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Imaging modalities for characterising focal pancreatic lesions (Review)

Best LMJ, Rawji V, Pereira SP, Davidson BR, Gurusamy KS

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Imaging modalities for characterising focal pancreatic lesions (Review)
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[Diagnostic Test Accuracy Review]

Imaging modalities for characterising focal pancreatic lesions

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ABSTRACT

Background

Increasing numbers of incidental pancreatic lesions are being detected each year. Accurate characterisation of pancreatic lesions into benign, precancerous, and cancer masses is crucial in deciding whether to use treatment or surveillance. Distinguishing benign lesions from precancerous and cancerous lesions can prevent patients from undergoing unnecessary major surgery. Despite the importance of accurately classifying pancreatic lesions, there is no clear algorithm for management of focal pancreatic lesions.

Objectives

To determine and compare the diagnostic accuracy of various imaging modalities in detecting cancerous and precancerous lesions in people with focal pancreatic lesions.

Search methods

We searched the CENTRAL, MEDLINE, Embase, and Science Citation Index until 19 July 2016. We searched the references of included studies to identify further studies. We did not restrict studies based on language or publication status, or whether data were collected prospectively or retrospectively.

Selection criteria

We planned to include studies reporting cross-sectional information on the index test (CT (computed tomography), MRI (magnetic resonance imaging), PET (positron emission tomography), EUS (endoscopic ultrasound), EUS elastography, and EUS-guided biopsy or FNA (fine-needle aspiration)) and reference standard (confirmation of the nature of the lesion was obtained by histopathological examination of the entire lesion by surgical excision, or histopathological examination for confirmation of precancer or cancer by biopsy and clinical follow-up of at least six months in people with negative index tests) in people with pancreatic lesions irrespective of language or publication status or whether the data were collected prospectively or retrospectively.

Data collection and analysis

Two review authors independently searched the references to identify relevant studies and extracted the data. We planned to use the bivariate analysis to calculate the summary sensitivity and specificity with their 95% confidence intervals and the hierarchical summary receiver operating characteristic (HSROC) to compare the tests and assess heterogeneity, but used simpler models (such as univariate random-effects model and univariate fixed-effect model) for combining studies when appropriate because of the sparse data. We were unable to compare the diagnostic performance of the tests using formal statistical methods because of sparse data.

Main results

We included 54 studies involving a total of 3,196 participants evaluating the diagnostic accuracy of various index tests. In these 54 studies, eight different target conditions were identified with different final diagnoses constituting benign, precancerous, and cancerous lesions. None of the studies was of high methodological quality. None of the comparisons in which single studies were included was of sufficiently high methodological quality to warrant highlighting of the results. For differentiation of cancerous lesions from benign or precancerous lesions, we identified only one study per index test. The second analysis, of studies differentiating cancerous versus benign lesions, provided three tests in which meta-analysis could be performed. The sensitivities and specificities for diagnosing cancer were: EUS-FNA: sensitivity 0.79 (95% confidence interval (CI) 0.07 to 1.00), specificity 1.00 (95% CI 0.91 to 1.00); EUS: sensitivity 0.95 (95% CI 0.84 to 0.99), specificity 0.53 (95% CI 0.31 to 0.74); PET: sensitivity 0.92 (95% CI 0.80 to 0.97), specificity 0.65 (95% CI 0.39 to 0.84). The third analysis, of studies differentiating precancerous or cancerous lesions from benign lesions, only provided one test (EUS-FNA) in which meta-analysis was performed. EUS-FNA had moderate sensitivity for diagnosing precancerous or cancerous lesions (sensitivity 0.73 (95% CI 0.01 to 1.00) and high specificity 0.94 (95% CI 0.15 to 1.00), the extremely wide confidence intervals reflecting the heterogeneity between the studies). The fourth analysis, of studies differentiating cancerous (invasive carcinoma) from precancerous (dysplasia) provided three tests in which meta-analysis was performed. The sensitivities and specificities for diagnosing invasive carcinoma were: CT: sensitivity 0.72 (95% CI 0.50 to 0.87), specificity 0.92 (95% CI 0.81 to 0.97); EUS: sensitivity 0.78 (95% CI 0.44 to 0.94), specificity 0.91 (95% CI 0.61 to 0.98); EUS-FNA: sensitivity 0.66 (95% CI 0.03 to 0.99), specificity 0.92 (95% CI 0.73 to 0.98). The fifth analysis, of studies differentiating cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) provided six tests in which meta-analysis was performed. The sensitivities and specificities for diagnosing cancer (high-grade dysplasia or invasive carcinoma) were: CT: sensitivity 0.87 (95% CI 0.00 to 1.00), specificity 0.96 (95% CI 0.00 to 1.00); EUS: sensitivity 0.86 (95% CI 0.74 to 0.92), specificity 0.91 (95% CI 0.83 to 0.96); EUS-FNA: sensitivity 0.47 (95% CI 0.24 to 0.70), specificity 0.91 (95% CI 0.32 to 1.00); EUS-FNA carcinoembryonic antigen 200 ng/mL: sensitivity 0.58 (95% CI 0.28 to 0.83), specificity 0.51 (95% CI 0.19 to 0.81); MRI: sensitivity 0.69 (95% CI 0.44 to 0.86), specificity 0.93 (95% CI 0.43 to 1.00); PET: sensitivity 0.90 (95% CI 0.79 to 0.96), specificity 0.94 (95% CI 0.81 to 0.99). The sixth analysis, of studies differentiating cancerous (invasive carcinoma) from precancerous (low-grade dysplasia) provided no tests in which meta-analysis was performed. The seventh analysis, of studies differentiating precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) from precancerous (low-grade dysplasia) provided two tests in which meta-analysis was performed. The sensitivity and specificity for diagnosing cancer were: CT: sensitivity 0.83 (95% CI 0.68 to 0.92), specificity 0.83 (95% CI 0.64 to 0.93) and MRI: sensitivity 0.80 (95% CI 0.58 to 0.92), specificity 0.81 (95% CI 0.53 to 0.95), respectively. The eighth analysis, of studies differentiating precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) from precancerous (low-grade dysplasia) or benign lesions provided no test in which meta-analysis was performed.

There were no major alterations in the subgroup analysis of cystic pancreatic focal lesions (42 studies; 2086 participants). None of the included studies evaluated EUS elastography or sequential testing.

Authors' conclusions

We were unable to arrive at any firm conclusions because of the differences in the way that study authors classified focal pancreatic lesions into cancerous, precancerous, and benign lesions; the inclusion of few studies with wide confidence intervals for each comparison; poor methodological quality in the studies; and heterogeneity in the estimates within comparisons.

PLAIN LANGUAGE SUMMARY

Accuracy of different imaging techniques for determining whether a pancreatic tumour is cancerous

Background

The pancreas is an organ in the abdomen that secretes pancreatic juice, which aids digestion and contains cells that produce important hormones such as insulin. Increasingly, abnormalities in the pancreas are noted in people undergoing routine scans, such as ultrasound or computed tomography (CT) scans, in the form of what are known as 'shadows', which may be described as focal pancreatic lesion, pancreatic mass, pancreatic tumour, pancreatic cyst, or pancreatic nodule. A significant proportion of focal pancreatic lesions are benign (non-cancerous) lesions requiring no treatment. Surgical removal of the tumour is the main method of treatment for precancerous (i.e. focal pancreatic lesions that are not full-blown cancer and do not have the ability to spread like cancer, but can turn into cancer) and cancerous focal pancreatic lesions. New methods are being developed for treating precancerous lesions, such as using heat to destroy the tumour. Surgical removal remains the only potentially curative treatment for people with limited pancreatic cancer. It is thus important to characterise whether a focal pancreatic lesion is non-cancerous, precancerous, or cancerous. A number of scans are available for characterising the nature of the focal pancreatic lesion, which include the following.

- Computed tomography (CT) scan: a series of X-rays taken from different angles, which are then reconstructed using a computer.
- Magnetic resonance imaging (MRI): the use of a powerful magnet to produce images of different tissues of the body.
- Positron emission tomography (PET): the use of a small amount of radioactive glucose (sugar) to differentiate between different tissues. It takes advantage of the tendency of cancer cells to use more glucose than normal cells.

- Endoscopic ultrasound (also known as endosonography or EUS): the use of an endoscope, a camera introduced into a body cavity to view the inside of the body. An ultrasound (high-energy sound waves) probe at the end of the endoscope is used to differentiate tissues.
- EUS elastography: this measures the stiffness of the lesion, which is used to identify whether the lesion is cancerous.
- EUS-guided biopsy: the removal of cells or tissues for examination under a microscope or to perform other tests on the cells or tissue.

At present it is unclear how effective different scans are in characterising focal pancreatic lesions.

Study characteristics

We performed a thorough literature search for studies reporting the accuracy of different scans until 19 July 2016. We identified 54 studies reporting information on 3196 people with focal pancreatic lesions. These studies evaluated one or more of the above tests and compared these test results with the eventual diagnosis provided by surgical removal of the lesion and examination under microscope. There were no diagnostic test accuracy studies of EUS elastography or studies that looked at multiple scans rather than single scans.

Key results

Variations in how studies defined precancerous and cancerous lesions meant that we were not able to combine the data to provide the overall results for many tests. We were unable to arrive at any firm conclusions for the following reasons.

- The way that study authors classified focal pancreatic lesions into cancerous, precancerous, and benign lesions was not consistent in different studies.
- The studies included few participants, leading to significant uncertainty in the results.
- The studies were of poor methodological quality, which introduced additional uncertainty in the results.
- Even among the studies that classified focal pancreatic lesions into cancerous, precancerous, and benign lesions in a similar manner, the results were not consistent.

Quality of evidence

All of the studies were of low methodological quality, which may result in arriving at false conclusions.

SUMMARY OF FINDINGS

Summary of findings 1. Imaging modalities for characterising focal pancreatic lesions

Name of test	Number of studies (number of participants)	Sensitivity (95% CI)	Specificity (95% CI)	Post-test probability of positive test* (95% CI)	Post-test probability of negative test* (95% CI)	Number of false positives per 100 positive index test results (95% CI)	Number of false negatives per 100 negative index test results (95% CI)	Risk of bias	Applicability concerns	Uncertainty (due to inconsistency or inability to assess inconsistency, and random errors because of overall small sample size)
Cancerous versus benign or precancerous (median pre-test probability: 63%)										
EUS-FNA (cytology)	1 (45)	0.79 (0.60 to 0.91)	1.00 (0.85 to 1.00)	98% (79% to 100%)	26% (14% to 43%)	2 (0 to 21)	26 (14 to 43)	Unclear	High	High
EUS-FNA (CEA > 500 ng/mL)	1 (24)	0.93 (0.70 to 0.99)	0.33 (0.12 to 0.65)	70% (59% to 79%)	25% (4% to 73%)	30 (21 to 41)	25 (4 to 73)	High	High	High
PET (criteria unspecified)	1 (76)	0.85 (0.73 to 0.92)	0.91 (0.72 to 0.97)	94% (81% to 98%)	21% (12% to 34%)	6 (2 to 19)	21 (12 to 34)	Unclear	High	High
Cancerous versus benign (median pre-test probability: 70%)										
EUS	2 (133)	0.95 (0.84 to 0.99)	0.53 (0.31 to 0.74)	82% (74% to 88%)	18% (6% to 45%)	18 (12 to 26)	18 (6 to 45)	Unclear or high	High	High
EUS-FNA (cytology)	3 (147)	0.79 (0.07 to 1.00)	1.00 (0.91 to 1.00)	99% (90% to 100%)	32% (2% to 92%)	0 (0 to 9)	32 (2 to 92)	High	High	High

PET (criteria unspecified)	3 (99)	0.92 (0.80 to 0.97)	0.65 (0.39 to 0.85)	86% (75% to 92%)	22% (9% to 44%)	14 (8 to 25)	22 (9 to 44)	High	High	High
PET (SU-Vmax > 3.5)	1 (80)	0.96 (0.87 to 0.99)	0.62 (0.43 to 0.78)	85% (78% to 90%)	12% (3% to 36%)	15 (10 to 22)	12 (3 to 36)	High	High	High
CT	2 (123)	0.98 (0.00 to 1.00)	0.76 (0.02 to 1.00)	90% (17% to 100%)	6% (0% to 100%)	10 (0 to 83)	6 (0 to 100)	Unclear or high	High	High
MRI	1 (29)	0.80 (0.58 to 0.92)	0.89 (0.57 to 0.98)	94% (72% to 99%)	34% (17% to 56%)	6 (1 to 28)	34 (17 to 56)	High	High	High
Precancerous or cancerous versus benign (median pre-test probability: 71%)										
EUS	1 (34)	0.92 (0.74 to 0.98)	0.60 (0.31 to 0.83)	85% (72% to 92%)	25% (7% to 58%)	15 (8 to 28)	25 (7 to 58)	High	High	High
EUS-FNA (cytology)	2 (52)	0.73 (0.01 to 1.00)	0.94 (0.15 to 1.00)	97% (25% to 100%)	41% (1% to 98%)	3 (0 to 75)	41 (1 to 98)	Unclear or high	High	High
EUS-FNA (CEA > 50 ng/mL)	1 (11)	0.29 (0.08 to 0.64)	0.25 (0.05 to 0.70)	48% (20% to 77%)	87% (54% to 98%)	52 (23 to 80)	87 (54 to 98)	High	High	High
PET (SU-Vmax 2.4)	1 (32)	0.94 (0.74 to 0.99)	0.93 (0.69 to 0.99)	97% (83% to 100%)	13% (2% to 49%)	3 (0 to 17)	13 (2 to 49)	High	High	High
CT	1 (48)	0.62 (0.45 to 0.76)	0.64 (0.39 to 0.84)	81% (66% to 90%)	59% (44% to 72%)	19 (10 to 34)	59 (44 to 72)	Unclear	High	High
MRI	1 (27)	0.93 (0.69 to 0.99)	0.85 (0.58 to 0.96)	94% (80% to 98%)	17% (3% to 58%)	6 (2 to 20)	17 (3 to 58)	High	High	High
Cancerous (invasive carcinoma) versus precancerous (dysplasia) (median pre-test probability: 27%)										
EUS	5 (156)	0.78 (0.45 to 0.94)	0.91 (0.61 to 0.98)	75% (37% to 94%)	8% (3% to 22%)	25 (6 to 63)	8 (3 to 22)	Unclear or high	High	High
EUS-FNA (cytology)	3 (158)	0.66 (0.03 to 0.99)	0.92 (0.73 to 0.98)	75% (29% to 95%)	12% (1% to 69%)	25 (5 to 71)	12 (1 to 69)	Unclear or high	High	High

EUS-FNA (CEA > 200 ng/mL)	1 (41)	1.00 (0.57 to 1.00)	0.64 (0.48 to 0.78)	51% (40% to 61%)	Not estimable	49 (39 to 60)	Not estimable	High	High	High
CT	6 (326)	0.72 (0.50 to 0.87)	0.92 (0.81 to 0.97)	78% (57% to 91%)	10% (5% to 18%)	22 (9 to 43)	10 (5 to 18)	Unclear or high	High	High
MRI	1 (32)	0.75 (0.30 to 0.95)	0.93 (0.77 to 0.98)	80% (48% to 94%)	9% (2% to 35%)	20 (6 to 52)	9 (2 to 35)	High	High	High
Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) (median pre-test probability: 45%)										
EUS	4 (196)	0.86 (0.74 to 0.92)	0.91 (0.83 to 0.96)	89% (80% to 94%)	11% (7% to 19%)	11 (6 to 20)	11 (7 to 19)	High	High	High
EUS-FNA (cytology)	3 (310)	0.47 (0.24 to 0.70)	0.91 (0.32 to 1.00)	81% (19% to 99%)	32% (22% to 45%)	19 (1 to 81)	32 (22 to 45)	Unclear or high	High	High
EUS-FNA (CEA > 200 ng/mL)	3 (160)	0.58 (0.28 to 0.83)	0.51 (0.19 to 0.81)	49% (28% to 70%)	40% (19% to 65%)	51 (30 to 72)	40 (19 to 65)	High	High	High
EUS-FNA (CA 19-9 > 1000 U/mL)	1 (41)	0.90 (0.60 to 0.98)	0.42 (0.26 to 0.59)	56% (47% to 65%)	16% (3% to 57%)	44 (35 to 53)	16 (3 to 57)	High	High	High
EUS-FNA (CEA > 692.8 ng/mL)	1 (20)	0.80 (0.49 to 0.94)	0.90 (0.60 to 0.98)	87% (50% to 98%)	15% (5% to 39%)	13 (2 to 50)	15 (5 to 39)	Unclear	High	High
PET (SU-Vmax > 2 to 2.5)	4 (124)	0.90 (0.79 to 0.96)	0.94 (0.81 to 0.99)	93% (78% to 98%)	8% (4% to 16%)	7 (2 to 22)	8 (4 to 16)	High	High	High
CT	3 (139)	0.87 (0.00 to 1.00)	0.96 (0.00 to 1.00)	95% (0% to 100%)	10% (0% to 100%)	5 (0 to 100)	10 (0 to 100)	Unclear or high	High	High
MRI	3 (189)	0.69 (0.44 to 0.86)	0.93 (0.43 to 1.00)	89% (35% to 99%)	21% (12% to 36%)	11 (1 to 65)	21 (12 to 36)	High	High	High
Cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia) (median pre-test probability: 21%)										

EUS	1 (51)	0.77 (0.50 to 0.92)	0.89 (0.76 to 0.96)	67% (43% to 84%)	7% (3% to 16%)	33 (16 to 57)	7 (3 to 16)	Unclear	High	High
CT	1 (46)	0.50 (0.22 to 0.78)	0.95 (0.83 to 0.99)	72% (36% to 92%)	13% (7% to 22%)	28 (8 to 64)	13 (7 to 22)	High	High	High
Precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia) (median pre-test probability: 59%)										
CT	3 (106)	0.83 (0.68 to 0.92)	0.83 (0.64 to 0.93)	89% (56% to 98%)	33% (18% to 52%)	11 (2 to 44)	33 (18 to 52)	High	High	High
MRI	2 (71)	0.80 (0.58 to 0.92)	0.81 (0.53 to 0.95)	86% (67% to 95%)	27% (13% to 47%)	14 (5 to 33)	27 (13 to 47)	High	High	High
Precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia) or benign (median pre-test probability: 43%)										
EUS	1 (70)	0.97 (0.83 to 0.99)	0.40 (0.26 to 0.55)	55% (48% to 61%)	6% (1% to 31%)	45 (39 to 52)	6 (1 to 31)	High	High	High

*Post-test probability was calculated at the median pre-test probability.

