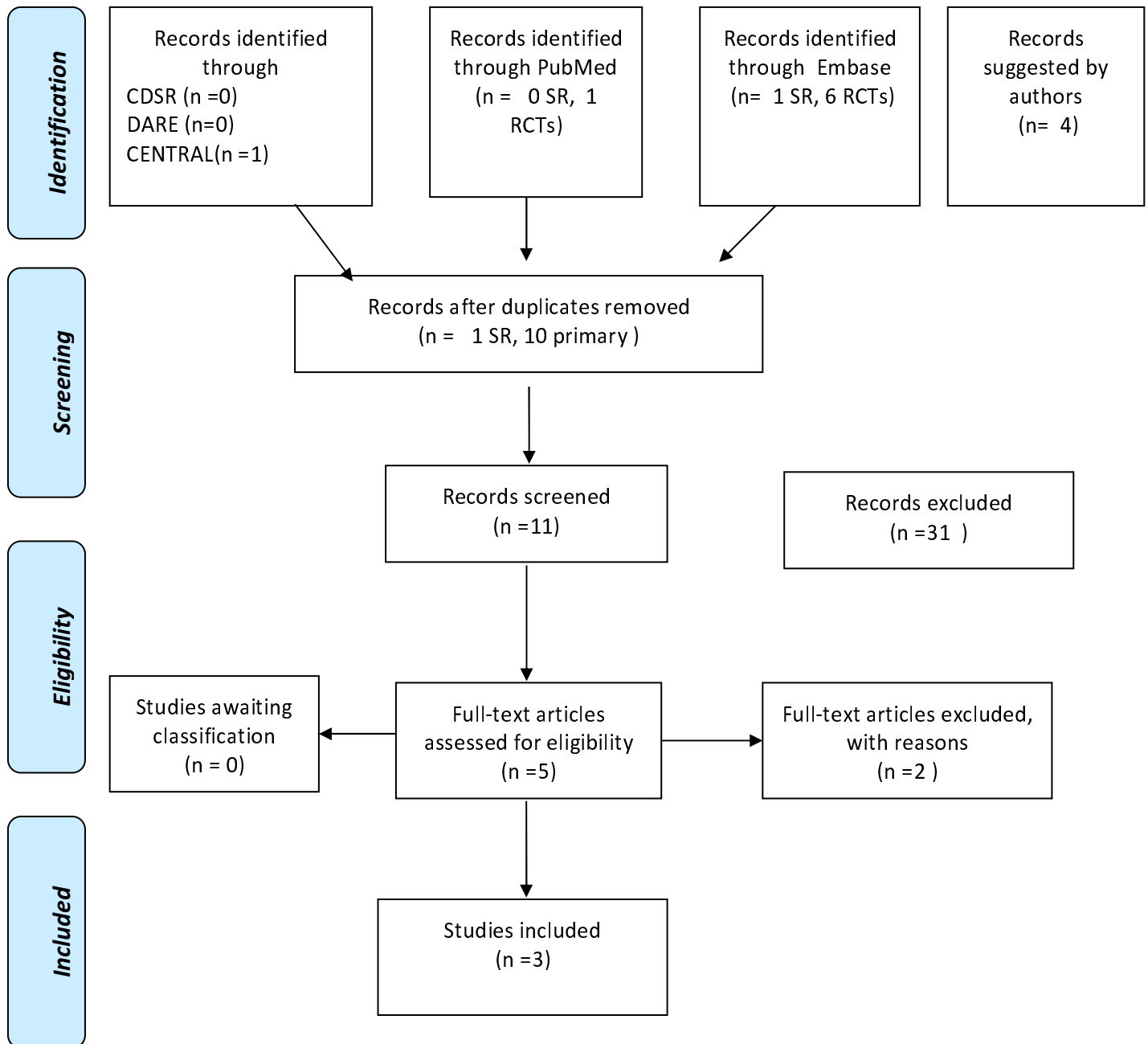
References

Included studies
  1. Collen MJ, Hanan MR, Maher JA, Stubrin SE. Modification of endoscopic retrograde cholangiopancreatography (ERCP) septic complications by the addition of an antibiotic to the contrast media. Randomized controlled investigation. Am J Gastroenterol. 1980;74(6):493-6.
  2. Norouzi A, Khatibian M, Afroogh R, Chaharmahali M, Sotoudehmanesh R.The effect of adding gentamicin to contrast media for prevention of cholangitis after biliary stenting for non-calculous biliary obstruction, a randomized controlled trial.Indian J Gastroenterol. 2013;32(1):18-21.
  3. Pugliese V, Saccomanno S, Bonelli L, Aste H. [Is it useful to add gentamycin to contrast media in endoscopic retrograde cholangiopancreatography? Prospective evaluation of 330 cases].Minerva Dietol Gastroenterol. 1986;32(2):149-56.

Excluded studies
  4. Jendrzejewski JW, McAnally T, Jones SR, Katon RM. Antibiotics and ERCP: in vitro activity of aminoglycosides when added to iodinated contrast agents. Gastroenterology. 1980;78(4):745-8.
  5. Ramirez FC, Osato MS, Graham DY, Woods KL. Addition of gentamicin to endoscopic retrograde cholangiopancreatography (ERCP) contrast medium towards reducing the frequency of septic complications of ERCP.J Dig Dis. 2010 ;11(4):237-43

PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n =0)
DARE (n=0)
CENTRAL(n =1)

Records identified through PubMed
(n = 0 SR, 1 RCTs)

Records identified through Embase
(n= 1 SR, 6 RCTs)

Records suggested by authors
(n= 4)

Screening

Records after duplicates removed
(n = 1 SR, 10 primary)

Records screened
(n =11)

Records excluded
(n =31)

Eligibility

Studies awaiting classification
(n = 0)

Full-text articles assessed for eligibility
(n =5)

Full-text articles excluded, with reasons
(n =2)

Included

Studies included
(n =3)

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CPO
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e la Prevenzione Oncologica in Piemonte

EUS-FNA IN PATIENTS WITH SUSPECTED PANCREATIC CANCER

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4 (D). **Risks of performing EUS-FNA in patients with suspected pancreatic cancer**
4.1 (D I).   **Due to the potential risk of seeding metastases EUS-FNA is often not performed in patients with unclear pancreatic masses**

Population
Patients with unclear pancreatic mass / suspected pancreatic cancer undergoing EUS-FNA

Intervention
Performing EUS-FNA to clarify the diagnosis

Control
No EUS-FNA

Outcome
Tumor spread, seeding metastases

Suggested statement. The risks of performing EUS-FNA in patients with undiagnosed pancreatic masses include tumour spread and seeding of metastases.

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/8/2015 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
(((Suspect*[Title/Abstract]   OR   unclear[Title/Abstract])   AND   (mass[Title/Abstract]   OR masses[Title/Abstract]   OR   malign*[Title/Abstract]   OR   cancer[Title/Abstract]   OR tumor[Title/Abstract]   OR   tumour[Title/Abstract])   AND   (pancrea*[Title/Abstract]))   OR

("Pancreatic Neoplasms"[Mesh] AND (Suspect*[Title/Abstract] OR unclear[Title/Abstract]))) **AND** ("Endosonography"[Mesh] OR "Biopsy, Fine-Needle"[Mesh] OR ("endoscopic ultrasound" [Title/Abstract] AND fine[Title/Abstract] AND needle[Title/Abstract]) OR (EUS[Title/Abstract] AND FNA[Title/Abstract])) **AND** ("Tumor Burden"[Mesh] OR infiltration[Title/Abstract] OR metastasis[Title/Abstract] OR metastases[Title/Abstract] OR "Lymphatic Metastasis"[Mesh] OR "Neoplasm Metastasis"[Mesh] OR "tumor spread"[Title/Abstract] OR "tumour spread"[Title/Abstract] OR "cancer spread"[Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
((((suspect*:ab,ti OR unclear:ab,ti) AND (mass:ab,ti OR masses:ab,ti OR malign:ab,ti OR cancer:ab,ti OR tumor:ab,ti OR tumour:ab,ti) AND pancreas*:ab,ti) OR ('pancreas cancer'/exp AND (suspect*:ab,ti OR unclear:ab,ti))) **AND** ('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) **AND** ('tumor volume'/exp OR 'lymph node metastasis'/exp OR 'metastasis'/exp OR infiltration:ab,ti OR metastasis:ab,ti OR metastases:ab,ti OR 'cancer spread':ab,ti OR 'tumor spread':ab,ti OR 'tumour spread':ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and Database of Abstracts of Reviews of Effects (DARE)
#1   MeSH descriptor: [Endosonography] explode all trees
#2   MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#3   endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#4   EUS and FNA:ti,ab,kw (Word variations have been searched)
#5   #1 or #2 or #3 or #4
#6   MeSH descriptor: [Tumor Burden] explode all trees
#7   MeSH descriptor: [Lymphatic Metastasis] explode all trees
#8   MeSH descriptor: [Neoplasm Metastasis] explode all trees
#9   infiltration or metastasis or tumor spread or cancer spread:ti,ab,kw (Word variations have been searched)
#10   #6 or #7 or #8 or #9
#11   suspected or unclear:ti,ab,kw (Word variations have been searched)
#12   mass or malign* or cancer or tumor:ti,ab,kw (Word variations have been searched)
#13   pancreas or pancreatic:ti,ab,kw (Word variations have been searched)
#14   MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#15   #12 and #13 and #11
#16   #11 and #14
#17   #16 or #15
#18   #17 and #10 and #5 Publication Year from 2000 to 2015

Primary studies

PubMed
((((Suspect*[Title/Abstract] OR unclear[Title/Abstract]) AND (mass[Title/Abstract] OR masses[Title/Abstract] OR malign*[Title/Abstract] OR cancer[Title/Abstract] OR

tumor[Title/Abstract] OR tumour[Title/Abstract]) AND (pancrea*[Title/Abstract])) OR ("Pancreatic Neoplasms"[Mesh] AND (Suspect*[Title/Abstract] OR unclear[Title/Abstract]))) **AND** ("Endosonography"[Mesh] OR "Biopsy, Fine-Needle"[Mesh] OR ("endoscopic ultrasound" [Title/Abstract] AND fine[Title/Abstract] AND needle[Title/Abstract]) OR (EUS[Title/Abstract] AND FNA[Title/Abstract])) **AND** ("Tumor Burden"[Mesh] OR infiltration[Title/Abstract] OR metastasis[Title/Abstract] OR metastases[Title/Abstract] OR "Lymphatic Metastasis"[Mesh] OR "Neoplasm Metastasis"[Mesh] OR "tumor spread"[Title/Abstract] OR "tumour spread"[Title/Abstract] OR "cancer spread"[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