Abbreviations:

CA 19-9: carbohydrate antigen 19-9

CEA: carcinoembryonic antigen

CI: confidence interval

CT: computed tomography

EUS: endoscopic ultrasound

FNA: fine-needle aspiration

MRI: magnetic resonance imaging

PET: positron emission tomography

SUVmax: maximum standardised uptake values

BACKGROUND

(Please see the glossary in [Appendix 1](#) for terms that have not been described in the main text.)

A 'shadow' identified in the pancreas on imaging may be variously described as a focal pancreatic lesion, pancreatic mass, pancreatic tumour, pancreatic cyst, or pancreatic nodule. This phrasing refers to focal lesions, as opposed to diffuse changes of the pancreas, and includes solid and cystic lesions of the pancreas. In the Western world, the prevalence of focal pancreatic lesions is approximately 1.2% and is increasing steadily (by approximately 8%) each year, with smaller and asymptomatic lesions being identified more frequently ([Gaujoux 2011](#); [Spinelli 2004](#)). An incidental pancreatic lesion is one that is detected in the pancreas of a patient who undergoes radiological investigations for an unrelated medical condition ([Sachs 2009](#)). Such asymptomatic incidental lesions represent 55% to 60% of pancreatic tumours ([Gaujoux 2011](#); [Spinelli 2004](#)). Some focal pancreatic lesions may be associated with symptoms, depending upon their size and nature. The symptoms of pancreatic cancer, which generally refers to pancreatic adenocarcinoma, can include obstructive jaundice (yellowish discolouration of the skin and the whites of the eyes with dark urine and pale stool due to blockage of bile duct ([National Cancer Institute 2011a](#)), a tube that transports the bile from the liver), loss of appetite, and abdominal pain ([Holly 2004](#)). The symptoms of pancreatic neuroendocrine tumours (tumours arising from cells that secrete hormones), some of which may be cancer, are related to the excessive secretion of hormones (by the tumour) such as insulin, glucagon, gastrin, somatostatin, and vasoactive peptide resulting in hypoglycaemia (decreased blood sugar), hyperglycaemia (increased blood sugar, a rare cause of diabetes), and gastrointestinal disturbances such as peptic ulcer and diarrhoea ([Batcher 2011](#)). The symptoms of chronic pancreatitis (chronic inflammation of the pancreas that can result in alteration in the structure and function of the pancreas) are abdominal and back pain and those symptoms related to pancreatic insufficiency, which include steatorrhoea, malabsorption, vitamin deficiency, diabetes, or weight loss ([Braganza 2011](#); [Nair 2007](#)). About 40% of people with focal pancreatic lesions have chronic pancreatitis ([Spinelli 2004](#)). In the remaining 60% of people with focal pancreatic lesions, the remaining pancreas is normal.

Focal pancreatic lesions can be benign (serous pancreatic cystadenoma, acinar cell cystadenoma, papillary cysts, lymphoepithelial cysts, simple cysts), precancerous (intraductal papillary mucinous neoplasm (IPMN) with dysplasia but without invasive cancer, mucinous cystic neoplasm (MCN), benign neuroendocrine tumours), or cancer (ductal adenocarcinoma, acinar cell carcinoma, IPMN with invasive carcinoma, cystadenocarcinoma, pancreatoblastoma, solid pseudo-papillary neoplasm, cancer neuroendocrine tumours) ([Luttges 2011](#); [Sachs 2009](#); [Spinelli 2004](#); [WHO 2016](#)). Dysplasia can be low grade, intermediate grade, or high grade ([WHO 2016](#)). About 80% of benign lesions, 50% of precancerous lesions, and 20% of cancerous lesions are asymptomatic ([Spinelli 2004](#)). Focal pancreatic lesions can be solid or cystic or mixed solid and cystic tumours ([Cho 2011](#)).

Surgical resection is generally considered to be the only curative treatment for pancreatic cancer. Worldwide, only 15% to 20% of people with pancreatic cancer undergo potentially curative resection ([Conlon 1996](#); [Engelken 2003](#); [Katz 2009](#); [Michelassi](#)

[1989](#); [Shahrudin 1997](#); [Smith 2008](#)). In the remaining patients, the cancers are not resected because of infiltration of local structures or disseminated disease. Early diagnosis of pancreatic cancer might enable resection of the pancreatic cancer before it is too late to resect. Pancreatic resection is a major surgery, with an approximately 1% to 25% risk of perioperative death reported worldwide ([Conlon 1996](#); [Katz 2009](#); [Michelassi 1989](#); [Shahrudin 1997](#); [van Oost 2006](#)). High-volume centres show a lower perioperative mortality of less than 5% compared to low-volume centres, which are associated with a perioperative mortality of up to 25% ([Gurusamy 2013](#); [van Oost 2006](#)). Pancreatic resection is also associated with an about 40% morbidity rate ([Gurusamy 2013](#); [van der Gaag 2010](#)). Only 5% to 25% of patients survive for five years ([Conlon 1996](#); [Katz 2009](#); [Michelassi 1989](#); [Shahrudin 1997](#)). Surgery is generally offered if there are features suggestive of precancerous or cancerous lesions ([Lee 2005c](#)), although some clinicians prefer sequential follow-up (by imaging) of precancerous lesions to surgical resection ([Irie 2004](#)). Surgery is offered when there is an increase in the size or morphology (the way the lesion appears) of the lesion in sequential imaging ([Gaujoux 2011](#)). Surgery is also offered when there is considerable uncertainty as to the nature of the lesion. In some ways, surgery can be considered as a diagnostic test for characterisation of the lesion and as a treatment for people with cancerous and precancerous lesions. Histological confirmation of the lesion by percutaneous biopsy is generally not performed because of difficulty in accessing the lesion percutaneously and because of dissemination of cancer cells.

Target condition being diagnosed

1. Cancerous versus benign or precancerous lesions.
2. Precancerous or cancerous (including the type of cancerous lesion) versus benign lesions.

Index test(s)

Computed tomography (CT) scan

This involves a series of X-rays taken from different angles, which are then reconstructed using a computer ([National Cancer Institute 2011a](#)). Morphological features of the lesion, such as density, regularity of margins, vascularity, and the diameter of the pancreatic duct, are taken into account to characterise the lesion. The main side effect of CT scan is the ionising radiation (radioactivity) associated with it. Everyone is exposed to very small amounts of radiation (background radiation). One CT scan of the abdomen is equivalent to approximately three years of background radiation ([Fred 2004](#)). In addition, the contrast material (dye used to view the structures better) can cause allergic reactions, such as difficulty breathing, or kidney damage, particularly in people with pre-existing kidney disease ([Namasivayam 2006](#)).

Magnetic resonance imaging (MRI)

This involves the use of a powerful magnet to produce images of different tissues of the body. Magnetic resonance imaging is also known as nuclear magnetic resonance imaging (NMRI) ([National Cancer Institute 2011b](#)). Similar features as those employed in CT scan are used to characterise the lesion. While MRI does not use radiation, it is contraindicated in people with metallic implants such as artificial joints, those with cardiac pacemakers (devices used to control heart rhythm), and those with claustrophobia (fear of closed spaces) ([Dill 2008](#)). Some of the contrasts used can also cause kidney damage ([Dill 2008](#)).

Positron emission tomography (PET)

This involves the use of a small amount of radioactive glucose (sugar) to differentiate between different tissues. It takes advantage of the tendency of cancer cells to use more glucose than normal cells. Positron emission tomography is also known as PET scan ([National Cancer Institute 2011c](#)). Cancerous lesions appear as areas of increased uptake. Positron emission tomography also uses ionising radiation ([Leide-Svegborn 2010](#)). The radiation exposure to one PET scan is similar to that in one CT scan of abdomen ([Fred 2004](#); [Leide-Svegborn 2010](#)).

Endoscopic ultrasound (EUS)

This involves the use of an endoscope, a camera introduced into a body cavity to view the inside of the body. An ultrasound (high-energy sound waves) probe at the end of the endoscope is used to differentiate tissues. Endoscopic ultrasound is also known as endosonography ([National Cancer Institute 2011d](#)). Features such as echogenicity and regularity of margins are taken into account and used to characterise the lesion. Complications following EUS are rare and include perforation ([Benson 2010](#); [Niv 2011](#)).

EUS elastography

This measures the stiffness of the lesion, which can be used to identify whether the lesion is benign or cancerous ([Iglesias-Garcia 2010](#)). The complications associated with EUS elastography are the same as with EUS.

EUS-guided biopsy

This is the removal of cells or tissues for examination by a pathologist. The pathologist may study the tissue under a microscope or perform other tests on the cells or tissue. There are many different types of biopsy procedures. The most common types include:

1. incisional biopsy, in which only a sample of tissue is removed;
2. excisional biopsy, in which an entire lump or suspicious area is removed; and
3. needle biopsy, in which a sample of tissue or fluid is removed with a needle. When a wide needle is used the procedure is called a core biopsy. When a thin needle is used the procedure is called a fine-needle aspiration biopsy (FNAB) ([National Cancer Institute 2011e](#)).

Because of the risk of dissemination from cancer, EUS-guided biopsy is preferable to percutaneous (image-guided) biopsy

([Micames 2003](#)). The examinations under the microscope used may include the routine haematoxylin and eosin stain for core biopsy and special staining for FNAB ([Mehta 2010](#)). Immunocytochemistry and proteomic profiling to identify the presence of biomarkers in the tissue may also be used in the diagnosis ([Cui 2009](#); [Mehta 2010](#)). A positive core biopsy can confirm cancer, but a negative core biopsy cannot rule out cancer. Cytology results are not quite as reliable as core biopsy as false-positive cytology has been reported ([Hancke 1984](#)).

Complications associated with EUS-guided biopsy include those associated with EUS as well as bleeding ([Benson 2010](#); [Niv 2011](#)).

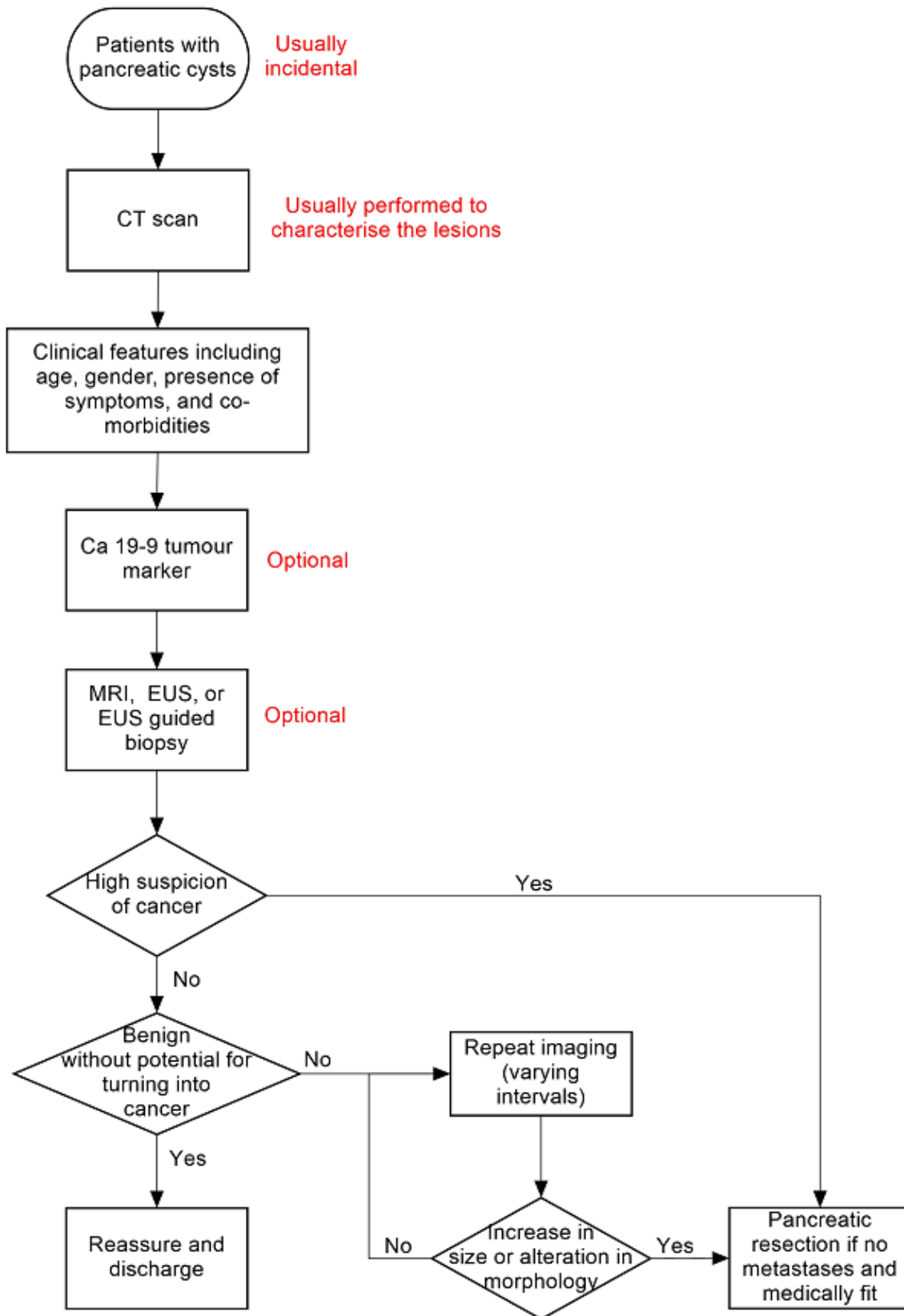
Of these index tests, the commonly available tests are CT scan and MRI. The remaining tests (PET, EUS, EUS elastography, and EUS-guided biopsy) are available in major tertiary centres only.

Clinical pathway

There is no standard algorithm in the diagnosis or management of focal pancreatic lesions. The algorithm may vary from one centre to another and even within the same centre ([Gaujoux 2011](#); [Goh 2006b](#)). One possible diagnostic clinical pathway is shown in [Figure 1](#). As noted in [Figure 1](#), an increase in the size of or change of morphological features is one of the reasons that surgeons recommend surgical excision, as this may indicate that the lesion was malignant in the first instance (without features suggestive of malignancy in the original scan) or has transformed into a malignant lesion. The interval for sequential scans is variable. Our local protocol advises sequential scanning in one year in the absence of malignant features. It is important to distinguish whether the focal pancreatic lesion is benign with no cancer potential so that unnecessary surgery and anxiety can be avoided. It is also important to know whether the lesion is precancerous or cancerous so that an informed decision about surgery can be made after weighing the potential benefits and harms. In addition, new alternative treatments such as radiofrequency ablation (destruction of tissue using radiofrequency waves) are being evaluated for precancerous lesions ([Pereira 2015](#)). It is also necessary to differentiate the different types of cancer, since different malignancies carry different prognoses ([Klempnauer 1995](#)). Some surgeons follow the single-test strategy, that is making decisions based on the features of the lesion in a single test, while others follow repeated testing (repeating the imaging modality or using a different imaging modality), particularly if the nature of the lesion is indeterminate. The optimal interval between the tests in the repeated-testing strategy is unknown.

**Figure 1. Clinical pathway. Abbreviations: Ca 19-9: carbohydrate antigen 19-9
CT: computed tomography
EUS: endoscopic ultrasound
MRI: magnetic resonance imaging**

PET: positron emission tomography



Prior test(s)

The tests that occur prior to pancreatic imaging depend on how the patient presents. The investigation may be targeted if the patient presents with abdominal symptoms, however it is equally possible that the pancreatic lesion is an incidental finding on an abdominal scan for an alternative reason. As pancreatic cancer is relatively late presenting (Porta 2005), the number of incidental lesions found will be high comparative to other cancers where symptoms will primarily drive discovery. Whilst CT, MRI, and PET may identify incidental lesions, EUS and EUS-guided fine-needle aspiration (EUS-FNA) are the likely second test for known lesions of symptomatic individuals.

Role of index test(s)

All of the index tests described are used primarily to characterise pancreatic lesions as either benign or cancerous, or more importantly as needing significant or more conservative treatment. The location of the pancreas makes percutaneous biopsy dangerous because of the risk of cancer spread, therefore determination of cancer stage and consequently required treatment must be made non-invasively by the imaging techniques and by EUS-FNA.

Alternative test(s)

Computed tomography is usually part of a standard algorithm for assessing focal pancreatic lesions (Gaujoux 2011). If the incidental lesion is detected on CT scan, then CT scan can be the only investigation, since the added value of the other tests is not known. One or more of the above tests may be used in addition to, or instead of, CT scan. Diagnostic laparoscopy and laparoscopic ultrasound are other tests that may be used in the differential diagnosis of focal pancreatic lesions; however, these tests are not used routinely. Serum carbohydrate antigen 19-9 (CA 19-9) is a substance released into the bloodstream by both cancer cells and normal cells and is used as a type of tumour marker (National Cancer Institute 2011f). Excessive CA 19-9 in the blood can be a sign of pancreatic cancer or other types of cancer or conditions. The amount of CA 19-9 in the blood can be used to measure how effective cancer treatments are or if cancer has returned. It can be used in conjunction with other imaging modalities in the assessment of the focal pancreatic lesion.

Rationale

The various imaging modalities use different methods to differentiate normal and diseased tissues. Endoscopic ultrasound is closer to the tissues and therefore high-frequency ultrasound waves can be used, which have better resolution but poorer penetration than an external ultrasound. Image-guided biopsy can be performed and the tissue can be examined under the microscope to differentiate between types of focal pancreatic lesion.

Accurate characterisation of lesions will help in patient management. Patients with cancerous lesions will be offered surgery if there is no distant spread of cancer and assuming they are fit for major surgery. Patients with cancerous lesions who are not eligible for surgery because of distant spread of cancer or lack of fitness for major surgery will be offered other treatments such as chemotherapy. Patients with precancerous lesions may also undergo surgery or ablation depending upon the clinician and

patient preferences. Unnecessary major surgery can be avoided in patients with benign lesions.

There is currently no Cochrane review of studies assessing the diagnostic accuracy of different imaging modalities in the assessment of focal pancreatic lesions.

OBJECTIVES

To determine and compare the diagnostic accuracy of various imaging modalities in detecting cancerous and precancerous lesions in people with focal pancreatic lesions.

Secondary objectives

We planned to explore the following sources of heterogeneity.

1. Studies at low risk of bias versus those at unclear or high risk of bias (as assessed by the revised Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool as recommended by the [Cochrane Screening and Diagnostic Tests Methods Group](#)) (Whiting 2006). In particular, we considered the studies classified as 'yes' for the items differential verification, uninterpretable results, and withdrawals as the most important sources of heterogeneity.
2. Full-text publications versus abstracts (this might be indicative of publication bias, since there may be an association between the results of the study and the study reaching full publication) (Eloubeidi 2001).
3. Prospective studies versus retrospective studies.
4. Different types of reference standard.
5. Symptomatic versus asymptomatic lesions (the presence of symptoms may increase the pre-test probability).
6. Solid versus cystic lesions (as the diagnostic accuracy of the imaging modalities may vary depending upon whether the lesion is solid or cystic).
7. Participants with chronic pancreatitis versus those without chronic pancreatitis.
8. Different criteria used by the authors to classify the lesions.
9. Single imaging versus sequential imaging (repeated imaging).
10. Different intervals of sequential imaging (e.g. imaging every six months versus annual review).

METHODS

Criteria for considering studies for this review

Types of studies

We included studies reporting on cross-sectional information of the index test and reference test in the appropriate patient population (see below), irrespective of language or publication status or whether the data were collected prospectively or retrospectively. However, we excluded case series in which only true-positive results or true-negative results were reported without any information on the other participants who underwent the test.

Participants

Adults with focal pancreatic lesions.

Index tests

CT scan, MRI scan, PET scan, EUS, EUS elastography, and EUS-guided biopsy either alone or in combination as replacement for major surgery for diagnostic purposes.

We accepted the criteria stated by the authors to classify the lesion as benign, precancerous, and cancerous for different imaging modalities.

There is no standard algorithm in the diagnosis or management of focal pancreatic lesions. Other tests that may be used in the diagnosis of focal pancreatic lesions include diagnostic laparoscopy, laparoscopic ultrasound, serum levels of CA 19-9, and surgical resection (surgical resection may be considered diagnostic when the diagnosis is uncertain after all other diagnostic modalities have been attempted).

Target conditions

1. Benign versus precancerous and cancerous lesions (including the type of cancerous lesion).
2. Benign and precancerous versus cancerous lesions.

Reference standards

We accepted the following reference standards.

- Histopathological examination of the entire lesion by surgical resection (gold standard). This classified the lesion as benign, precancerous, or cancerous.
- Histopathological examination (irrespective of how the tissues were obtained for histopathological examination) in people with positive test (for cancerous or precancerous lesions) and clinical follow-up by a doctor (with or without sequential follow-up with imaging but using appropriate criteria such as metastases or confirmation of cancer by biopsy or death of participants due to cancer) of all participants with negative test for a period of at least six months and for a maximum period of 24 months. Until a definitive diagnosis is available, percutaneous biopsy is generally avoided because of the fear of seeding of cancer cells in potentially resectable cancers. As anticipated, the tissues obtained for histopathological examination were obtained from surgical resection. It is unlikely that patients with a low likelihood for cancer based on clinical symptoms and signs and test results (may include the results of index test) are subject to surgery or biopsy. Even if a biopsy is performed in such patients, a cancerous or precancerous lesion cannot be ruled out because of sampling error. Consequently, such patients are usually followed up clinically with sequential imaging. Pancreatic adenocarcinoma will cause clinical deterioration or increase in tumour size during a period of six months, and so we accepted clinical follow-up or sequential follow-up imaging (irrespective of the modality of the imaging) of all participants with a negative biopsy or no biopsy for at least six months as one of the reference standards. However, we accepted clinical follow-up as a reference standard only when the criteria used for diagnosis were appropriate (e.g. identification of metastases, later biopsy of the lesion confirming the nature of the lesion, and death of participants due to cancer). The choice of a maximum period of 24 months was an arbitrary choice based on the low probability of precancerous lesions becoming cancerous during 24 months. Clinical follow-up of patients is unlikely to classify

precancerous lesions correctly since patients are unlikely to develop metastases or die within this interval.

Search methods for identification of studies

Electronic searches

We searched the following databases.

1. Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library (Issue 7, 2016) ([Appendix 2](#)).
2. MEDLINE via PubMed (January 1946 to 19 July 2016) ([Appendix 3](#)).
3. Embase via OvidSP (January 1947 to 19 July 2016) ([Appendix 4](#)).
4. Science Citation Index Expanded via ISI Web of Knowledge (January 1980 to 19 July 2016) ([Appendix 5](#)).

Searching other resources

We searched the references of included studies to identify further studies ([Horsley 2011](#)). We also searched for additional articles related to the included studies by performing the 'related search' function in MEDLINE (PubMed) and Embase (OvidSP) and 'citing reference' search (search the articles that cited the included articles) in Science Citation Index Expanded and Embase (OvidSP) ([Sampson 2008](#)).

Data collection and analysis

Selection of studies

Two review authors independently searched the references to identify relevant studies. We obtained the full text of references that at least one of the review authors consider relevant and used these full texts to further exclude irrelevant references. We selected references to studies that met the inclusion criteria for data extraction. Any differences in study selection were arbitrated by review author BR Davidson.

Data extraction and management

Two review authors independently extracted the following data from each included study.

- First author of report.
- Year of publication of report.
- Study design (prospective or retrospective; cross-sectional studies or randomised clinical trials).
- Inclusion and exclusion criteria for individual studies.
- Total number of participants.
- Number of females.
- Mean age of the participants.
- Criteria used for classification of lesions.
- Preoperative tests carried out prior to index test.
- Index test.
- Reference standard.
- True positive (TP), false positive (FP), true negative (TN), and false negative (FN) data.

Main analysis

The unit of analysis was the participant. We extracted the TP, FP, TN, and FN information for each index test for the following situations (when data were available).

1. Precancerous or cancerous lesions (positive test) versus benign lesions with no cancer potential (negative test) (this helps determine whether the patient needs further follow-up).
2. Cancerous lesions (positive test) versus non-cancerous lesions (negative test) (this helps determine whether the patient needs immediate surgery).
3. In the group of participants with precancerous or cancerous lesions (i.e. those with positive test in the analysis of benign lesions with no cancer potential (negative test) versus precancerous or cancerous lesions (positive test)), we extracted the TP, FP, TN, and FN information for cancerous lesions (positive test) versus precancerous lesions (negative test) (this helps in assessing whether or not surgery is appropriate; surgery is the only curative option for cancerous lesions, while follow-up may be an option for precancerous lesions).

We extracted the information on indeterminate results separately from the TP, FP, TN, and FN data. There is no standard algorithm of management of patients with indeterminate results in the first scan. Some surgeons may recommend surgical resection for indeterminate lesions, while others may advise additional scans or sequential follow-up imaging. We therefore planned to perform a sensitivity analysis as described in [Sensitivity analyses](#).

For tests performed for sequential follow-up imaging (repeated-testing strategy), we planned to extract the TP, FP, TN, and FN data for the strategy as a whole. We considered increase in size or change in the lesion on sequential follow-up imaging (performed within 12 months) a positive index test. If the lesion remained static (or decreased in size) without any change in the characteristics of the lesion, we considered this a negative index test. The majority of surgeons will recommend further follow-up imaging or no follow-up if the sequential follow-up image shows no change in the lesion, and there is no clinical deterioration for the comparison between precancerous and cancerous lesions. We therefore considered indeterminate results on sequential follow-up imaging as negative results for this comparison.

We sought further information from study authors where necessary. Any differences between the review authors were resolved by discussion.

Assessment of methodological quality

Two review authors independently assessed the quality of the studies using the QUADAS-2 assessment tool ([Whiting 2006](#); [Whiting 2011](#)). We resolved any differences in assessment using the QUADAS-2 assessment algorithm published in the protocol. We sought further information from the authors of the studies in order to accurately assess the methodological quality of the studies.

We assessed the quality items derived from the QUADAS-2 tool using the methodology stated in [Table 1](#).

Statistical analysis and data synthesis

We have plotted study estimates of sensitivity and specificity on forest plots and in receiver operating characteristic (ROC) space to explore between-study variation in the performance of each test. To estimate the summary sensitivity and specificity of each test, we planned to perform the meta-analysis by fitting the bivariate model ([Chu 2006](#); [Reitsma 2005](#)), which accounts for between-study variability in estimates of sensitivity and specificity through the inclusion of random effects for the logit sensitivity

and logit specificity parameters of the bivariate model. As there was lack of convergence due to sparse data, we tried other alternate models suggested by [Takwoingi 2015](#) and colleagues. These included the random-effects model, ignoring the inverse correlation between sensitivities and specificities in the different studies due to intrinsic threshold effect, and the fixed-effect model for either sensitivity or specificity or both after visualising the forest plots and summary receiver operating characteristics (SROC) plots ([Takwoingi 2015](#)). We based our choice between the different models on the distribution of sensitivities and specificities as noted in the forest plots or ROC space. We also used the model fit as indicated by the -2 log likelihood and considered the model with the lower -2 log likelihood to be the better model.

We planned to compare the diagnostic accuracy of the tests by including covariate terms for test type (CT scan, MRI, PET, EUS, EUS-FNA, EUS elastography) in the bivariate model to estimate differences in the sensitivity and specificity of the tests. We planned to allow both the sensitivity and specificity to vary by covariate. In addition, we planned to permit the variances of the random effects and their covariance to also depend on test type, thus allowing the variances to differ between tests. We planned to use likelihood ratio tests to compare the model with and without covariate (test type). We planned to use a P value of less than 0.05 for the likelihood ratio test to indicate differences in the diagnostic accuracy between the tests. If studies that reported different tests in the same study population were available from at least four studies, we planned to perform a direct head-to-head comparison by limiting the test comparison to such studies. We planned to calculate the relative sensitivities and specificities for each pair-wise comparison of tests.

We performed the meta-analysis using the NLMIXED command in SAS version 9.4 (SAS Institute Inc, Cary, North Carolina, USA) ([Takwoingi 2012](#)). The post-test probabilities were calculated using these pre-test probabilities and the summary positive and negative likelihood ratios. We calculated the summary likelihood ratios and their confidence intervals from the functions of the parameter estimates from the model that we fitted to estimate the summary sensitivities and specificities. Post-test probability associated with a positive test is the probability of having the target condition (e.g. precancer or cancer) on the basis of a positive test result (e.g. positive CT) and is the same as the term 'positive predictive value' used in a single diagnostic accuracy study. Post-test probability associated with a negative test is the probability of having the target condition (e.g. precancer or cancer) on the basis of a negative test result (e.g. negative CT) and is $1 -$ 'negative predictive value'. 'Negative predictive value' is the term used in a single diagnostic accuracy study to indicate the chance that the participant has no target condition when the test is negative. We have reported the summary sensitivity, specificity, and post-test probabilities for the median pre-test probabilities whenever possible.

Investigations of heterogeneity

We visually inspected forest plots of sensitivity and specificity and the ROC curve to identify heterogeneity. We planned to explore heterogeneity by using the different sources of heterogeneity as covariates in the METADAS macro ([Takwoingi 2012](#)), but due to the sparseness of the data we were unable to do this. We planned to assess whether there was a statistically significant difference in the likelihood ratios in order to identify heterogeneity. Although we did not formally compare the diagnostic test accuracy of different index tests between solid and cystic lesions, we have presented a

subgroup analysis of solid and cystic lesions, since some clinicians consider the diagnostic test accuracies to differ between the two.

Sensitivity analyses

In the presence of indeterminate results (for any reason) for the initial test, we planned to consider two scenarios: the participants with indeterminate results as positive for the test, as some surgeons will recommend surgical resection for indeterminate lesions; and the indeterminate results as negative for the test, as some surgeons will recommend sequential follow-up imaging. We planned to assess the diagnostic accuracy in both of these scenarios. However, due to sparse data and few studies reporting indeterminate results we did not perform the above.

We also planned to assess the comparative performance of tests by direct comparison (i.e. the tests performed in the same participant) versus indirect comparison (the tests performed in different participants across studies).

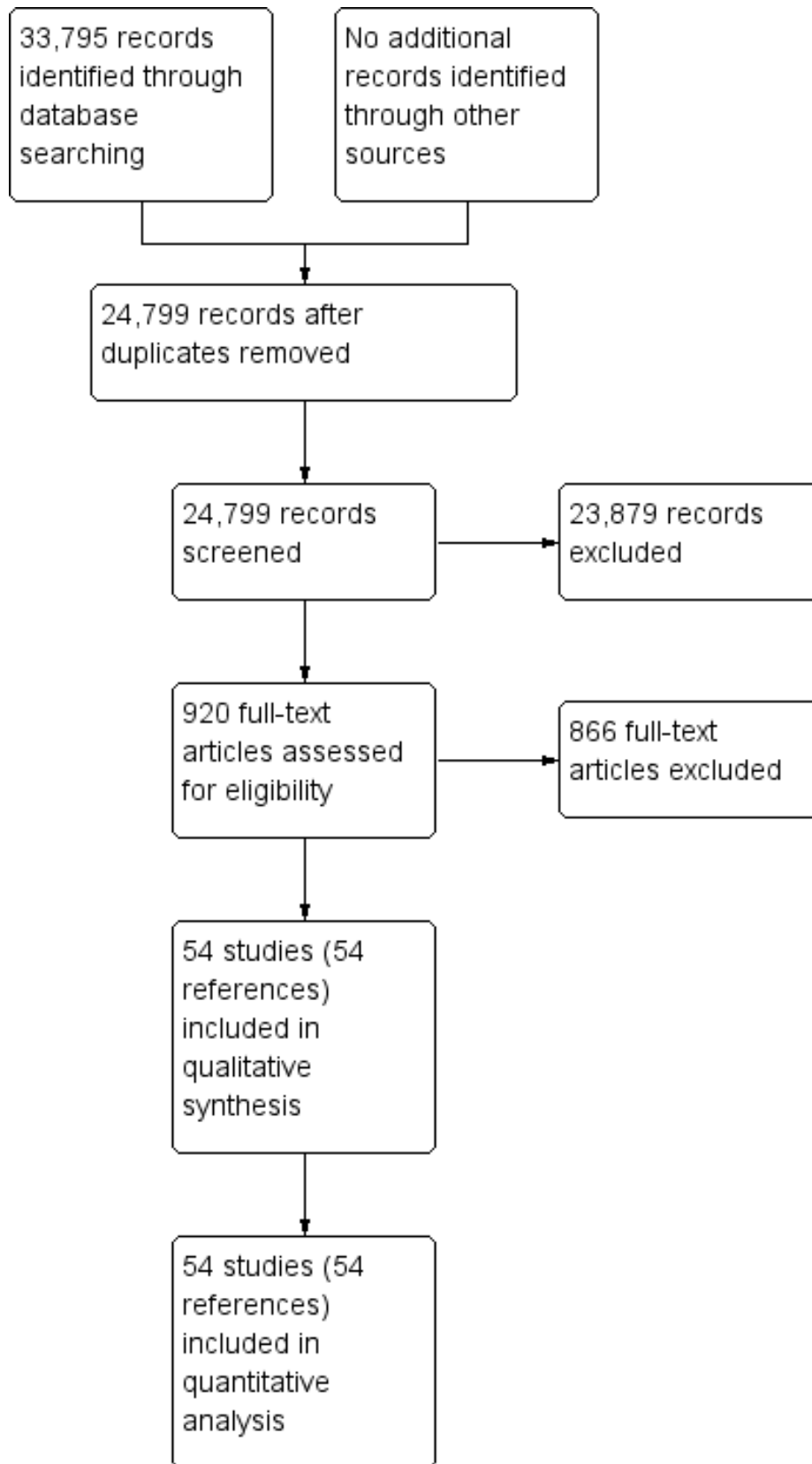
RESULTS

Results of the search

We identified 33,795 references through electronic searches of the Cochrane Central Register of Controlled Trials (CENTRAL),

MEDLINE, Embase, and Science Citation Index. We were left with 24,799 references after removing duplicate references. We excluded 23,879 clearly irrelevant references through reading the abstracts. We sought the full text for 920 references for further assessment. We did not identify any additional references to studies through other searches. We excluded 866 references for the reasons described in the [Characteristics of excluded studies](#) tables. Fifty-two studies (54 references) met the inclusion criteria. Two studies reported the diagnostic test data on solid and cystic lesions separately ([Brandwein 2001 - Cystic](#); [Brandwein 2001 - Solid](#); [Fischer 2009 - Cystic](#); [Fischer 2009 - Solid](#)) therefore, we considered them as separate studies. We thus included a total of 54 studies in the review ([Brand 2000](#); [Brandwein 2001 - Cystic](#); [Brandwein 2001 - Solid](#); [Cellier 1998](#); [Choi 2003](#); [Correa-Gallego 2009](#); [de Jong 2012](#); [Doi 2002](#); [Erkan 2012](#); [Fischer 2009 - Cystic](#); [Fischer 2009 - Solid](#); [Fisher 2008](#); [Grieser 2010](#); [Harrison 1999](#); [Higashi 1997](#); [Hong 2010](#); [Hu 2013](#); [Jafarimehr 2010](#); [Jang 2014a](#); [Jang 2014b](#); [Jin 2013a](#); [Jin 2015](#); [Kalha 2003](#); [Kamata 2016a](#); [Kato 1995](#); [Kim 2015](#); [Klau 2011](#); [Kobayashi 2012](#); [Kubo 2001](#); [Kucera 2012](#); [Le Baleur 2011a](#); [Lee 2014](#); [Maire 2008](#); [McHenry 2002](#); [Nakagawa 2009](#); [Nara 2009](#); [Ogawa 2008](#); [Ogawa 2014](#); [Otomi 2014](#); [Pais 2007](#); [Sahani 2006](#); [Saito 2013](#); [Salla 2007](#); [Sedlack 2002](#); [Smith 2016](#); [Takanami 2011](#); [Takeshita 2008](#); [Tan 2009](#); [Taouli 2000](#); [Tomimaru 2010](#); [Yamao 2001](#); [Zhan 2011](#); [Zhan 2013](#)). The reference flow diagram is shown in [Figure 2](#).

Figure 2. Study flow diagram.