((((suspect*:ab,ti OR unclear:ab,ti) AND (mass:ab,ti OR masses:ab,ti OR malign:ab,ti OR cancer:ab,ti OR tumor:ab,ti OR tumour:ab,ti) AND pancreas*:ab,ti) OR ('pancreas cancer'/exp AND (suspect*:ab,ti OR unclear:ab,ti))) **AND** ('endoscopic echography'/exp OR 'endoscopic ultrasound guided fine needle biopsy'/exp OR ('endoscopic ultrasound':ab,ti AND fine:ab,ti AND needle:ab,ti) OR (EUS:ab,ti AND FNA:ab,ti)) **AND** ('tumor volume'/exp OR 'lymph node metastasis'/exp OR 'metastasis'/exp OR infiltration:ab,ti OR metastasis:ab,ti OR metastases:ab,ti OR 'cancer spread':ab,ti OR 'tumor spread':ab,ti OR 'tumour spread':ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)
#1   MeSH descriptor: [Endosonography] explode all trees
#2   MeSH descriptor: [Biopsy, Fine-Needle] explode all trees
#3   endoscopic ultrasound and fine and needle:ti,ab,kw (Word variations have been searched)
#4   EUS and FNA:ti,ab,kw (Word variations have been searched)
#5   #1 or #2 or #3 or #4
#6   MeSH descriptor: [Tumor Burden] explode all trees
#7   MeSH descriptor: [Lymphatic Metastasis] explode all trees
#8   MeSH descriptor: [Neoplasm Metastasis] explode all trees
#9   infiltration or metastasis or tumor spread or cancer spread:ti,ab,kw (Word variations have been searched)
#10   #6 or #7 or #8 or #9
#11   suspected or unclear:ti,ab,kw (Word variations have been searched)
#12   mass or malign* or cancer or tumor:ti,ab,kw (Word variations have been searched)
#13   pancreas or pancreatic:ti,ab,kw (Word variations have been searched)
#14   MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#15   #12 and #13 and #11
#16   #11 and #14
#17   #16 or #15
#18   #17 and #10 and #5 Publication Year from 2000 to 2015
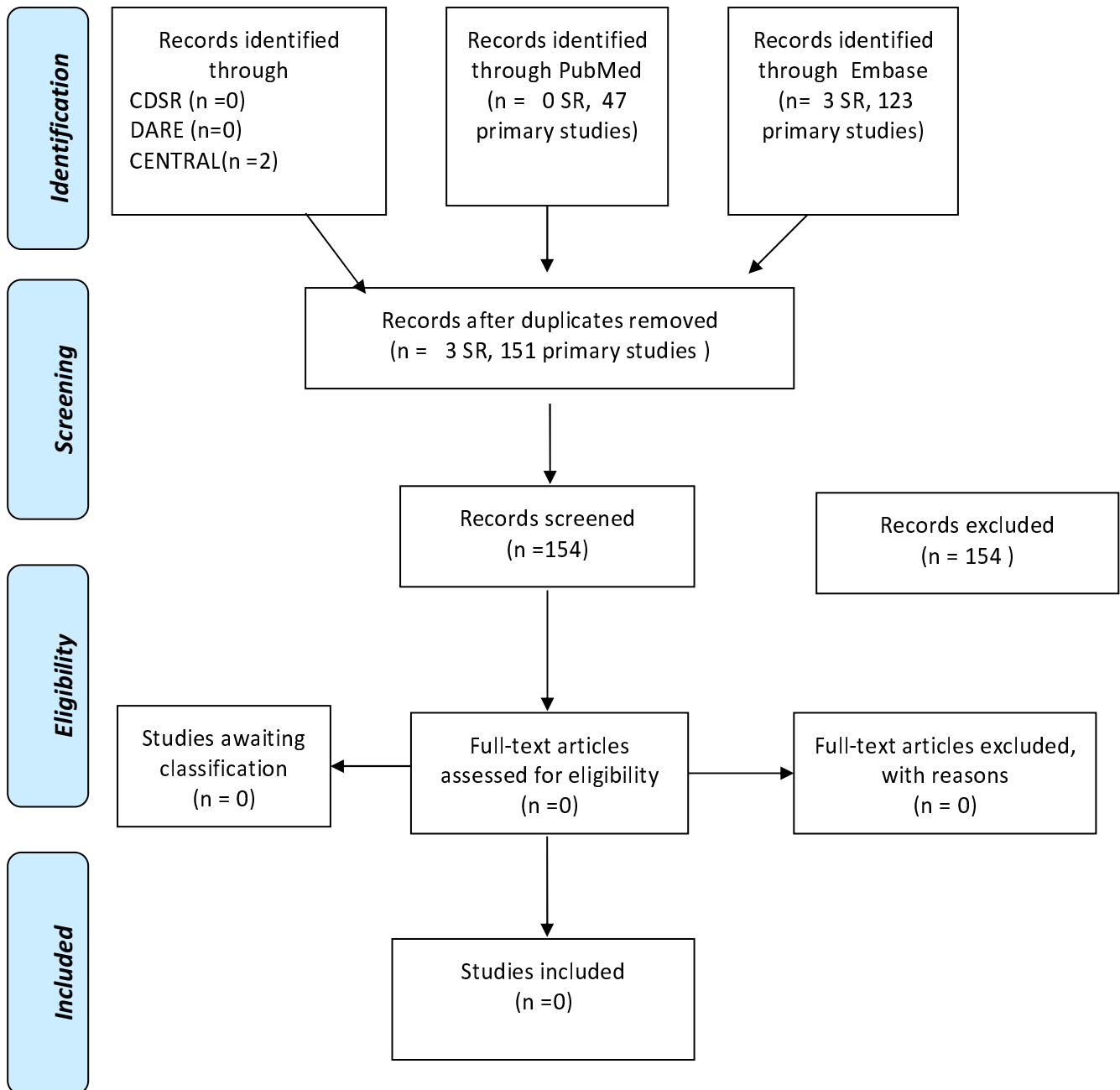
Results

<u>Results of the bibliographic searches</u>
After removing duplicates, 154 articles (3 reviews and 151 primary studies) were found. No relevant studies were found addressing this question.

Conclusions

No conclusion can be drawn about tumor spread and seeding metastases performing EUS-FNA in patients with unclear pancreatic masses because no evidence was found.

PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n =0)
DARE (n=0)
CENTRAL(n =2)

Records identified through PubMed
(n = 0 SR, 47 primary studies)

Records identified through Embase
(n= 3 SR, 123 primary studies)

Screening

Records after duplicates removed
(n = 3 SR, 151 primary studies)

Records screened
(n =154)

Records excluded
(n = 154)

Eligibility

Studies awaiting classification
(n = 0)

Full-text articles assessed for eligibility
(n =0)

Full-text articles excluded, with reasons
(n = 0)

Included

Studies included
(n =0)

**S.C. Epidemiologia screening, registro tumori –
CPO Piemonte**

Direttore: Dr. Nereo Segnan
via Cavour 31, 10123 Torino
tel. 011.6333881 - fax 011.6333861
www.cpo.it - email: info@cpo.it

Centro di Riferimento per l'Epidemiologia
e la Prevenzione Oncologica in Piemonte

SUCCESFUL STAGING AND DOCUMENTATION RATE FOR GI-CANCER

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Cristina Bellisario, MSc, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte
Literature Group Coordinator: Carlo Senore, MD, S.C. Epidemiologia, Screening e Registro Tumori- CPO Piemonte

Clinical question 4

Population
patients undergoing EUS for staging of GI-cancer, (e.g. - esophageal cancer, - pancreatic cancer, - biliary cancer, - rectal cancer)

Intervention
endoscopic ultrasound

Control
None

Outcome
successful staging (TNM)

Clinical question 5

Population
Patients with pancreatic cancer undergoing EUS

Intervention
Documentation of pancreatic masses along with vascular involvement, lymphadenopathy and distant metastases

Control
none

Outcome
documentation rate

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 25/9/2016 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed
("Endosonography"[Mesh] OR EUS[Title/Abstract]) **AND** ("Neoplasm Staging"[Mesh] OR stag*[Title/Abstract] OR infiltration[Title/Abstract] OR TNM[Title/Abstract] OR (("Lymph Nodes"[Mesh] OR "lymph node"[Title/Abstract] OR "lymph nodes"[Title/Abstract] OR "lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract]) AND (metastasis[Title/Abstract] OR metastases[Title/Abstract])) OR "Lymphatic Metastasis"[Mesh]) **AND** ((("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct"[Title/Abstract] OR biliary[Title/Abstract] OR pancreatic[Title/Abstract] OR rectal[Title/Abstract] OR gastric[Title/Abstract] OR esophageal[Title/Abstract] OR oesophageal[Title/Abstract]) AND (cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign* [Title/Abstract] OR tumor [Title/Abstract] OR tumour [Title/Abstract] OR tumors [Title/Abstract] OR tumours [Title/Abstract] OR carcinom* [Title/Abstract] OR mass[Title/Abstract] OR masses[Title/Abstract])) OR "Biliary Tract Neoplasms"[Mesh] OR "Pancreatic Neoplasms"[Mesh] OR "Gastrointestinal Neoplasms"[Mesh] OR "Rectal Neoplasms"[Mesh]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase
('endoscopic echography'/exp OR EUS:ab,ti) **AND** ('cancer staging'/exp OR stag*:ab,ti OR infiltration:ab,ti OR TNM:ab,ti OR (('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti) AND (metastasis:ab,ti OR metastases:ab,ti)) OR 'lymph node metastasis'/exp) **AND** ((('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti OR rectal:ab,ti OR gastric:ab,ti OR esophageal:ab,ti OR oesophageal:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti)) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR 'rectum cancer'/exp OR 'esophagus cancer'/exp OR 'digestive system cancer'/exp) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