Characteristics of included studies

For a summary of the characteristics of included studies see the [Characteristics of included studies](#) table.

We included a total of 54 studies involving 31,196 participants in this systematic review. The studies reported investigation of eight different target conditions:

- cancerous versus benign or precancerous lesions;
- cancerous versus benign lesions;
- precancerous or cancerous lesions versus benign lesions;
- cancerous (invasive carcinoma) versus precancerous (dysplasia) lesions;
- cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) lesions;
- cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia) lesions;
- precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia) lesions; and
- precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia) or benign lesions.

The variation in target condition was due to different definitions of what constitutes a benign, precancerous, and cancerous lesion. For example, the World Health Organization pancreatic tumour classification system classifies intraductal papillary mucinous neoplasms' (IPMNs) as precancerous tumours regardless of dysplasia (Luttges 2011). However, many of the included studies considered IPMNs to be benign lesions or even classified them as benign or cancerous based on the grade of dysplasia. This meant that the index tests were actually used for differentiating between very different populations of cancerous and benign tumours, and therefore the combination of all studies as simply cancer versus benign would have been inappropriate. In addition, different surgeons will have different thresholds for recommending surgery. Consequently, we have presented the results for all of the various definitions used by authors to classify a lesion as benign, precancerous, or cancerous.

Three studies reported data on tests differentiating cancerous from benign or precancerous lesions. Of these three studies, one reported the performance of EUS-FNA using cytology (McHenry 2002); another reported the performance of EUS-FNA using a carcinoembryonic antigen (CEA) threshold of 500 ng/mL (Kalha 2003); and the third reported the performance of PET to differentiate between benign or precancerous and cancerous lesions (Jafarimehr 2010). The median pre-test probability of a cancerous lesion in these studies was 0.625 or 62.5% (minimum 0.533, maximum 0.711).

Twelve studies reported data on tests differentiating cancerous from benign lesions. Of these 12 studies, two reported the performance of EUS (Brand 2000; Harrison 1999); three reported the performance of EUS-FNA (Brandwein 2001 - Cystic; Brandwein 2001 - Solid; Cherian 2010); three reported the performance of PET (Erkan 2012; Higashi 1997; Kato 1995); one reported the performance of PET with a standard uptake value (SUV) maximum of greater than 3.5 as its threshold for positivity (Hu 2013); two reported the performance of CT (Grieser 2010; Harrison 1999); and

one reported the performance of MRI to differentiate between cancerous and benign lesions (Klau 2011). The median pre-test probability of a cancerous lesion in these studies was 0.697 or 69.7% (minimum 0.231, maximum 0.889).

Six studies reported data on tests differentiating precancerous or cancerous from benign lesions, with one study providing data for multiple imaging modalities (Sedlack 2002). One study reported the performance of EUS (Sedlack 2002); three studies reported the performance of EUS-FNA (Fischer 2009 - Cystic; Fischer 2009 - Solid; Sedlack 2002); one study reported the performance of EUS-FNA using a CEA threshold of 50 ng/mL (Sedlack 2002); one study reported the performance of PET with an SUV maximum threshold of greater than 2.4 as its threshold for positivity (Otomi 2014); one study reported the performance of CT (Fisher 2008); and one study reported the performance of MRI (Jang 2014a). The median pre-test probability of a precancerous or cancerous lesion in these studies was 0.706 or 70.6% (minimum 0.519, maximum 0.75).

Twelve studies reported data on tests differentiating cancerous invasive carcinomas from precancerous dysplastic lesions, with some studies reporting the diagnostic test accuracy or more than one index test. Five studies reported the performance of EUS (Cellier 1998; de Jong 2012; Nakagawa 2009; Yamao 2001; Zhan 2011); three studies reported the performance of EUS-FNA (Jin 2015; Pais 2007; Salla 2007); and one study reported the performance of EUS-FNA using a CEA threshold of 200 ng/mL (Maire 2008). Six studies reported the performance of CT (Cellier 1998; Nakagawa 2009; Nara 2009; Ogawa 2008; Taouli 2000; Yamao 2001), and one study reported the performance of MRI (de Jong 2012). The median pre-test probability of a cancerous invasive carcinoma was 0.270 or 27% (minimum 0.122, maximum 0.618).

Eighteen studies reported data on tests differentiating cancerous lesions defined by high-grade dysplasia or invasive carcinoma from precancerous lesions with a low or intermediate grade of dysplasia, with some studies reporting the diagnostic test accuracy or more than one index test. Four studies reported the performance of EUS (Doi 2002; Kobayashi 2012; Lee 2014; Yamao 2001). Three studies reported the performance of EUS-FNA (Jin 2013a; Smith 2016; Zhan 2013). Three studies reported the performance of EUS-FNA using a CEA threshold of 200 ng/mL (Correa-Gallego 2009; Kucera 2012; Maire 2008). One study reported the performance of EUS-FNA using a carbohydrate antigen 19-9 threshold of greater than 1000 U/mL (Maire 2008). One study reported the performance of EUS-FNA using a CEA threshold of 692.8 ng/mL (Zhan 2013). Four studies reported the performance of PET with an SUVmax value between 2 and 2.5 as their threshold for positivity (Hong 2010; Saito 2013; Takanami 2011; Tomimaru 2010). Three studies reported the performance of CT (Hong 2010; Le Baleur 2011a; Yamao 2001). Three studies reported the performance of MRI (Jang 2014b; Kim 2015; Ogawa 2014). The median pre-test probability of a cancerous lesion defined by high-grade dysplasia or invasive carcinoma in these studies was 0.449 or 44.9% (minimum 0.167, maximum 0.875).

Two studies reported data on tests differentiating cancerous invasive carcinomas from precancerous lesions with a low grade of dysplasia. One study reported the performance of EUS (Kubo 2001), and one study reported the performance of CT (Takeshita 2008). The median pre-test probability of cancerous invasive carcinoma in these studies was 0.214 or 21.4% (minimum 0.174, maximum 0.255).

Imaging modalities for characterising focal pancreatic lesions (Review)

Five studies reported data on tests differentiating precancerous or cancerous lesions that may be moderately or highly dysplastic or invasive carcinomas from precancerous lesions with a low grade of dysplasia. Three studies reported the performance of CT (Ogawa 2008; Sahani 2006; Tan 2009), and two studies reported the performance of MRI (Choi 2003; Sahani 2006). None of the studies reported the diagnostic accuracy of EUS elastography or sequential testing. The median pre-test probability of a cancerous lesion that may be moderately or highly dysplastic or an invasive carcinoma in these studies was 0.593 or 59.3% (minimum 0.574, maximum 0.68).

One study reported data on tests differentiating precancerous or cancerous lesions that may be moderately or highly dysplastic or invasive carcinomas from benign or precancerous lesions with a low grade of dysplasia. This study reported the performance of EUS. The median pre-test probability of a cancerous lesion that may be moderately or highly dysplastic or an invasive carcinoma in this study was 0.429 or 42.9%.

Forty-six studies were full-text publications (Brand 2000; Brandwein 2001 - Cystic; Brandwein 2001 - Solid; Cellier 1998; Cherian 2010; Choi 2003; Correa-Gallego 2009; de Jong 2012; Doi 2002; Fisher 2008; Grieser 2010; Harrison 1999; Higashi 1997; Hong 2010; Hu 2013; Jang 2014a; Jang 2014b; Jin 2015; Kamata 2016a; Kato 1995; Kim 2015; Klau 2011; Kobayashi 2012; Kubo 2001; Kucera 2012; Le Baleur 2011a; Lee 2014; Maire 2008; Nakagawa 2009; Nara 2009; Ogawa 2008; Ogawa 2014; Otomi 2014; Pais 2007; Sahani 2006; Saito 2013; Salla 2007; Sedlack 2002; Smith 2016; Takanami 2011; Takeshita 2008; Tan 2009; Taouli 2000; Tomimaru 2010; Yamao 2001; Zhan 2013). The remaining studies were abstracts (Erkan 2012; Fischer 2009 - Cystic; Fischer 2009 - Solid; Jafarimehr 2010; Jin 2013a; Kalha 2003; McHenry 2002; Zhan 2011). Three studies were prospective (Brand 2000; de Jong 2012; Erkan 2012); 39 were retrospective (Brandwein 2001 - Cystic; Brandwein 2001 - Solid; Cellier 1998; Cherian 2010; Correa-Gallego 2009; Doi 2002; Fisher 2008; Grieser 2010; Harrison 1999; Hong 2010; Hu 2013; Jafarimehr 2010; Jang 2014a; Jang 2014b; Jin 2013a; Jin 2015; Kalha 2003; Kamata 2016a; Kim 2015; Klau 2011; Kobayashi 2012; Kubo 2001; Kucera 2012; Lee 2014; Maire 2008; McHenry 2002; Nakagawa 2009; Ogawa 2008; Otomi 2014; Pais 2007; Sahani 2006; Saito 2013; Salla 2007; Sedlack 2002; Smith 2016; Takanami 2011; Taouli 2000; Zhan 2011; Zhan 2013); and 12 did not state whether they were prospective or retrospective (Choi 2003; Fischer 2009 - Cystic; Fischer 2009 - Solid; Higashi 1997; Kato 1995; Le Baleur 2011a; Nara 2009; Ogawa 2014; Takeshita 2008; Tan 2009; Tomimaru 2010; Yamao 2001).

None of the studies reported data on symptomatic and asymptomatic participants separately. Forty-two studies (2086 participants) reported on cystic pancreatic lesions (Brandwein 2001 - Cystic; Cellier 1998; Choi 2003; Correa-Gallego 2009; de Jong 2012; Doi 2002; Fischer 2009 - Cystic; Fisher 2008; Hong 2010; Hu 2013; Jang 2014a; Jang 2014b; Jin 2013a; Jin 2015; Kalha 2003; Kamata 2016a; Kim 2015; Kobayashi 2012; Kubo 2001; Kucera 2012; Le Baleur 2011a; Lee 2014; Maire 2008; McHenry 2002; Nakagawa 2009; Nara 2009; Ogawa 2008; Ogawa 2014; Pais 2007; Sahani 2006; Saito 2013; Salla 2007; Sedlack 2002; Smith 2016; Takanami 2011; Takeshita 2008; Tan 2009; Taouli 2000; Tomimaru 2010; Yamao 2001; Zhan 2011; Zhan 2013). Four studies reported on solid pancreatic lesions (Brandwein 2001 - Solid; Cherian 2010; Fischer 2009 - Solid; Klau 2011). The remaining eight studies either did not mention whether the lesions were cystic or solid, or did not report this information separately (Brand 2000; Erkan 2012; Grieser 2010; Harrison 1999; Higashi 1997; Jafarimehr 2010; Kato 1995; Otomi 2014). None of the studies reported data on people with chronic pancreatitis separately.

Overall, 12 studies reported data on EUS results (Brand 2000; Cellier 1998; de Jong 2012; Doi 2002; Harrison 1999; Kamata 2016a; Kobayashi 2012; Kubo 2001; Lee 2014; Nakagawa 2009; Sedlack 2002; Yamao 2001); 19 studies reported data on EUS-FNA (Brandwein 2001 - Cystic; Brandwein 2001 - Solid; Cherian 2010; Correa-Gallego 2009; Fischer 2009 - Cystic; Fischer 2009 - Solid; Fisher 2008; Jin 2013a; Jin 2015; Kalha 2003; Kucera 2012; Maire 2008; McHenry 2002; Pais 2007; Salla 2007; Sedlack 2002; Smith 2016; Zhan 2011; Zhan 2013); 10 studies reported data on PET (Erkan 2012; Higashi 1997; Hong 2010; Hu 2013; Jafarimehr 2010; Kato 1995; Otomi 2014; Saito 2013; Takanami 2011; Tomimaru 2010); 13 studies reported data on CT (Cellier 1998; Grieser 2010; Harrison 1999; Hong 2010; Le Baleur 2011a; Nakagawa 2009; Nara 2009; Ogawa 2008; Sahani 2006; Takeshita 2008; Tan 2009; Taouli 2000; Yamao 2001); and eight studies reported data on MRI (Choi 2003; de Jong 2012; Jang 2014a; Jang 2014b; Kim 2015; Klau 2011; Ogawa 2014; Sahani 2006).

The criteria for a positive test result varied widely by study and are described in detail in [Characteristics of included studies](#). The reference standards in all of the included studies was surgical excision.

Methodological quality of included studies

The methodological quality of the included studies is summarised in [Figure 3](#) and [Figure 4](#). None of the included studies was of high methodological quality.

Figure 3. Risk of bias and applicability concerns graph: review authors' judgements about each domain presented as percentages across included studies.

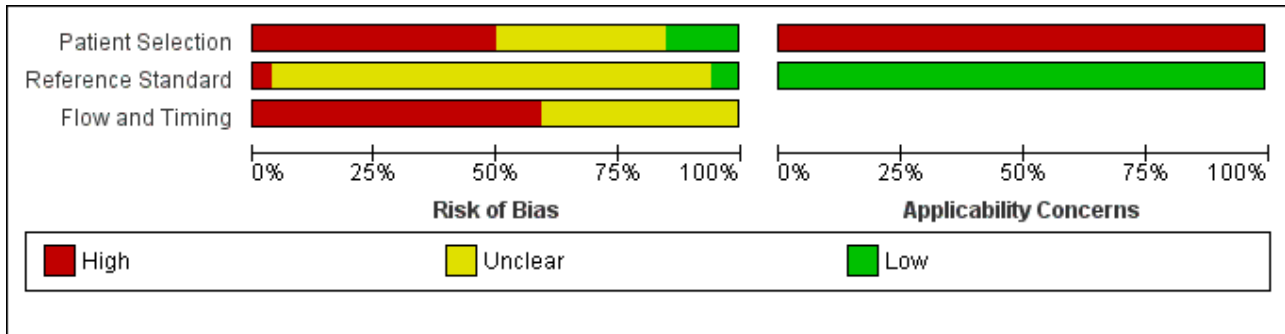


Figure 4. Risk of bias and applicability concerns summary: review authors' judgements about each domain for each included study.

	Risk of Bias			Applicability Concerns	
	Patient Selection	Reference Standard	Flow and Timing	Patient Selection	Reference Standard
Brand 2000	-	?	-	-	+
Brandwein 2001 - Cystic	-	?	-	-	+
Brandwein 2001 - Solid	-	?	-	-	+
Cellier 1998	-	?	-	-	+
Cherian 2010	+	-	-	-	+
Choi 2003	-	?	-	-	+
Correa-Gallego 2009	+	+	-	-	+
de Jong 2012	-	?	-	-	+
Doi 2002	-	?	-	-	+
Erkan 2012	-	?	-	-	+
Fischer 2009 - Cystic	?	?	?	-	+
Fischer 2009 - Solid	?	?	?	-	+
Fisher 2008	+	?	?	-	+
Grieser 2010	?	+	?	-	+
Harrison 1999	?	?	?	-	+
Higashi 1997	?	?	?	-	+
Hong 2010	?	?	-	-	+
Hu 2013	?	+	?	-	+
Jafarimehr 2010	?	?	?	-	+
Jang 2014a	-	?	-	-	+
Jang 2014b	-	?	-	-	+
Jin 2013a	?	?	?	-	+
Jin 2015	-	?	-	-	+
Kalha 2003	-	?	-	-	+
Kamata 2016a	-	?	-	-	+
Kato 1995	?	?	-	-	+

Figure 4. (Continued)

Kato 1995	?	?	-	-	+
Kim 2015	-	?	-	-	+
Klau 2011	+	?	?	-	+
Kobayashi 2012	-	?	-	-	+
Kubo 2001	?	?	?	-	+
Kucera 2012	-	?	-	-	+
Le Baleur 2011 a	?	?	?	-	+
Lee 2014	-	?	-	-	+
Maire 2008	?	?	?	-	+
McHenry 2002	?	?	?	-	+
Nakagawa 2009	-	?	-	-	+
Nara 2009	+	?	?	-	+
Ogawa 2008	-	?	-	-	+
Ogawa 2014	-	?	-	-	+
Otomi 2014	+	?	?	-	+
Pais 2007	?	-	-	-	+
Sahani 2006	?	?	?	-	+
Saito 2013	+	?	?	-	+
Salla 2007	+	?	?	-	+
Sedlack 2002	-	?	-	-	+
Smith 2016	-	?	-	-	+
Takanami 2011	-	?	-	-	+
Takeshita 2008	?	?	?	-	+
Tan 2009	-	?	-	-	+
Taouli 2000	-	?	-	-	+
Tomimaru 2010	-	?	-	-	+
Yamao 2001	-	?	-	-	+
Zhan 2011	?	?	?	-	+
Zhan 2013	?	?	?	-	+

● High
 ? Unclear
 + Low

Participant selection domain

In the participant selection domain, nine studies had a low risk of bias (Cherian 2010; Correa-Gallego 2009; Fisher 2008; Kamata 2016a; Klau 2011; Nara 2009; Otomi 2014; Saito 2013; Salla 2007). All of the studies had high applicability concerns because of concerns that the participants did not match the review question. The review question was to find out the diagnostic accuracy of these index tests in people with focal lesions. However, all of the studies meeting the inclusion criteria for this review except Cherian 2010 used surgical excision as the reference standard, suggesting that the surgeons considered these patients to be at high risk of malignancy based on the results of the index tests or the tests that patients had prior to or subsequent to the index test. Cherian 2010 was also at high risk of applicability concern because it excluded participants with resectable lesions on CT scan and included only those equivocal lesions on CT scan.