Cochrane Database of Systematic Reviews (CDSR) and **Database of Abstracts of Reviews of Effects (DARE)**
#1   MeSH descriptor: [Endosonography] explode all trees
#2   EUS:ti,ab,kw (Word variations have been searched)
#3   MeSH descriptor: [Neoplasm Staging] explode all trees
#4   stage or infiltration or TNM:ti,ab,kw (Word variations have been searched)
#5   MeSH descriptor: [Lymph Nodes] explode all trees
#6   lymphnode:ti,ab,kw (Word variations have been searched)
#7   #5 or #6

#8 metastasis:ti,ab,kw (Word variations have been searched)
#9 MeSH descriptor: [Lymphatic Metastasis] explode all trees
#10 #7 and #8
#11 #3 or #4 or #9 or #10
#12 #1 or #2
#13 cancer or malign or mass or neoplasm or tumor or carcinoma:ti,ab,kw (Word variations have been searched)
#14 rectal:ti,ab,kw (Word variations have been searched)
#15 gastric:ti,ab,kw (Word variations have been searched)
#16 pancreatic:ti,ab,kw (Word variations have been searched)
#17 biliary or CBD or bile duct:ti,ab,kw (Word variations have been searched)
#18 MeSH descriptor: [Common Bile Duct] explode all trees
#19 esophageal:ti,ab,kw (Word variations have been searched)
#20 #14 or #15 or #16 or #17 or #18 or #19
#21 #20 and #13
#22 MeSH descriptor: [Rectal Neoplasms] explode all trees
#23 MeSH descriptor: [Gastrointestinal Neoplasms] explode all trees
#24 MeSH descriptor: [Biliary Tract Neoplasms] explode all trees
#25 MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#26 MeSH descriptor: [Esophageal Neoplasms] explode all trees
#27 #21 or #22 or #23 or #24 or #25 or #26
#18 #11 and #12 and #27 Publication Year from 2000 to 2016

Primary studies

PubMed
("Endosonography"[Mesh] OR EUS[Title/Abstract]) **AND** ("Neoplasm Staging"[Mesh] OR stag*[Title/Abstract] OR infiltration[Title/Abstract] OR TNM[Title/Abstract] OR (("Lymph Nodes"[Mesh] OR "lymph node"[Title/Abstract] OR "lymph nodes"[Title/Abstract] OR "lymphnode"[Title/Abstract] OR "lymphnodes"[Title/Abstract]) AND (metastasis[Title/Abstract] OR metastases[Title/Abstract])) OR "Lymphatic Metastasis"[Mesh]) **AND** ((("Common Bile Duct"[Mesh] OR CBD[Title/Abstract] OR "Bile Duct"[Title/Abstract] OR biliary[Title/Abstract] OR pancreatic[Title/Abstract] OR rectal[Title/Abstract] OR gastric[Title/Abstract] OR esophageal[Title/Abstract] OR oesophageal[Title/Abstract]) AND (cancer [Title/Abstract] OR neoplasm*[Title/Abstract] OR malign* [Title/Abstract] OR tumor [Title/Abstract] OR tumour [Title/Abstract] OR tumors [Title/Abstract] OR tumours [Title/Abstract] OR carcinom* [Title/Abstract] OR mass[Title/Abstract] OR masses[Title/Abstract])) OR "Biliary Tract Neoplasms"[Mesh] OR "Pancreatic Neoplasms"[Mesh] OR "Gastrointestinal Neoplasms"[Mesh] OR "Rectal Neoplasms"[Mesh]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase
('endoscopic echography'/exp OR EUS:ab,ti) **AND** ('cancer staging'/exp OR stag*:ab,ti OR infiltration:ab,ti OR TNM:ab,ti OR (('lymph node'/exp OR 'lymph node':ab,ti OR 'lymph nodes':ab,ti OR 'lymphnode':ab,ti OR 'lymphnodes':ab,ti) AND (metastasis:ab,ti OR metastases:ab,ti)) OR 'lymph node metastasis'/exp) **AND** ((('common bile duct'/exp OR CBD:ab,ti OR 'bile duct':ab,ti OR biliary:ab,ti OR pancreatic:ab,ti OR rectal:ab,ti OR gastric:ab,ti OR

esophageal:ab,ti OR oesophageal:ab,ti) AND (cancer:ab,ti OR neoplasm*:ab,ti OR malign*:ab,ti OR tumor:ab,ti OR tumour:ab,ti OR tumors:ab,ti OR tumours:ab,ti OR carcinom*:ab,ti OR mass:ab,ti OR masses:ab,ti)) OR 'biliary tract tumor'/exp OR 'pancreas tumor'/exp OR 'rectum cancer'/exp OR 'esophagus cancer'/exp OR 'digestive system cancer'/exp) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)

#1   MeSH descriptor: [Endosonography] explode all trees
#2   EUS:ti,ab,kw (Word variations have been searched)
#3   MeSH descriptor: [Neoplasm Staging] explode all trees
#4   stage or infiltration or TNM:ti,ab,kw (Word variations have been searched)
#5   MeSH descriptor: [Lymph Nodes] explode all trees
#6   lymphnode:ti,ab,kw (Word variations have been searched)
#7   #5 or #6
#8   metastasis:ti,ab,kw (Word variations have been searched)
#9   MeSH descriptor: [Lymphatic Metastasis] explode all trees
#10   #7 and #8
#11   #3 or #4 or #9 or #10
#12   #1 or #2
#13   cancer or malign or mass or neoplasm or tumor or carcinoma:ti,ab,kw (Word variations have been searched)
#14   rectal:ti,ab,kw (Word variations have been searched)
#15   gastric:ti,ab,kw (Word variations have been searched)
#16   pancreatic:ti,ab,kw (Word variations have been searched)
#17   biliary or CBD or bile duct:ti,ab,kw (Word variations have been searched)
#18   MeSH descriptor: [Common Bile Duct] explode all trees
#19   esophageal:ti,ab,kw (Word variations have been searched)
#20   #14 or #15 or #16 or #17 or #18 or #19
#21   #20 and #13
#22   MeSH descriptor: [Rectal Neoplasms] explode all trees
#23   MeSH descriptor: [Gastrointestinal Neoplasms] explode all trees
#24   MeSH descriptor: [Biliary Tract Neoplasms] explode all trees
#25   MeSH descriptor: [Pancreatic Neoplasms] explode all trees
#26   MeSH descriptor: [Esophageal Neoplasms] explode all trees
#27   #21 or #22 or #23 or #24 or #25 or #26
#18   #11 and #12 and #27 Publication Year from 2000 to 2016

Results

Results of the bibliographic searches
After removing duplicates, 4627 articles (197 reviews and 4430 primary studies) were found. 34 potentially relevant systematic reviews were considered potentially relevant and acquired in full text. In first instance, given the high number of updated systematic reviews, only systematic reviews were considered.

Excluded studies

12 articles were excluded: 5 because conference abstracts (Gentry 2009, Puli 2009 A498, Puli 2009 AB341, Thosani 2011, Vetro 2011); 1 because did not report the outcomes of interest (De Witt 2006); 1 because assessed the diagnostic accuracy of EUS only as an add on test after CT foe periampullary and pancreatic cancer (Tamburrino 2016); 1 because assessed the diagnostic accuracy of EUS-FNA (Treadwell 2016); 1 because pooled together studies assessing patients with colon and rectal cancer (Li 2015 Asian Pac J Cancer Prev); 1 because it was a narrative review without useful data (Skandarajah 2006); 1 because did not report TNM staging (Qumseya 2015) and 1 because in Chinese language (Zhou 2014).

Included studies

We finally included 22 systematic reviews (one for gastric cancer and esophageal cancer): 2 on biliary cancers, 3 on pancreatic cancer, 7 on gastric cancer, 4 on rectal cancer , 7 on esophageal cancer.

All the reviews assessed the diagnostic accuracy of EUS for TNM staging, but none reported data about the successful staging, defined as the percentage of patients for whom the TNM staging were successful (irrespective to its accuracy) over the total number of patients for whom TNM staging was attempted.

Table 1. Successful Staging and Documentation Rate for biliary cancer

Authors, publication date	n. of studies included, n. of participants Reference standard	Successful staging/ documentation rate	Accuracy of EUS to diagnose T stage tumor	Accuracy of EUS to diagnose N stage tumor	Accuracy of EUS to detect vascular invasion
Al-Taan 2015 EUS for the staging of periampullary cancers	22 articles included with 1003 patients Reference standard: intraoperative findings and final histopathological analysis cancers		Sensitivity: 97% (474/488) Specificity: / PV: 93% (213/240) NPV : 83% (10/12)	Sensitivity: 56% (75/133) Specificity: 76% (78/103) PV: 62% (40/65) NPV : /	Sensitivity: 83.9% (47/56) Specificity:97% (101/104) PV: 91% (41/45) NPV : 91% (89/98)/

Trikudanathan 2014	14 studies included with 422 patients		T1, 11 studies 327 patients	N stage, 12 studies 332 patients	
EUS staging for ampullary cancers	Reference standard: histopathology		Sensitivity (95% CI): 0.77 (0.69–0.83) Specificity (95% CI): 0.78 (0.72–0.84)	Sensitivity (95% CI): 0.70 (95% CI: 0.62–0.77),	
			T2, 12 studies 351 patients Sensitivity (95% CI): 0.73 (0.65–0.80) Specificity (95% CI): 0.76 (0.70–0.82)	Specificity (95% CI): 0.74 (0.67–0.0.80), Positive LR: (95% CI): 2.49 (1.91–3.24)	
			T3, 11 studies 327 patients Sensitivity (95% CI): 0.79 (0.71–0.85) Specificity (95% CI): 0.76 (0.71–0.83)	Negative LR (95% CI): 0.46 (0.36–0.59) DOR: (95% CI): 6.53 (3.81–11.19)	
			T4, 4 studies 148 pz Sensitivity (95% CI): 0.84 (0.73–0.92) Specificity (95% CI) 0.74 (0.63–0.83)	The EUS definition of N-stage disease varied across studies, with some studies relying exclusively on lymph node size (>10 mm) and others on characteristic malignant lymph node morphology (e.g. uniformly hypoechoic, rounded contour, sharply demarcated borders, close proximity to ampullary tumour).	