Index test domain

In the index test domain, nine studies were at low risk of bias (Correa-Gallego 2009; Hong 2010; Jang 2014b; Kim 2015; Kubo 2001; Nara 2009; Ogawa 2014; Tan 2009; Taouli 2000). Of the remaining studies, 31 were at unclear risk of bias because it was unclear whether the index test results were interpreted without knowledge of the results of the reference standard (Brand 2000; Brandwein 2001 - Cystic; Brandwein 2001 - Solid; Cellier 1998; Choi 2003; Cherian 2010; de Jong 2012; Doi 2002; Erkan 2012; Fischer 2009 - Cystic; Fischer 2009 - Solid; Fisher 2008; Harrison 1999; Jafarimehr 2010; Jin 2013a; Jin 2015; Kalha 2003; Kamata 2016a; Kato 1995; Kobayashi 2012; Kucera 2012; Le Baleur 2011a; McHenry 2002; Ogawa 2008; Pais 2007; Salla 2007; Sedlack 2002; Smith 2016; Yamao 2001; Zhan 2011; Zhan 2013). Fifteen studies were at high risk of bias because the threshold for the index test was not prespecified (Grieser 2010; Higashi 1997; Hu 2013; Jang 2014a; Klau 2011; Lee 2014; Maire 2008; Nakagawa 2009; Otomi 2014; Sahani 2006; Saito 2013; Takanami 2011; Takeshita 2008; Tomimaru 2010; Zhan 2013). Twenty-eight studies had low applicability concerns (Brand 2000; Brandwein 2001 - Cystic; Brandwein 2001 - Solid; Cellier 1998; Choi 2003; Cherian 2010; Correa-Gallego 2009; de Jong 2012; Doi 2002; Hong 2010; Hu 2013; Jang 2014b; Jin 2013a; Jin 2015; Kalha 2003; Kamata 2016a; Kim 2015; Kubo 2001; Le Baleur 2011a; Nara 2009; Ogawa 2008; Ogawa 2014; Pais 2007; Sahani 2006; Sedlack 2002; Smith 2016; Yamao 2001; Zhan 2013), and the remaining 27 studies had high applicability concerns because of concerns that the index test, its conduct, or interpretation differed from the review question (Erkan 2012; Fischer 2009 - Cystic; Fischer 2009 - Solid; Fisher 2008; Grieser 2010; Harrison 1999; Higashi 1997; Jafarimehr 2010; Jang 2014a; Kato 1995; Klau 2011; Kobayashi 2012; Kucera 2012; Lee 2014; Maire 2008; McHenry 2002; Nakagawa 2009; Otomi 2014; Saito 2013; Salla 2007; Sedlack 2002; Takanami 2011; Takeshita 2008; Tan 2009; Taouli 2000; Tomimaru 2010; Zhan 2011).

Reference standard domain

In the reference standard domain, three studies were at low risk of bias (Correa-Gallego 2009; Grieser 2010; Hu 2013). Two studies were at high risk of bias because the reference standard results were not interpreted without knowledge of the index test results (Pais 2007), or because radiological and clinical follow-up was used in some of the participants as the reference standard. The remaining 49 studies were at unclear risk of bias as it was unclear if the reference standard was interpreted without knowledge of

the results of index tests (Brand 2000; Brandwein 2001 - Cystic; Brandwein 2001 - Solid; Cellier 1998; Choi 2003; de Jong 2012; Doi 2002; Erkan 2012; Fischer 2009 - Cystic; Fischer 2009 - Solid; Fisher 2008; Harrison 1999; Higashi 1997; Hong 2010; Jafarimehr 2010; Jang 2014a; Jang 2014b; Jin 2013a; Jin 2015; Kalha 2003; Kamata 2016a; Kato 1995; Kim 2015; Klau 2011; Kobayashi 2012; Kubo 2001; Kucera 2012; Le Baleur 2011a; Lee 2014; Maire 2008; McHenry 2002; Nakagawa 2009; Nara 2009; Ogawa 2008; Ogawa 2014; Otomi 2014; Sahani 2006; Saito 2013; Salla 2007; Sedlack 2002; Smith 2016; Takanami 2011; Takeshita 2008; Tan 2009; Taouli 2000; Tomimaru 2010; Yamao 2001; Zhan 2011; Zhan 2013). All studies were at low concern for applicability, as we considered the definition of the target condition by the reference standard to match the review question.

Flow and timing domain

None of the studies were at low risk of bias in the flow and timing domain. Thirty studies were at high risk of bias because not all of the participants were included in the analysis, or there was an inappropriate interval between the index test and reference standard (Brand 2000; Brandwein 2001 - Cystic; Cellier 1998; Choi 2003; Correa-Gallego 2009; de Jong 2012; Doi 2002; Erkan 2012; Hong 2010; Jang 2014a; Jang 2014b; Jin 2015; Kalha 2003; Kamata 2016a; Kato 1995; Kim 2015; Kobayashi 2012; Kucera 2012; Lee 2014; Nakagawa 2009; Ogawa 2008; Ogawa 2014; Pais 2007; Sedlack 2002; Smith 2016; Takanami 2011; Tan 2009; Taouli 2000; Tomimaru 2010; Yamao 2001). One study was at high risk of bias because the reference standards that participants received were dependent on the index test results. The remaining 23 studies were at unclear risk of bias because it was either unclear if there was an appropriate interval between the index test and reference standard or if all participants were included in the analysis, or both (Brandwein 2001 - Solid; Fischer 2009 - Cystic; Fischer 2009 - Solid; Fisher 2008; Grieser 2010; Harrison 1999; Higashi 1997; Hu 2013; Jafarimehr 2010; Jin 2013a; Klau 2011; Kubo 2001; Le Baleur 2011a; Maire 2008; McHenry 2002; Nara 2009; Otomi 2014; Sahani 2006; Saito 2013; Salla 2007; Takeshita 2008; Zhan 2011; Zhan 2013).

Findings

The results are summarised in the [Summary of findings 1](#). The overall sensitivities and specificities for different tests for different target conditions are tabulated in [Table 2](#). A detailed description is given below.

Cancerous versus benign or precancerous

EUS-FNA cytology: We included one study reporting data on 45 participants for this test (McHenry 2002). The sensitivity and specificity for diagnosing cancer were 0.79 (95% confidence interval (CI) 0.60 to 0.91) and 1.00 (95% CI 0.85 to 1.00), respectively.

EUS-FNA (CEA > 500 ng/mL): We included one study reporting data on 24 participants for this test (Kalha 2003). The sensitivity and specificity for diagnosing cancer were 0.93 (95% CI 0.70 to 0.99) and 0.33 (95% CI 0.12 to 0.65), respectively.

PET (criteria: not specified): We included one study reporting data on 76 participants for this test (Jafarimehr 2010). The sensitivity and specificity for diagnosing cancer were 0.85 (95% CI 0.73 to 0.92) and 0.91 (95% CI 0.72 to 0.97), respectively.

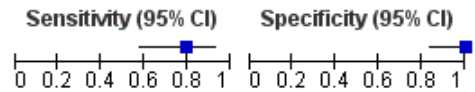
The results including sensitivities and specificities and post-test probabilities at median pre-test probabilities are summarised in

[Summary of findings 1](#). A forest plot summarising all of the sensitivity and specificity data for the 'cancerous versus benign or precancerous' studies is shown in [Figure 5](#).

Figure 5. Forest plot - Cancerous versus benign or precancerous.

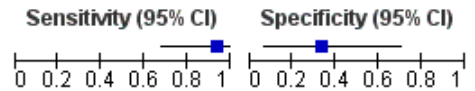
Cancerous versus benign or precancerous - EUS-FNA (cytology)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
McHenry 2002	19	0	5	21	0.79 [0.58, 0.93]	1.00 [0.84, 1.00]



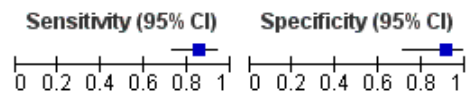
Cancerous versus benign or precancerous - EUS-FNA (CEA > 500 ng/mL)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kalha 2003	14	6	1	3	0.93 [0.68, 1.00]	0.33 [0.07, 0.70]



Cancerous versus benign or precancerous - PET

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Jafarimehr 2010	46	2	8	20	0.85 [0.73, 0.93]	0.91 [0.71, 0.99]



Cancerous versus benign

EUS: Two studies reporting data on 133 participants were included for this test, allowing meta-analysis to be performed ([Brand 2000](#); [Harrison 1999](#)). The summary sensitivity and summary specificity for diagnosing cancer were 0.95 (95% CI 0.84 to 0.99) and 0.53 (95% CI 0.31 to 0.74), respectively.

EUS-FNA cytology: Three studies reporting data on 147 participants were included for this test ([Brandwein 2001 - Cystic](#); [Brandwein 2001 - Solid](#); [Cherian 2010](#)). The sensitivity and specificity for diagnosing cancer were 0.79 (95% CI 0.07 to 1.00) and 1.00 (95% CI 0.91 to 1.00), respectively.

PET (criteria: not specified): Three studies reporting data on 99 participants were included for this test, allowing meta-analysis to be performed ([Erkan 2012](#); [Higashi 1997](#); [Kato 1995](#)). The summary sensitivity and summary specificity for diagnosing cancer were 0.92 (95% CI 0.80 to 0.97) and 0.65 (95% CI 0.39 to 0.85), respectively.

PET (SUVmax > 3.5): We included one study reporting data on 80 participants for this test ([Hu 2013](#)). The sensitivity and specificity for

diagnosing cancer were 0.96 (95% CI 0.87 to 0.99) and 0.62 (95% CI 0.43 to 0.78), respectively.

CT: Two studies reporting data on 123 participants were included for this test, allowing meta-analysis to be performed ([Grieser 2010](#); [Harrison 1999](#)). The summary sensitivity and summary specificity for diagnosing cancer were 0.98 (95% CI 0.00 to 1.00) and 0.76 (95% CI 0.02 to 1.00), respectively.

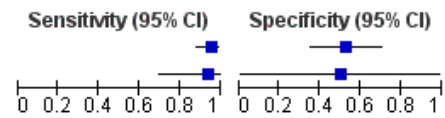
MRI: We included one study reporting data on 29 participants for this test ([Klau 2011](#)). The sensitivity and specificity for diagnosing cancer were 0.80 (95% CI 0.58 to 0.92) and 0.89 (95% CI 0.57 to 0.98), respectively.

The results including sensitivities and specificities and post-test probabilities at median pre-test probabilities are summarised in [Summary of findings 1](#). A forest plot summarising all of the sensitivity and specificity data for the 'cancerous versus benign' studies is shown in [Figure 6](#).

Figure 6. Forest plot - Cancerous versus benign.

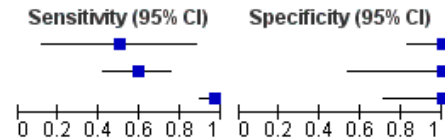
Cancerous versus benign - EUS

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Brand 2000	77	16	4	18	0.95 [0.88, 0.99]	0.53 [0.35, 0.70]
Harrison 1999	15	1	1	1	0.94 [0.70, 1.00]	0.50 [0.01, 0.99]



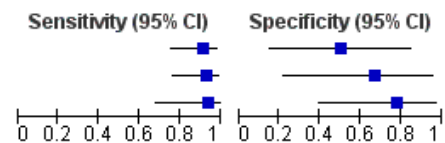
Cancerous versus benign - EUS-FNA

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Brandwein 2001 - Cystic	3	0	3	20	0.50 [0.12, 0.88]	1.00 [0.83, 1.00]
Brandwein 2001 - Solid	22	0	15	6	0.59 [0.42, 0.75]	1.00 [0.54, 1.00]
Cherian 2010	65	0	2	11	0.97 [0.90, 1.00]	1.00 [0.72, 1.00]



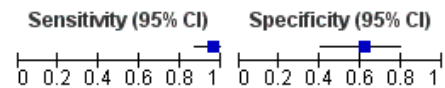
Cancerous versus benign - PET

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Erkan 2012	30	4	3	4	0.91 [0.76, 0.98]	0.50 [0.16, 0.84]
Higashi 1997	26	2	2	4	0.93 [0.76, 0.99]	0.67 [0.22, 0.96]
Kato 1995	14	2	1	7	0.93 [0.68, 1.00]	0.78 [0.40, 0.97]



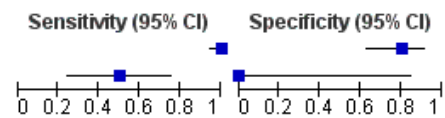
Cancerous versus benign - PET (SUVmax > 3.5)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Hu 2013	52	10	2	16	0.96 [0.87, 1.00]	0.62 [0.41, 0.80]



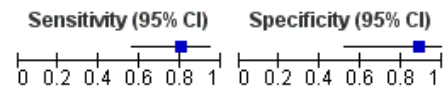
Cancerous versus benign - CT

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Grieser 2010	70	7	0	28	1.00 [0.95, 1.00]	0.80 [0.63, 0.92]
Harrison 1999	8	2	8	0	0.50 [0.25, 0.75]	0.00 [0.00, 0.84]



Cancerous versus benign - MRI

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Klau 2011	16	1	4	8	0.80 [0.56, 0.94]	0.89 [0.52, 1.00]



Precancerous or cancerous versus benign

EUS: We included one study reporting data on 34 participants for this test (Sedlack 2002). The sensitivity and specificity for diagnosing cancer or precancer were 0.92 (95% CI 0.74 to 0.98) and 0.60 (95% CI 0.31 to 0.83), respectively.

EUS-FNA cytology: We included three studies, reporting data on 52 participants for this test (Fischer 2009 - Cystic; Fischer 2009 - Solid; Sedlack 2002). The summary sensitivity and summary specificity for diagnosing cancer or precancer were 0.73 (95% CI 0.01 to 1.00) and 0.94 (95% CI 0.15 to 1.00), respectively.

EUS-FNA (CEA > 50 ng/mL): We included one study reporting data on 11 participants for this test (Sedlack 2002). The sensitivity and specificity for diagnosing cancer or precancer were 0.29 (95% CI 0.08 to 0.64) and 0.25 (95% CI 0.05 to 0.70), respectively.

PET (SUVmax > 2.4): We included one study reporting data on 32 participants for this test (Otomi 2014). The sensitivity and

specificity for diagnosing cancer or precancer were 0.94 (95% CI 0.74 to 0.99) and 0.93 (95% CI 0.69 to 0.99), respectively.

CT: We included one study reporting data on 48 participants for this test (Fisher 2008). The sensitivity and specificity for diagnosing cancer or precancer were 0.62 (95% CI 0.45 to 0.76) and 0.64 (95% CI 0.39 to 0.84), respectively.

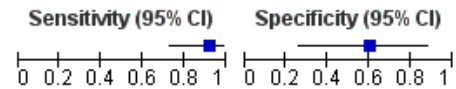
MRI: We included one study reporting data on 27 participants for this test (Jang 2014a). The sensitivity and specificity for diagnosing cancer or precancer were 0.93 (95% CI 0.69 to 0.99) and 0.85 (95% CI 0.58 to 0.96), respectively.

The results including sensitivities and specificities and post-test probabilities at median pre-test probabilities are summarised in Summary of findings 1. A forest plot summarising all of the sensitivity and specificity data for the 'precancerous or cancerous versus benign' studies is shown in Figure 7.

Figure 7. Forest plot - Precancerous or cancerous versus benign.

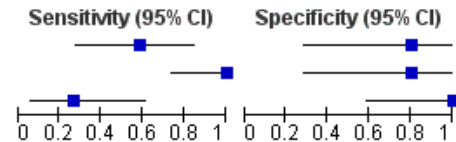
Precancerous or cancerous versus benign - EUS

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Sedlack 2002	22	4	2	6	0.92 [0.73, 0.99]	0.60 [0.26, 0.88]



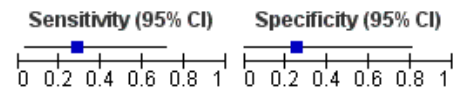
Precancerous or cancerous versus benign - EUS-FNA

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Fischer 2009 - Cystic	7	1	5	4	0.58 [0.28, 0.85]	0.80 [0.28, 0.99]
Fischer 2009 - Solid	12	1	0	4	1.00 [0.74, 1.00]	0.80 [0.28, 0.99]
Sedlack 2002	3	0	8	7	0.27 [0.06, 0.61]	1.00 [0.59, 1.00]



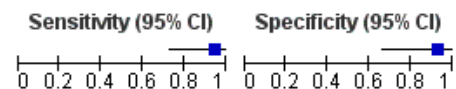
Precancerous or cancerous versus benign - EUS-FNA (CEA > 50 ng/mL)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Sedlack 2002	2	3	5	1	0.29 [0.04, 0.71]	0.25 [0.01, 0.81]



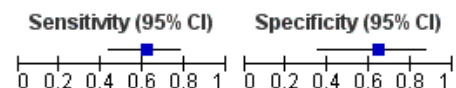
Precancerous or cancerous versus benign - PET (SUVmax > 2.4)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Otomi 2014	17	1	1	13	0.94 [0.73, 1.00]	0.93 [0.66, 1.00]



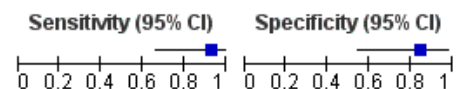
Precancerous or cancerous versus benign - CT

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Fisher 2008	21	5	13	9	0.62 [0.44, 0.78]	0.64 [0.35, 0.87]



Precancerous or cancerous versus benign - MRI

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Jang 2014a	13	2	1	11	0.93 [0.66, 1.00]	0.85 [0.55, 0.98]



Cancerous (invasive carcinoma) versus precancerous (dysplasia)

EUS: Five studies reporting data on 156 participants were included for this test, allowing meta-analysis to be performed (Cellier 1998; de Jong 2012; Nakagawa 2009; Yamao 2001; Zhan 2011). The summary sensitivity and summary specificity for diagnosing invasive cancer were 0.78 (95% CI 0.45 to 0.94) and 0.91 (95% CI 0.61 to 0.98), respectively.

EUS-FNA cytology: Three studies reporting data on 158 participants were included for this test, allowing meta-analysis to be performed (Jin 2013a; Pais 2007; Salla 2007). The summary sensitivity and summary specificity for diagnosing invasive cancer were 0.66 (95% CI 0.03 to 0.99) and 0.92 (95% CI 0.73 to 0.98), respectively.

EUS-FNA (CEA > 200 ng/mL): We included one study reporting data on 41 participants for this test (Maire 2008). The sensitivity and

specificity for diagnosing invasive cancer were 1.00 (95% CI 0.57 to 1.00) and 0.64 (95% CI 0.48 to 0.78), respectively.