Table 2. Successful Staging and Documentation Rate for gastric cancer

Authors, publication date	n. of studies included, n. of participants Reference standard	Successful staging/ documentation rate	Accuracy of EUS to diagnose T stage tumour	Accuracy of EUS to diagnose N stage tumour	Depth of invasion (mucosal (M), sub-mucosal (SM) invasion, serosal involvement)	Distant metastases
Cardoso 2013	22 articles included with 2445 patients Reference standard: histopathology		T2 staging pooled accuracy: 65% (95% CI: 57–73%) T1 staging, pooled accuracy: 77% (95% CI: 70–84%) T3 staging, pooled accuracy: 85% (95% CI: 82–88%) T4 staging, pooled accuracy: 79% (95% CI: 68–90%)	Pooled accuracy for N staging: 64% (95% CI: 43–84%) Pooled sensitivity: 74% (95% CI: 66–81%) Pooled specificity: 80% (95% CI: 74–87%)		
Kwee 2007	23 studies included with 2012 patients Reference standard: histopathology		Diagnostic accuracy of EUS for overall T staging varied between 65% and 92.1%.		**Serosal involvement** Sensitivity: varied between 77.8% and 100% Specificity: varied between 67.9% and 100%	

Kelly 2001	13 studies, no of patients not reported Reference standard: histopathology		sensitivity: range: 67% -100% specificity: range 87.5% - 100%		
Mocellin 2015	66 studies included with 7747 patients Reference standard: histopathology		Accuracy in discriminating T1 and T2 versus T3 and T4 (50 studies , 4397patients) Sensitivity: 0.86 (95%CI 0.81-0.90) Specificity: 0.90 (95%CI 0.87-0.93) Accuracy in discriminating T1 versus T2 (46 studies, 2742 patients) Sensitivity: 0.85 (95%CI 0.78-0.91) Specificity: 0.90 (95%CI 0.85-0.93)	44 studies, 3573 patients Sensitivity: 0.83 (95%CI 0.79-0.87) Specificity: 0.67 (95%CI 0.61-0.72)	Accuracy in discriminating T1a (mucosal) versus T1b (submucosal) (20 studies, 3321 patients) Sensitivity: 0.87 (95% CI 0.81- 0.92) Specificity: 0.75 (95%CI 0.62-0.84)	
Mocellin 2011	54 studies enrolling 5601 patients Reference standard: histopathology		Accuracy in discriminating T1/ T2 versus T3 and T4 (41 studies, 3510 patients) Sensitivity: 0.86 (95%CI 0.81-0.90) Specificity: 0.91 (95%CI 0.89-0.93)	39 studies, 3315 patients. Sensitivity: 0.69 (95%CI 0.63-0.74) Specificity: 0.84 (95%CI 0.81-0.88)		
Pei 2015	16 studies with				**Mucosal invasion**	

	3931 patients Reference standard: final histopathologic evaluation of endoscopically or surgically resected specimen				Sensitivity (%) 76 (74–78) Specificity (%) 72 (69–75) **Sub-mucosal invasion** Sensitivity (%) 62 (59–66) Specificity (%) 78 (76–80)	
Puli 2008	22 studies with 1896 patients		22 studies **T1** Sensitivity: 88.1% (84.5-91.1) Specificity:100.0% (99.7-100.0) **T2** Sensitivity: 82.3% (78.2-86.0) Specificity: 95.6% (94.4-96.6) **T3** Sensitivity: 89.7% (87.1-92.0) Specificity: 94.7% (93.3-95.9) **T4** Sensitivity: 99.2% (97.1-99.9) Specificity: 96.7% (95.7-97.6)	22 studies **N1** Sensitivity: 58.2% (53.5-62.8) Specificity: 87.2% (84.4-89.7) **N2** Sensitivity: 64.9% (60.8-68.8) Specificity: 92.4% (89.9-94.4)		4 studies Sensitivity 73.2% (95% CI: 63.2-81.7). Specificity: 88.6% (84.8-91.7).

Table 2. Successful Staging and Documentation Rate for pancreatic cancer

Authors, publication date	n. of studies included, n. of participants Reference standard	Successful staging/documentation rate	Accuracy of EUS to diagnose T stage tumor	Accuracy of EUS to diagnose N stage tumor	Vascular invasion
Li 2014	20 studies, with 726 patients Reference standard: intraoperative staging or postoperative histopathology		Accuracy in discriminating T1 and T2 versus T3 and T4 (16 studies, 588 patients) Sensitivity: 0.72 (95% CI, 0.65–0.79) Specificity: 0.90 (95% CI, 0.87–0.93)	14 studies, 506 patients Sensitivity (95% CI) 0.62 (0.56–0.68) Specificity (95% CI) 0.74 (0.68–0.80)	8 studies, 294 patients Sensitivity (95% CI) 0.87 (0.80–0.92) Specificity (95% CI) 0.92 (0.86–0.96)
Nawaz 2013	29 studies, with 1330 patients Reference standard: surgery or clinical follow-up			16 studies, with 512 patients sensitivity 69% (95% CI: 51–82%) specificity 81% (95% CI: 70–89%)	25 studies with 886 patients sensitivity 85% (95% CI: 76–91%) specificity 91% (95% CI: 85–94%)
Li 2013	8 studies , number of aptients not reported Reference				Sensitivity: 0.66 (95% CI 0.56 -0.75 Specificity: 0.94 (95% CI 0.85 - 0.97)

standard : surgery				

Table 3. Successful Staging and Documentation Rate for rectal cancer

Authors, publication date	n. of studies included, n. of participants **Reference standard**	Successful staging/ documentation rate	Accuracy of EUS to diagnose T stage tumour	Accuracy of EUS to diagnose N stage tumour	Accuracy of EUS to diagnose M stage tumour
Li 2015	71 studies with 5152 patients Reference standard: histopathology or follow-up data			Sensitivity 0.63 (0.58, 0.68) Specificity: 0.80 (0.77, 0.83)	
Puli 2010	11 studies, 1791 participants Reference standard: surgery		accuracy of T0 staging Sensitivity: 97.3% (95% CI: 93.7–99.1 Specificity : 96.3% (95% CI: 95.3–97.2)		
Puli 2009a	42 studies, with 5039 participants		T1 Sensitivity 87.8% (95%CI 85.3–90.0%) Specificity 98.3% (95% CI 97.8–98.7%		

	Reference standard: surgery		T2 Sensitivity 80.5% (95% CI 77.9–82.9%) Specificity 95.6% (95% CI 94.9–96.3%), T3 Sensitivity 96.4% (95% CI 95.4–97.2%) Specificity 90.6% (95% CI 89.5–91.7%) T4 Sensitivity 95.4% (95% CI 92.4–97.5%) Specificity 98.3% (95% CI 97.8–98.7%).		
Puli 2009b	35 studies, 2732 participants Reference standard: surgery			Sensitivity 73.2% (95% CI: 70.6–75.6 Specificity: 75.8% (95% CI 73.5–78.0).	

Table 4. Successful Staging and Documentation Rate for oesophageal cancer

Authors, publication date	n. of studies included, n. of participants Reference standard	Successful staging/ documentation rate	Accuracy of EUS to diagnose T stage tumour	Accuracy of EUS to diagnose N stage tumour	Accuracy of EUS to diagnose M stage tumor
Kelly 2001	13 studies, n of patients not reported Reference standard: histopathology		sensitivity: range: 71% - 100% specificity : range: 66.7% - 100%		
Luo 2016	44 studies, 2880 patients Reference standard: histopathology		42 studies T1 Sensitivity: 77% (95%CI: 73 to 80) Specificity: 95% (95%CI: 94 to 96 T2 Sensitivity: 66% (95%CI: 61,70 Specificity 88% (95%CI: 86,89) T3 Sensitivity: 87% (95%CI: 95%CI: 85,89 Specificity 87% (95%CI: 84,89) T4:	34 studies Sensitivity: 81% (95%CI: 79,82) Specificity 76% (95%CI: 73,78	

			Sensitivity: 84% (95%CI: 79,89) Specificity 96% (95%CI: 95,97))		
Puli 2008a	49 studies with 2558 patients Reference standard: surgery or appropriate follow-up		43 studies T1 Sensitivity: 81.6% (95% CI: 77.8-84.9) Specificity 99.4% (95% CI: 99.0-99.7) T2 Sensitivity: 81.4% (95% CI: 77.5-84.8) Specificity 96.3% (95% CI: 95.4-97.1) T3 Sensitivity: 91.4% (95% CI: 89.5-93.0) Specificity 94.4% (95% CI: 93.1-95.5), T4: Sensitivity: 92.4% (95% CI: 89.2-95.0) Specificity 97.4% (95% CI: 96.6-98.0)	44 studies Sensitivity: 84.7% (95% CI: 82.9-86.4) Specificity: 84.6% (95% CI: 83.2-85.9)	
Puli 2008b	25 studies with 2029 patients Reference standard: surgery or				**Distant metastases** Sensitivity: 67.2% (95% CI: 62.6–71.6). Specificity 97.9% (95% CI: 97.1–98.6

	appropriate follow-up				**Celiac lymph nodes metastases** Sensitivity: 66.6% (95% CI: 61.9–71.1 Specificity 98.1% (95% CI: 97.3–98.7).
Thosani 2012	19 studies with 1019 patients Reference standard: final pathologic staging per histologic evaluation of EMR or surgically resected specimen.		**T1a** Sensitivity: 0.85 (95% CI, 0.82-0.88) Specificity 0.87 (95% CI, 0.84-0.90), **T1b** Sensitivity: 0.86 (95% CI, 0.82-0.89) Specificity 0.86 (95% CI, 0.83-0.89)		
Van Vliet 2008	31 studies			Regional lymph nodes (N stage) Sensitivity: 0.80 (95% CI 0.75–0.84 Specificity 0.70 (95% CI 0.65–0.75)	Celiac and abdominal lymph node Sensitivity: 0.85 (95% CI 0.72–0.99) Specificity 0.96 (95% CI 0.92–1.00)
Young 2010	8 studies with 132 patients Reference standard: surgical or EMR pathology		accuracy for early oesophageal adenocarcinoma and HGD 0.33 (95%CI 0.21-0.45)		

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PRISMA 2009 Flow Diagram

Identification

Records identified through
CDSR (n =3)
DARE (n=14)
CENTRAL(n =48)

Records identified through PubMed (n =57 SR, 1732 primary studies)

Records identified through Embase (n= 184 SR, 3832 primary studies)

Screening

Records after duplicates removed (n = 197 SRs, 4430 primary studies)

Records screened (n =197)

Records excluded (n = 163)

Eligibility

Studies awaiting classification (n = 0)

Full-text articles assessed for eligibility (n =34)

Full-text articles excluded, with reasons (n =12)

Included

Studies included (n =22)