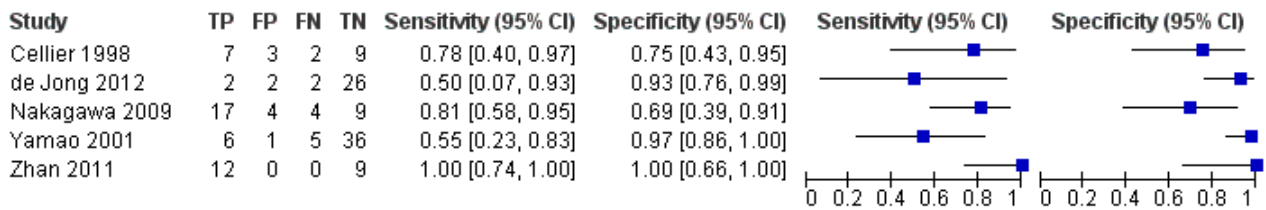
CT: Six studies reporting data on 326 participants were included for this test, allowing meta-analysis to be performed (Cellier 1998; Nakagawa 2009; Nara 2009; Ogawa 2008; Taouli 2000; Yamao 2001). The summary sensitivity and summary specificity for diagnosing invasive cancer were 0.72 (95% CI 0.50 to 0.87) and 0.92 (95% CI 0.81 to 0.97), respectively.

MRI: We included one study reporting data on 32 participants for this test (de Jong 2012). The sensitivity and specificity for diagnosing invasive cancer were 0.75 (95% CI 0.30 to 0.95) and 0.93 (95% CI 0.77 to 0.98), respectively.

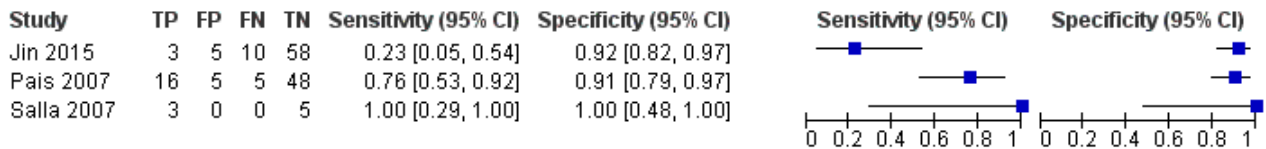
The results including sensitivities and specificities and post-test probabilities at median pre-test probabilities are summarised in [Summary of findings 1](#). A forest plot summarising all of the sensitivity and specificity data for the 'cancer (invasive carcinoma) versus precancerous (dysplasia)' studies is shown in [Figure 8](#).

Figure 8. Forest plot - Cancerous (invasive carcinoma) versus precancerous (dysplasia).

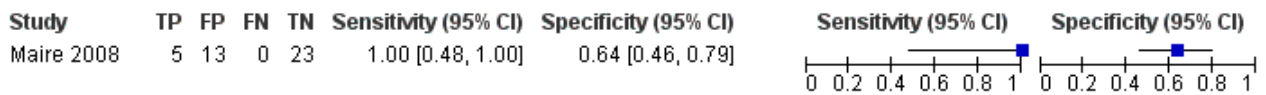
Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS



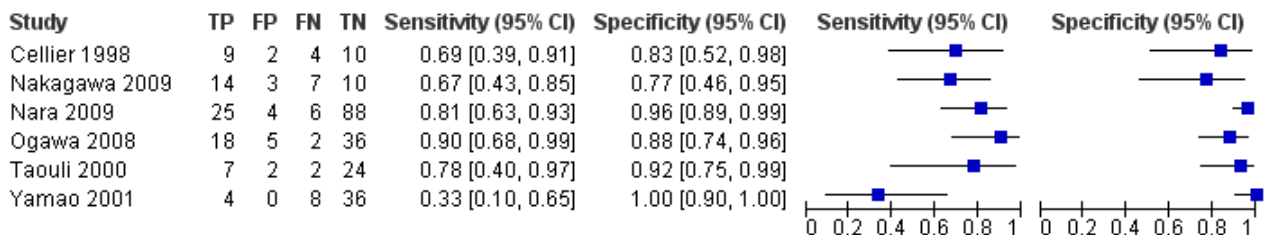
Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS-FNA



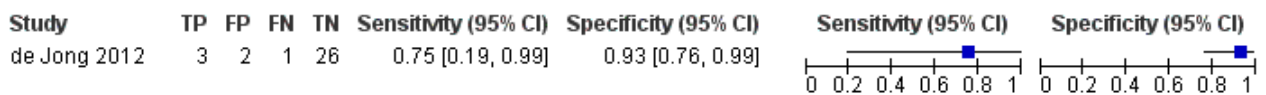
Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS-FNA (CEA > 200 ng/mL)



Cancerous (invasive carcinoma) versus precancerous (dysplasia) - CT



Cancerous (invasive carcinoma) versus precancerous (dysplasia) - MRI



Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia)

EUS: Four studies reporting data on 196 participants were included for this test, allowing meta-analysis to be performed (Doi 2002; Kobayashi 2012; Lee 2014; Yamao 2001). The summary sensitivity and summary specificity for diagnosing high-grade dysplasia or invasive cancer were 0.86 (95% CI 0.74 to 0.92) and 0.91 (95% CI 0.83 to 0.96), respectively.

EUS-FNA cytology: Three studies reporting data on 310 participants were included for this test, allowing meta-analysis to be performed (Jin 2013a; Smith 2016; Zhan 2013). The summary sensitivity and summary specificity for diagnosing high-grade dysplasia or invasive cancer were 0.47 (95% CI 0.24 to 0.70) and 0.91 (95% CI 0.32 to 1.00), respectively.

EUS-FNA (CEA > 200 ng/mL): Three studies reporting data on 160 participants were included for this test, allowing meta-analysis to be performed (Correa-Gallego 2009; Kucera 2012; Maire 2008). The

summary sensitivity and summary specificity for diagnosing high-grade dysplasia or invasive cancer were 0.58 (95% CI 0.28 to 0.83) and 0.51 (95% CI 0.19 to 0.81), respectively.

EUS-FNA (carbohydrate antigen 19-9 > 1000 U/mL): We included one study reporting data on 41 participants for this test (Maire 2008). The sensitivity and specificity for diagnosing high-grade dysplasia or invasive cancer were 0.90 (95% CI 0.60 to 0.98) and 0.42 (95% CI 0.26 to 0.59), respectively.

EUS-FNA (CEA > 692.8 ng/mL): We included one study reporting data on 20 participants for this test (Zhan 2013). The sensitivity and specificity for diagnosing high-grade dysplasia or invasive cancer were 0.80 (95% CI 0.49 to 0.94) and 0.90 (95% CI 0.60 to 0.98), respectively.

PET (SUVmax 2 to 2.5): Four studies reporting data on 124 participants were included for this test, allowing meta-analysis to be performed (Hong 2010; Saito 2013; Takanami 2011; Tomimaru 2010). The summary sensitivity and summary specificity for

diagnosing high-grade dysplasia or invasive cancer were 0.90 (95% CI 0.79 to 0.96) and 0.94 (95% CI 0.81 to 0.99), respectively.

CT: Three studies reporting data on 139 participants were included for this test, allowing meta-analysis to be performed ([Hong 2010](#); [Le Baleur 2011a](#); [Yamao 2001](#)). The summary sensitivity and summary specificity for diagnosing high-grade dysplasia or invasive cancer were 0.87 (95% CI 0.00 to 1.00) and 0.96 (95% CI 0.00 to 1.00), respectively.

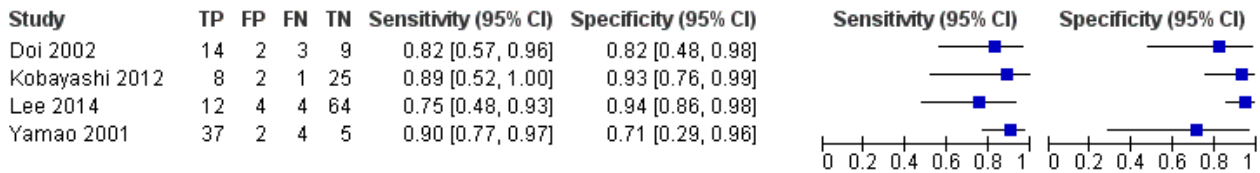
MRI: Three studies reporting data on 189 participants were included for this test, allowing meta-analysis to be performed

([Jang 2014b](#); [Kim 2015](#); [Ogawa 2014](#)). The summary sensitivity and summary specificity for diagnosing high-grade dysplasia or invasive cancer were 0.69 (95% CI 0.44 to 0.86) and 0.93 (95% CI 0.43 to 1.00), respectively.

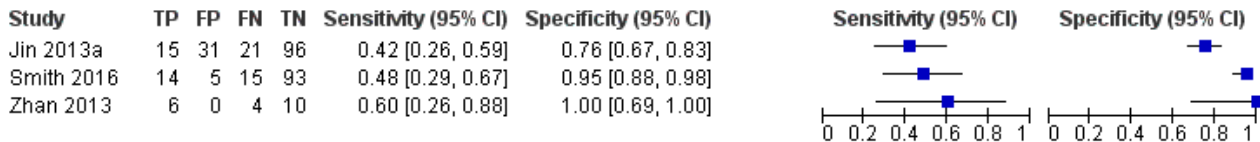
The results including sensitivities and specificities and post-test probabilities at median pre-test probabilities are summarised in [Summary of findings 1](#). A forest plot summarising all of the sensitivity and specificity data for the 'cancer (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia)' studies is shown in [Figure 9](#).

Figure 9. Forest plot - Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia).

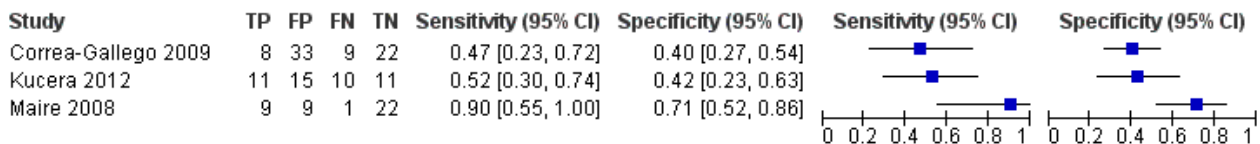
Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS



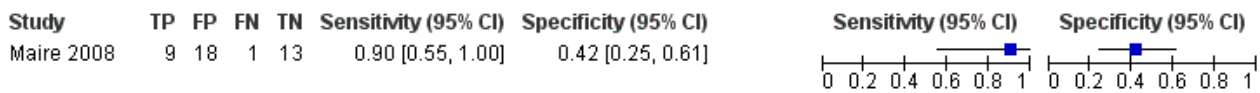
Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS-FNA



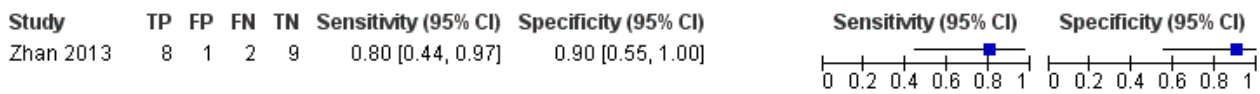
Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS-FNA (



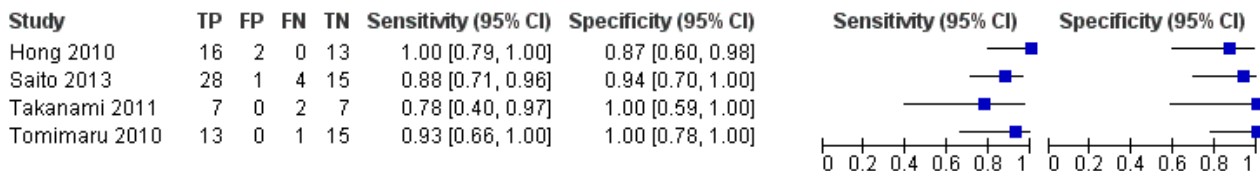
Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS-FNA (



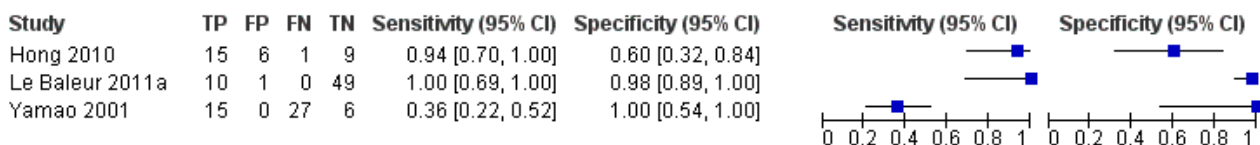
Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS-FNA (



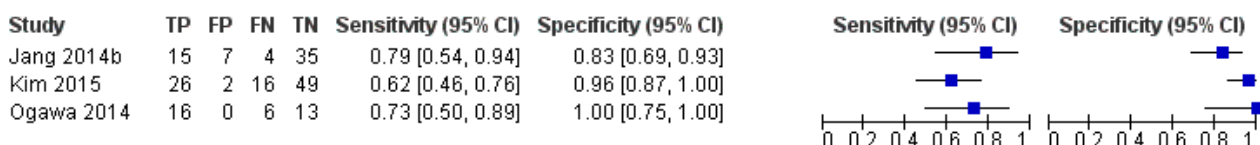
Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - PET (SUV



Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - CT



Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - MRI



Cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia)

EUS: We included one study reporting data on 51 participants for this test (Kubo 2001). The sensitivity and specificity for diagnosing invasive cancer were 0.77 (95% CI 0.50 to 0.92) and 0.89 (95% CI 0.76 to 0.96), respectively.

CT: We included one study reporting data on 46 participants for this test (Takeshita 2008). The sensitivity and specificity for diagnosing

invasive cancer were 0.50 (95% CI 0.22 to 0.78) and 0.95 (95% CI 0.83 to 0.99), respectively.

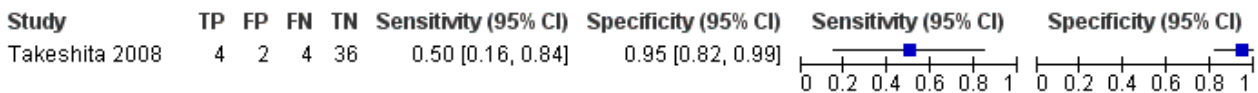
The results including sensitivities and specificities and post-test probabilities at median pre-test probabilities are summarised in [Summary of findings 1](#). A forest plot summarising all of the sensitivity and specificity data for the 'cancer (invasive carcinoma) versus precancerous (low-grade dysplasia)' studies is shown in [Figure 10](#).

Figure 10. Forest plot - Cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia).

Cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia) - EUS



Cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia) - CT



Precancerous or cancer (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia)

CT: Three studies reporting data on 106 participants were included for this test, allowing meta-analysis to be performed (Ogawa 2008; Sahani 2006; Tan 2009). The summary sensitivity and summary specificity for diagnosing intermediate- or high-grade dysplasia or invasive cancer were 0.83 (95% CI 0.68 to 0.92) and 0.83 (95% CI 0.64 to 0.93), respectively.

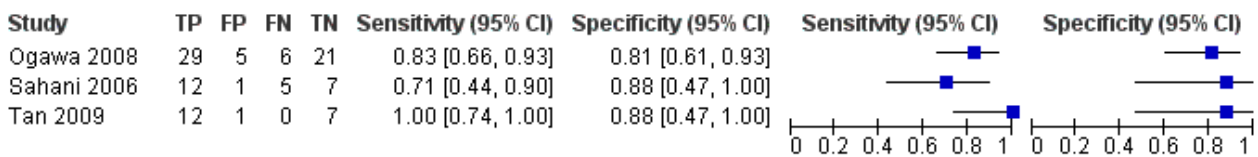
MRI: Two studies reporting data on 71 participants were included for this test, allowing meta-analysis to be performed (Choi

2003; Takeshita 2008). The summary sensitivity and specificity for diagnosing intermediate- or high-grade dysplasia or invasive cancer were 0.80 (95% CI 0.58 to 0.92) and 0.81 (95% CI 0.53 to 0.95), respectively.

The results including sensitivities and specificities and post-test probabilities at median pre-test probabilities are summarised in [Summary of findings 1](#). A forest plot summarising all of the sensitivity and specificity data for the 'precancerous or cancer (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia)' studies is shown in [Figure 11](#).

Figure 11. Forest plot - Precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia).

Precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-gr



Precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-gr

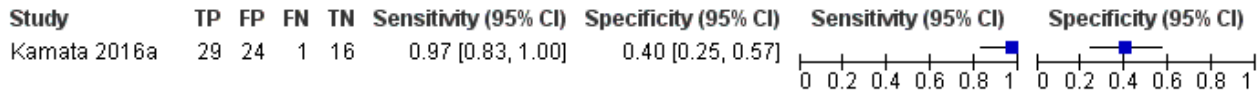


Precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia) or benign

EUS: We included one study reporting data on 70 participants for this test (Kamata 2016a). The sensitivity and specificity for diagnosing intermediate- or high-grade dysplasia or invasive carcinoma were 0.97 (95% CI 0.83 to 0.99) and 0.40 (95% CI 0.26 to 0.55), respectively.

The results including sensitivity and specificity and post-test probability at median pre-test probability are summarised in [Summary of findings 1](#). A forest plot summarising the sensitivity and specificity data for the 'precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia) or benign' study is shown in [Figure 12](#).

Figure 12. Forest plot of 33 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) or benign - EUS.



Subgroup analyses

We assessed the performance of the tests excluding any studies investigating participants with solid lesions and those in which information for solid and cystic lesions was not reported separately. All of the studies assessing the ability of different imaging modalities to differentiate precancerous versus cancerous lesions regardless of the definitions used by authors for precancer and cancer (Analysis 4 to Analysis 8) included participants with cystic focal pancreatic lesions only, therefore all the results reported are for cystic focal pancreatic lesions only.

In the analysis assessing the ability of different imaging modalities to differentiate benign or precancerous versus cancerous lesions, we excluded one study because it did not specify the type (solid or cystic) of lesions for which included participants were investigated (Jafarimehr 2010). However, as this study did not contribute to a meta-analysis, there were no changes to the analysis.

Cancerous versus benign

In the analysis assessing the ability of different imaging modalities to differentiate benign versus cancerous lesions, we excluded eight studies because they did not explicitly include participants with

cystic lesions (Brand 2000; Erkan 2012; Grieser 2010; Harrison 1999; Higashi 1997; Hu 2013; Kato 1995; Klau 2011), and one study that only had one component included (Brandwein 2001 - Cystic; Brandwein 2001 - Solid). This left two remaining studies, which did not contribute to a meta-analysis due to the exclusion of the other studies (Brandwein 2001 - Cystic; Hu 2013). We therefore performed no meta-analyses for this group. The new findings for benign versus cancerous lesions are described below.

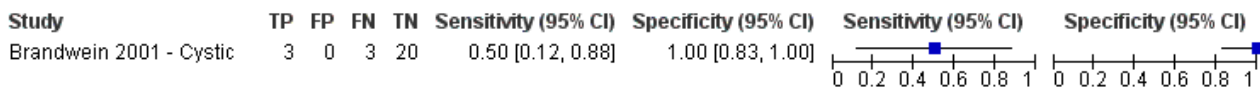
EUS-FNA: We included one study reporting data on 26 participants for this test (Brandwein 2001 - Cystic). The sensitivity and specificity for diagnosing cancer were 0.50 (95% CI 0.19 to 0.81) and 1.00 (95% CI 0.84 to 1.00), respectively.

PET: We included one study reporting data on 80 participants for this test (Hu 2013). The sensitivity and specificity for diagnosing cancer were 0.96 (95% CI 0.87 to 0.99) and 0.62 (95% CI 0.43 to 0.78), respectively.

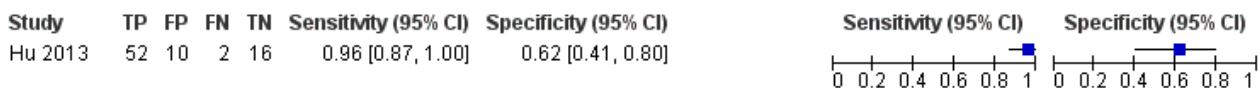
A forest plot summarising all the sensitivity and specificity data for the cystic subgroup analysis of 'cancerous versus benign lesion' studies is shown in [Figure 13](#).

Figure 13. Forest plot - Cystic lesion subgroup analysis: Cancerous versus benign.

Cystic lesion subgroup analysis - Cancerous versus benign - EUS-FNA



Cystic lesion subgroup analysis - Cancerous versus benign - PET



Precancerous or cancerous versus benign

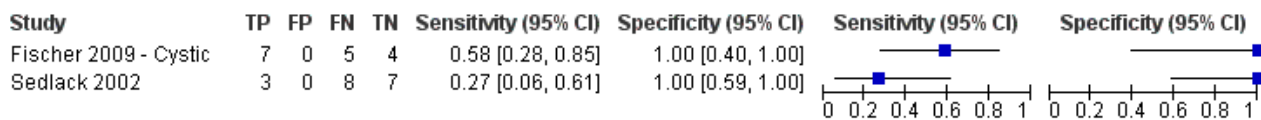
In the analysis assessing the ability of different imaging modalities to differentiate precancerous or cancerous versus benign lesions, we excluded a component of one study because the participants

had solid pancreatic lesions (Fischer 2009 - Solid). We therefore re-performed the meta-analysis for precancerous or cancerous versus benign lesions - EUS-FNA without these data. The remaining tests for this target condition did not have any studies excluded and were therefore not redone. The new findings are described below.

EUS-FNA: Two studies reporting data on 34 participants were included for this test, allowing meta-analysis to be performed (Fischer 2009 - Cystic; Sedlack 2002). The summary sensitivity and summary specificity for diagnosing precancer or cancer were 0.43 (95% CI 0.19 to 0.71) and 1.00 (95% CI 0.74 to 1.00), respectively.

A forest plot summarising the sensitivity and specificity data for the cystic subgroup analysis of 'precancerous or cancerous versus benign lesion' study is shown in Figure 14.

Figure 14. Forest plot - Cystic lesion subgroup analysis: Precancerous or cancerous versus benign - EUS-FNA.



DISCUSSION

Summary of main results

The results are summarised in [Summary of findings 1](#).

We included 54 studies involving a total of 3196 participants that evaluated the diagnostic accuracy of various imaging modalities (EUS, EUS-FNA, PET, CT, and MRI) for characterising focal pancreatic lesions. We identified eight different target conditions in these studies, with the studies using imaging modalities to differentiate: cancerous versus benign or precancerous lesions; cancerous versus benign lesions; precancerous or cancerous lesions versus benign lesions; cancerous (invasive carcinoma) versus precancerous (dysplasia) lesions; cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) lesions; cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia) lesions; precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia) lesions; and precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia) or benign lesions. The wide variety of tumour types that constituted benign and cancerous lesions within the studies meant that only a few meaningful meta-analyses could be performed. None of the comparisons in which single studies were included were of sufficiently high methodological quality to warrant highlighting of the results.

For differentiation of cancerous lesions from benign or precancerous lesions, only single studies were included and therefore meta-analysis was not performed. Overall, EUS-FNA (cytology) had a sensitivity of 0.79 (95% CI 0.60 to 0.91) and specificity of 1.00 (95% CI 0.85 to 1.00); EUS-FNA (CEA > 500 ng/mL) had a sensitivity of 0.93 (95% CI 0.70 to 0.99) and specificity of 0.33 (95% CI 0.12 to 0.65); and PET had a sensitivity of 0.85 (95% CI 0.73 to 0.92) and specificity of 0.91 (95% CI 0.72 to 0.97).

The second analysis, of studies differentiating cancerous versus benign lesions, provided three tests in which meta-analysis could be performed, however the data were sparse: one of these tests contained three studies, and the remaining two tests contained two studies, meaning the meta-analysis was of limited value. There was little difference in the diagnostic test accuracy between the imaging techniques. EUS-FNA achieved very high specificity (of 1.00, i.e. no false negatives) but modest sensitivity (0.79; 95% CI 0.07 to 1.00). A high specificity of EUS-FNA can be expected, since this involves physically sampling the lesion. However, the modest sensitivity may reflect that the sampling methods were inadequate.

Additional guidance such as identifying the location most likely to yield the correct results or additional guidance using optical endoscopy techniques such as confocal laser microendoscopy may overcome this problem and improve the sensitivity of EUS (Giovannini 2012), but there are major challenges, such as knowing the area within the lesion that is being examined by confocal laser microendoscopy, that must be addressed before such methods can be used routinely.

The third analysis, of studies differentiating precancerous or cancerous and benign lesions, only provided one test (EUS-FNA) for which meta-analysis was performed. The results were unreliable due to significant heterogeneity in the results between the studies.

The fourth analysis, of studies differentiating cancerous (invasive carcinoma) versus precancerous (dysplasia) lesions, provided three tests in which meta-analysis was performed, with one test containing five studies (EUS), one test containing three studies (EUS-FNA), and the third test containing six studies (CT). All five of the tests included in the analysis had a similar level of accuracy according to their respective ROC curves. EUS and CT showed the highest (and similar) accuracy estimates (EUS = sensitivity 0.78 and specificity 0.91; CT = sensitivity 0.72 and specificity 0.92) and included the largest number of studies (five and six, respectively) among all comparisons.

The fifth analysis, of studies differentiating cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) lesions, provided six tests in which meta-analysis was performed, with two tests containing four studies (EUS and PET SUVmax 2 to 2.5), one test containing two studies (EUS-FNA), three tests containing three studies (EUS-FNA > 200, CT, and MRI), and the remaining two tests providing single studies. PET performed with the highest accuracy (sensitivity 0.90 (95% CI 0.79 to 0.96) and specificity 0.94 (95% CI 0.81 to 0.99)).

The sixth analysis, of studies differentiating cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia) lesions, provided no tests in which meta-analysis was performed.

The seventh analysis, of studies differentiating precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia) lesions, provided two tests in which meta-analysis was performed. The meta-analysis results for CT (sensitivity 0.83 (95% CI 0.68 to 0.92) and specificity 0.83 (95% CI 0.64 to 0.93)) were similar to those of MRI (sensitivity 0.80 (95% CI 0.58 to 0.92) and specificity 0.81 (95% CI 0.53 to 0.95)), however lack of significant data means little can be inferred from this.

The eighth analysis, of studies differentiating precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia) or benign lesions, provided no tests in which meta-analysis was performed.

We performed a subgroup analysis to investigate the performance of imaging modalities for cystic pancreatic lesions. This only resulted in alterations to the 'cancerous versus benign or precancerous', 'cancerous versus benign', and 'precancerous or cancerous versus benign' groups, however when re-performed in these groups, the analysis did not result in any significant changes.

Overall, none of the tests assessed had sufficient overall diagnostic accuracy to be considered a definitive diagnostic modality. High sensitivity of the test is required so that precancer or cancer is not missed. High specificity is required to avoid major surgery. Sensitivity and specificity in excess of 90% are required to recommend the particular modality over other modalities. Only PET in differentiating precancerous (low- or intermediate-grade dysplasia) versus cancer (high-grade dysplasia or invasive carcinoma) approaches this level of accuracy. Overall, modalities other than EUS-FNA had moderate to high sensitivity but moderate specificity, while EUS-FNA had high specificity with moderate sensitivity in distinguishing the nature of focal pancreatic lesions.

Strengths and weaknesses of the review

We conducted a thorough literature search and included full-text publications and abstracts without any language restrictions. Two review authors independently identified and extracted data from the studies, potentially reducing the chance of error that would be associated with one person performing the data extraction. We used strict reference standards that are likely to diagnose the target condition with a high degree of accuracy. These were the major strengths of the review.

We included EUS-FNA as part of the review. Strictly speaking, EUS-FNA cannot be considered an imaging modality since it uses cytology criteria or levels of tumour markers in the aspirate rather than imaging features to make the diagnosis. We had mentioned at the protocol stage that we would include EUS-FNA in this review, as the searches for EUS return EUS-FNA as well and because EUS-FNA along with the imaging modalities included in this review are the most widely used tests for characterising focal pancreatic lesions. Our review provides the most important information about the tests performed to characterise focal lesions in one location and hence is probably more useful for clinicians, who would otherwise have to search for another review for information on EUS-FNA.

The major limitation in the review process was the diverse nature of the collected data, with a wide variety of definitions of benign, precancerous, and cancerous lesions. This limited the possible analysis of the data and the conclusions that could be made from our analyses. While some authors defined precancerous lesions as lesions with low- and intermediate-grade dysplasia, others defined it as low-grade dysplasia only, while yet others considered any form of dysplasia as precancerous lesions. In the comparison 'cancer versus benign', it is unclear how the study authors dealt with precancerous lesions, that is whether they included precancerous lesions in the 'cancer' group or the 'benign' group, or whether they simply excluded them, consequently undermining any conclusions that could be made for this comparison.

We could not perform a bivariate random-effects model that takes correlation between sensitivity and specificity into account and were unable to compare the diagnostic test accuracy of index tests using formal statistical methods due to the sparseness of data for each comparison. As a result, we performed the analysis using simpler models suggested by [Takwoingi 2015](#) and colleagues. We reported the model with the lowest -2 log likelihood and also visualised the forest plots and ROC plots in deciding the model to be reported. The confidence intervals were extremely wide for the following analyses: benign versus cancer: CT; benign versus cancer: EUS-FNA; benign versus precancer or cancer: EUS-FNA; and precancer (low- or intermediate-grade dysplasia) versus cancer (high-grade dysplasia or invasive carcinoma): CT. While fixed-effect model provided narrower confidence intervals for some of the above analyses, such models were inappropriate for these data because of the poor overlap of confidence intervals on the forest plot. This observation (i.e. that fixed-effect models were not appropriate) was supported by the -2 log likelihoods, which were higher for the univariate fixed-effect model than those of the models presented. The alternative was not to perform a meta-analysis at all, which is even more difficult to interpret. At least the current results allowed us to interpret that the sensitivity or specificity or both could not be estimated reliably. There was reasonable overlap of confidence intervals in the other meta-analyses performed. With regard to the tests for which meta-analysis could not be performed, the diagnostic test accuracy from single studies needs confirmation by other studies to assess whether the results are reproducible. Hence, we are unable to arrive at any major conclusions based on information by a single study.

A high proportion of studies were at high risk of bias and with high concern regarding applicability in all four domains of the QUADAS-2 tool. This makes the validity of the results questionable. Of particular concern was the type of people who underwent these tests. Because of the strict but appropriate reference standard, all of the participants in all of the studies included in this review except [Cherian 2010](#) underwent surgical resection. This suggested that the surgeons thought that these participants had high probability of having high-grade dysplasia or cancer, either because of the results of this test or other tests performed alongside the index tests. Since most of the studies were retrospective studies, if participants were operated on on the basis of the index test, and only participants who underwent surgery were included, participants with negative index tests but who had cancer would have been excluded inappropriately. This would have resulted in overestimation of sensitivity. The studies did not report the proportion of people in whom the different tests were feasible. This is particularly important for EUS and EUS-FNA, since the participants may have been selected to undergo EUS or EUS-FNA based on the proximity to the stomach or duodenum. This increases the concern regarding applicability. The studies did not report the complications associated with the index test. While this is unlikely to influence the diagnostic accuracy of the index test, it may have implications in determining the balance of benefits and harms in choosing a test.

Another limitation of this review was that we have included sensitivity-maximising diagnostic filters for searching MEDLINE and Embase databases ([Haynes 2004](#); [Wilczynski 2005](#)), and also used terms to limit the searches in Science Citation Index. We did this because the original searches without the filters retrieved more than 60,000 references. We had to balance the possibility of missing

some studies against the risk of not being able to complete the review. We decided that it is useful to have evidence from major studies rather than having no information at all. However, it must be noted that the diagnostic filters we used have a sensitivity of 98.6% for MEDLINE and 100% for Embase. Consequently, the chances that we missed some relevant diagnostic studies are extremely low. This was further reduced by performing a 'related search' and 'citing reference search', in which we found no studies that could be included in this review.

We identified six other systematic reviews on the topics included in this systematic review (Banafea 2016; Chen 2012; Fuccio 2013; Gillis 2015; Hewitt 2012; Mei 2013). These included the role of EUS-FNA (cytology), K-ras gene mutation analysis of FNA aspirate, and EUS elastography in focal pancreatic lesions. The diagnostic test accuracy in four of the studies showed that EUS cytology and K-ras gene mutation analysis of FNA aspirate had a reasonably high sensitivity (0.80 to 0.86) and very high specificity (96% to 98%) in solid pancreatic lesions (Banafea 2016; Chen 2012; Fuccio 2013; Hewitt 2012). These studies accepted cytology and clinical follow-up (without specifying the exact nature of acceptable clinical follow-up) in addition to histopathology as reference standards (Chen 2012; Fuccio 2013; Hewitt 2012). It is likely that this methodological difference was responsible for the major differences between our observations and these systematic reviews. In addition, these systematic reviews restricted participants to those with solid pancreatic lesions (Banafea 2016; Chen 2012; Fuccio 2013; Hewitt 2012), which could be another explanation for the differences between our observations and these systematic reviews. One systematic review evaluated EUS elastography in focal pancreatic lesions and reported a high sensitivity of 0.95 and a specificity of 0.67 (Mei 2013). We did not identify any study evaluating EUS elastography that met our inclusion criteria with respect to our reference standard, therefore we are unable to comment on the observation by Mei 2013. The last systematic review evaluated the role of EUS-FNA and EUS-FNA molecular analysis (i.e. check for abnormal genes) in people with cystic pancreatic lesions. The authors found poor sensitivity and high specificity of EUS-FNA, which is similar to our findings (Gillis 2015).

Applicability of findings to the review question

All studies had high applicability concerns, making the applicability of findings to the target patient population of all incidental lesions questionable. The findings are applicable only for people who are suspected to be at high risk of high-grade dysplasia or cancer. The review question was to find out the diagnostic accuracy of these index tests in people with focal pancreatic lesions, usually

detected incidentally. However, all of the studies that met the inclusion criteria for this review used surgical excision as the reference standard, suggesting that the surgeons considered these patients to have a high risk of malignancy based on the results of the index tests or any additional tests. In terms of current availability of these tests, CT scan and MRI are likely to be available in most secondary centres. EUS is likely to be available in limited secondary centres and most tertiary centres that treat pancreatic lesions. PET is likely to be available only in limited tertiary centres, although the tertiary centres are likely to have access to a PET scan. However, based on the observations in this review, there do not appear to be any major differences between the different imaging modalities. The improved sensitivity of EUS-FNA compared to other imaging modalities is compensated by a corresponding decrease in sensitivity, consequently there do not appear to be major advantages to using EUS for characterising focal pancreatic lesions compared to other non-invasive methodologies.

AUTHORS' CONCLUSIONS

Implications for practice

We were unable to arrive at any firm conclusions because of the differences in the way that study authors classified focal pancreatic lesions into cancerous, precancerous, and benign lesions; the inclusion of few studies with wide confidence intervals for each comparison; poor methodological quality in the studies; and heterogeneity in the estimates within comparisons.

Implications for research

Further studies of high methodological quality are necessary. Future research should be conducted in a prospective manner, however most importantly the definition of benign and cancerous lesions in the analysis of studies should be standardised according to World Health Organization (WHO) classification. The threshold for positivity of endoscopic ultrasound-guided fine-needle aspiration cancer markers should be prespecified. Future studies should avoid any inappropriate exclusions to ensure that true diagnostic accuracy can be determined. Long-term follow-up of participants with negative tests will help in understanding the implications of false-negative results and will aid clinical decision-making.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES
Characteristics of included studies [ordered by study ID]
Brand 2000
Study characteristics

Patient sampling	Type of study: prospective study. Consecutive or random sample: neither.
Patient characteristics and setting	Sample size: 179. Females: 47 (26.3%). Age: 61 years. Presentation: Patients with pancreatic lesions who had undergone EUS and surgical resection with histological confirmation. Setting: secondary care, Germany.
Index tests	Index test: EUS. Further details: Technical specifications: Olympus GF-UM 3, GF-UM 20, and GF-UM 200. Performed by: gastroenterologist. Criteria for positive diagnosis: a mass lesion with irregular borders, non-homogeneous echotexture, and/or loss of vascular interface or obvious vascular involvement, without any signs of chronic pancreatitis in the lesion or the rest of the gland. However, in the presence of obvious chronic pancreatitis, an associated malignancy was suspected if the EUS morphology of the focal lesion suggested involvement of the adjacent structures.
Target condition and reference standard(s)	Target condition: cancerous versus benign. Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: 64 (35.8%).
Comparative	
Notes	Possible overlap with Binmoeller 1998a and Binmoeller 1998b ; out of 179 patients, only 115 patients with histologically confirmed diagnosis were included.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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Imaging modalities for characterising focal pancreatic lesions (Review)

Brand 2000 (Continued)

DOMAIN 1: Patient Selection

Was a consecutive or random sample of patients enrolled?	No
----------------------------------------------------------	----

Was a case-control design avoided?	Yes
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Did the study avoid inappropriate exclusions?	No
-----------------------------------------------	----

High
High
DOMAIN 2: Index Test Cancerous versus benign - EUS

If a threshold was used, was it pre-specified?	Yes
------------------------------------------------	-----

Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear
-----------------------------------------------------------------------------------------------------	---------

Unclear
Low
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	Yes
-------------------------------------------------------------------------------	-----

Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
------------------------------------------------------------------------------------------------------	---------

Unclear
Low
DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Unclear
------------------------------------------------------------------------------	---------

Did all patients receive the same reference standard?	Yes
-------------------------------------------------------	-----

Were all patients included in the analysis?	No
---------------------------------------------	----

High
Brandwein 2001 - Cystic
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: neither.
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Patient characteristics and setting	Sample size: 26. Females: not stated.
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Brandwein 2001 - Cystic (Continued)

Age: not stated.
Presentation:
Patients with cystic and solid pancreatic lesions who had undergone surgical resection; only patients with cystic lesions included in our analysis.
Setting: secondary care, USA.

Index tests

Index test: EUS-FNA.
Further details:
Technical specifications: Pentax echoendoscope (model not stated); 22-gauge needle.
Performed by: endoscopist and cytologist.
Criteria for positive diagnosis: a malignant mass was defined as a focal hypoechoic heterogeneous lesion within the pancreatic parenchyma and cytology reported stated malignancy.

Target condition and reference standard(s)

Target condition: cancerous versus benign.
Reference standard: surgical excision.
Further details:
Technical specifications: not applicable.
Performed by: clinicians.
Criteria for positive diagnosis: not stated.

Flow and timing

Number of indeterminates for whom the results of reference standard were available: not stated.
Number of patients who were excluded from the analysis: not stated.

Comparative

Notes

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High
DOMAIN 2: Index Test Cystic lesion subgroup analysis - Cancerous versus benign - EUS FNA			
If a threshold was used, was it pre-specified?	Unclear		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	Low
DOMAIN 2: Index Test Cancerous versus benign - EUS FNA			
If a threshold was used, was it pre-specified?	Yes		

Brandwein 2001 - Cystic *(Continued)*

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

Unclear

Low

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Unclear

Low

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Unclear

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

High

Brandwein 2001 - Solid
Study characteristics

Patient sampling Type of study: retrospective study.
Consecutive or random sample: neither.

Patient characteristics and setting Sample size: 43.
Females: not stated.
Age: not stated.
Presentation:
Patients with cystic and solid pancreatic lesions who had undergone surgical resection.
Setting: secondary care, USA.

Index tests Index test: EUS-FNA.
Further details:
Technical specifications: Pentax echoendoscope (model not stated); 22-gauge needle.
Performed by: endoscopist and cytologist.
Criteria for positive diagnosis: a malignant mass was defined as a focal hypoechoic heterogeneous lesion within the pancreatic parenchyma and cytology reported stated malignancy.

Target condition and reference standard(s) Target condition: cancerous versus benign.
Reference standard: surgical excision.
Further details:
Technical specifications: not applicable.
Performed by: clinicians.

Brandwein 2001 - Solid (Continued)

Criteria for positive diagnosis: not stated.

Flow and timing

 Number of indeterminates for whom the results of reference standard were available: not stated.
 Number of patients who were excluded from the analysis: not stated.

Comparative

Notes

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High
DOMAIN 2: Index Test Cancerous versus benign - EUS FNA			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	Low
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
		High	

Cellier 1998

Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: consecutive patients.
Patient characteristics and setting	Sample size: 46. Females: not stated. Age: not stated. Presentation: Patients with IPMN undergoing surgery. Setting: secondary care, France.
Index tests	Index test: EUS. Further details: Technical specifications: Olympus GFUM3 or GF UM20. Performed by: endoscopist. Criteria for positive diagnosis: <ul style="list-style-type: none"> • Rupture of main pancreatic duct wall with tumoural intrapancreatic spread. • Intrapancreatic mass. • Tumour invasion of duodenum or common bile duct. • Metastatic peripancreatic lymph nodes. • Extrapancreatic spread. Index test: CT. Further details: Technical specifications: conventional CT (further details not available). Performed by: not stated. Criteria for positive diagnosis: <ul style="list-style-type: none"> • Intraductal proliferation. • Intrapancreatic tumoural mass. • Extrapancreatic tumoural spread. • Metastatic peripancreatic nodes.
Target condition and reference standard(s)	Target condition: cancerous (invasive carcinoma) versus precancerous (dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: 22 (46.8%).
Comparative	
Notes	A number of patients were excluded from the analysis. The reasons were not reported.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			

Cellier 1998 (Continued)

Was a consecutive or random sample of patients enrolled?	Yes	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	No	
		High High

DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS

If a threshold was used, was it pre-specified?	Yes	
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear	
		Unclear Low

DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (dysplasia) - CT

If a threshold was used, was it pre-specified?	Yes	
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear	
		Unclear Low

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
		Unclear Low

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	No	
		High

Cherian 2010
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: consecutive patients.
Patient characteristics and setting	Sample size: 78. Females: not stated. Age: not stated. Presentation: 1. Patients with solid pancreatic lesions and suspected pancreatic cancer who required definitive diagnosis. 2. Atypical histories and symptoms. 3. Equivocal CT findings. 4. Deemed unresectable or unfit for surgery. Setting: secondary care, UK.
Index tests	Index test: EUS-FNA. Further details: Technical specifications: Olympus GF-UCT240-AL5. Performed by: endoscopist and cytologist. Criteria for positive diagnosis: not stated.
Target condition and reference standard(s)	Target condition: benign versus malignant. Reference standard: surgical excision and histology in people who had undergone surgery and clinical follow-up, defined as serial imaging at 12 months that demonstrated progression of disease or patients had clinical deterioration or death. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		

Cherian 2010 (Continued)

		Low	High
DOMAIN 2: Index Test Cancerous versus benign - EUS FNA			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	Low
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	No		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		High	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Yes		
		High	

Choi 2003
Study characteristics

Patient sampling	Type of study: unclear whether prospective or retrospective study. Consecutive or random sample: neither.
Patient characteristics and setting	Sample size: 64. Females: 14 (21.9%). Age: 61 years. Presentation: Patients with IPMN undergoing surgical resection. Setting: secondary care, Korea.
Index tests	Index test: MRI. Further details: Technical specifications: 1.5-T MR system (Magnetom Vision; Siemens, Erlangen, Germany). Performed by: radiologist. Criteria for positive diagnosis: presence of mural nodules.

Choi 2003 (Continued)

Target condition and reference standard(s)	Target condition: precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
--------------------------------------------	----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Flow and timing	Number of indeterminates for whom the results of reference standard were available: 0 (0%). Number of patients who were excluded from the analysis: 18 (28.1%).
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Comparative

Notes

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
		High	High
DOMAIN 2: Index Test Precancerous or cancerous (intermediate or high grade dysplasia or invasive carcinoma) versus precancerous (low grade dysplasia) - MRI			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
		Unclear	Low
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		

Choi 2003 (Continued)

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

High
Correa-Gallego 2009
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: consecutive patients.
Patient characteristics and setting	Sample size: 72. Females: not stated. Age: not stated. Presentation: Patients with IPMN who had undergone surgical resection. Setting: secondary care, USA.
Index tests	Index test: EUS-FNA. Further details: Technical specifications: not stated. Performed by: not stated. Criteria for positive diagnosis: cyst CEA fluid \geq 200 ng/mL.
Target condition and reference standard(s)	Target condition: cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.

Comparative

Notes

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		

Correa-Gallego 2009 (Continued)

	Low	High
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - EUS FNA (CEA > 200 ng/ml)		
If a threshold was used, was it pre-specified?	Yes	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	
	Low	Low
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes	
	Low	Low
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	No	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Yes	
	High	

de Jong 2012
Study characteristics

Patient sampling	Type of study: prospective study. Consecutive or random sample: consecutive patients.
Patient characteristics and setting	Sample size: 32. Females: 19 (59.4%). Age: 62 years. Presentation: Inclusion criteria <ul style="list-style-type: none"> • Patients above 18 years of age with a pancreatic cystic lesion of unknown aetiology detected on cross-sectional imaging (transabdominal ultrasound, CT, MRI). • Patients undergoing surgical resection. Exclusion criteria

de Jong 2012 (Continued)

- Patients with a recent episode of acute pancreatitis or with known chronic pancreatitis.
- Clotting disorders.
- Acute pancreatitis or a synchronic malignancy elsewhere in the body.

Setting: secondary care, Netherlands.

Index tests	Index test: EUS. Further details: Technical specifications: Olympus GF-UC(T)140(P). Performed by: endoscopists. Criteria for positive diagnosis: diffuse main duct dilatation (> 10 mm), and/or mural nodes were present, and/or a solid component was seen outside the cyst. Index test: MRI. Further details: Technical specifications: Avanto 1.5 Tesla MR. Performed by: radiologist. Criteria for positive diagnosis: diffuse main duct dilatation (> 10 mm), and/or mural nodes were present, and/or a solid component was seen outside the cyst.
Target condition and reference standard(s)	Target condition: cancerous (invasive carcinoma) versus precancerous (dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	Interval between index test and reference standard varied, with a median of 78 days.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High
DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS			
If a threshold was used, was it pre-specified?	Yes		

de Jong 2012 (Continued)

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

Unclear

Low

DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (dysplasia) - MRI

If a threshold was used, was it pre-specified? Yes

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

Unclear

Low

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Unclear

Low

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? No

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

High

Doi 2002
Study characteristics

Patient sampling Type of study: retrospective study.
 Consecutive or random sample: neither.

Patient characteristics and setting Sample size: 38.
 Females: 12 (31.6%).
 Age: 60 years.
 Presentation:
 Patients with IPMN who had undergone a pancreatic resection.
 Setting: secondary care, Japan.

Index tests Index test: EUS.

Doi 2002 (Continued)

Further details:
 Technical specifications: not stated.
 Performed by: not stated.
 Criteria for positive diagnosis: presence of mural nodule or papillary projection.

Target condition and reference standard(s)	Target condition: cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	Out of 38 participants included in the study, only 28 underwent EUS. We obtained diagnostic accuracy information from the discussion. The tables provide information on the number of participants who underwent EUS and the diagnostic accuracy of EUS in identifying the presence of the lesion.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - EUS			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	Low
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		

Doi 2002 (Continued)

	Unclear	Low
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	No	
High		

Erkan 2012

Study characteristics	
Patient sampling	Type of study: prospective study. Consecutive or random sample: neither.
Patient characteristics and setting	Sample size: 46. Females: not stated. Age: not stated. Presentation: Patients undergoing PET/CT scan for suspected pancreatic lesions and surgical resection. Setting: secondary care, Germany.
Index tests	Index test: PET. Further details: Technical specifications: model and manufacturer not stated. Performed by: radiologist. Criteria for positive diagnosis: not stated.
Target condition and reference standard(s)	Target condition: cancerous versus benign. Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: 5 (10.9%).
Comparative	
Notes	FLT-PET was also available.

Methodological quality			
Item	Authors' judgement	Risk of bias	Applicability concerns

Erkan 2012 (Continued)

DOMAIN 1: Patient Selection

Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High

DOMAIN 2: Index Test Cancerous versus benign - PET

If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	High

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
		High	

Fischer 2009 - Cystic
Study characteristics

Patient sampling	Type of study: unclear whether prospective or retrospective study. Consecutive or random sample: unclear.
Patient characteristics and setting	Sample size: 33. Females: not stated. Age: not stated. Presentation: Patients with pancreatic lesions undergoing EUS-FNA. Setting: secondary care, country not stated.

Fischer 2009 - Cystic (Continued)

Index tests	Index test: EUS-FNA. Further details: Technical specifications: not stated. Performed by: not stated. Criteria for positive diagnosis: not stated.
Target condition and reference standard(s)	Target condition: precancerous or cancerous versus benign. Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
		Unclear	High
DOMAIN 2: Index Test Precancerous or cancerous versus benign - EUS FNA			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	High
DOMAIN 2: Index Test Cystic lesion subgroup analysis - Precancerous or cancerous versus benign - EUS FNA			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	High
DOMAIN 3: Reference Standard			

Fischer 2009 - Cystic *(Continued)*

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Unclear

Low

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Unclear

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Unclear

Fischer 2009 - Solid
Study characteristics

Patient sampling Type of study: unclear whether prospective or retrospective study. Consecutive or random sample: unclear.

Patient characteristics and setting Sample size: 33. Females: not stated. Age: not stated. Presentation: Patients with pancreatic lesions undergoing EUS-FNA. Setting: secondary care, country not stated.

Index tests Index test: EUS-FNA. Further details: Technical specifications: not stated. Performed by: not stated. Criteria for positive diagnosis: not stated.

Target condition and reference standard(s) Target condition: precancerous or cancerous versus benign. Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.

Flow and timing Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.

Comparative

Notes

Methodological quality

Fischer 2009 - Solid (Continued)

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
		Unclear	High
DOMAIN 2: Index Test Precancerous or cancerous versus benign - EUS FNA			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
		Unclear	

Fisher 2008
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: consecutive patients.
Patient characteristics and setting	Sample size: 48. Females: 33 (68.8%). Age: 60 years.

Imaging modalities for characterising focal pancreatic lesions (Review)

Fisher 2008 (Continued)

Presentation:

Inclusion criteria

- Patients with cystic pancreatic lesions who had undergone surgical resection.

Exclusion criteria

- Patients with a clear history of acute pancreatitis and subsequent development of a pseudocyst were excluded from the study.

Setting: secondary care, USA.

Index tests	Index test: CT. Further details: Technical specifications: not stated. Performed by: radiologist. Criteria for positive diagnosis: not stated.
Target condition and reference standard(s)	Target condition: precancerous or cancerous versus benign. Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
		Low	High
DOMAIN 2: Index Test Precancerous or cancerous versus benign - CT			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
		Unclear	High

Fisher 2008 (Continued)

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
	Unclear
	Low

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
	Unclear

Grieser 2010
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: consecutive patients.
Patient characteristics and setting	Sample size: 105. Females: 32 (30.5%). Age: 58 years. Presentation: Patients undergoing surgical exploration or resection for pancreatic mass and CT scan. Setting: secondary care, Germany.
Index tests	Index test: CT. Further details: Technical specifications: Siemens Somatom Plus 4; GE Healthcare LightSpeed Ultra, LightSpeed 16/Pro16, LightSpeed VCT. Performed by: radiologist. Criteria for positive diagnosis: not stated.
Target condition and reference standard(s)	Target condition: cancerous versus benign. Reference standard: surgical excision or biopsy during exploratory laparotomy for non-resectable cancers. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.

Grieser 2010 (Continued)

Comparative

Notes

Another radiologist has a lower specificity.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
		Unclear	High
DOMAIN 2: Index Test Cancerous versus benign - CT			
If a threshold was used, was it pre-specified?	No		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
		High	High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
		Low	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
		Unclear	

Harrison 1999
Study characteristics

Harrison 1999 (Continued)

Patient sampling	Type of study: retrospective study. Consecutive or random sample: unclear.
Patient characteristics and setting	Sample size: 18. Females: 10 (55.6%). Age: 62 years. Presentation: Patients undergoing surgery for suspected pancreatic cancer. Setting: secondary care, USA.
Index tests	Index test: EUS. Further details: Technical specifications: Olympus UM20. Performed by: endoscopist. Criteria for positive diagnosis: not stated. Index test: CT. Further details: Technical specifications: not stated. Performed by: endoscopist. Criteria for positive diagnosis: not stated.
Target condition and reference standard(s)	Target condition: cancerous versus benign. Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
		Unclear	High
DOMAIN 2: Index Test Cancerous versus benign - EUS			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		

Harrison 1999 (Continued)

		Unclear	High
DOMAIN 2: Index Test Cancerous versus benign - CT			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
		Unclear	

Higashi 1997
Study characteristics

Patient sampling	Type of study: unclear whether prospective or retrospective study. Consecutive or random sample: unclear.
Patient characteristics and setting	Sample size: 34. Females: 16 (47.1%). Age: 61 years. Presentation: Patients with suspected pancreatic tumours undergoing PET and surgery. Setting: secondary care, Japan.
Index tests	Index test: PET. Further details: Technical specifications: not stated. Performed by: not stated. Criteria for positive diagnosis: not stated.
Target condition and reference standard(s)	Target condition: cancerous versus benign. Reference standard: surgical excision.

Higashi 1997 (Continued)

Further details:
 Technical specifications: not applicable.
 Performed by: clinicians.
 Criteria for positive diagnosis: not stated.

Flow and timing

Number of indeterminates for whom the results of reference standard were available: not stated.
 Number of patients who were excluded from the analysis: not stated.

Comparative

Notes

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
		Unclear	High
DOMAIN 2: Index Test Cancerous versus benign - PET			
If a threshold was used, was it pre-specified?	No		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		High	High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		

Higashi 1997 (Continued)

Unclear

Hong 2010

Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: consecutive patients.
Patient characteristics and setting	Sample size: 31. Females: 16 (51.6%). Age: 65 years. Presentation: Patients with IPMN who had undergone CT/PET. Setting: secondary care, Korea.
Index tests	Index test: PET. Further details: Technical specifications: DSTe (GE Healthcare). Performed by: radiologist. Criteria for positive diagnosis: SUVmax > 2.5. Index test: CT. Further details: Technical specifications: LightSpeed Plus (GE Healthcare) or Somatom Sensation 64 (Siemens Healthcare). Performed by: radiologist. Criteria for positive diagnosis: <ul style="list-style-type: none"> • Main duct-type. • Marked dilatation of the main pancreatic duct (> 10 mm). • Large mural nodule (> 1 cm). • Large cyst size (> 3 cm). • Irregular or septate cyst. • Calcification. • Patulous duodenal papilla.
Target condition and reference standard(s)	Target condition: cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia). Reference standard: surgical excision, open laparotomy biopsy or biopsy of metastases. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	

Methodological quality

Hong 2010 (Continued)

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
		Unclear	High
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - PET (SUV max 2-2.5)			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
		Low	Low
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - CT			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Unclear		
		High	

Hu 2013

Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: unclear.
Patient characteristics and setting	Sample size: 80. Females: 36 (45.0%). Age: 57 years. Presentation: Inclusion criteria <ul style="list-style-type: none"> Patients with solitary pancreatic lesions who had undergone PET scan and surgical resection. Exclusion criteria <ul style="list-style-type: none"> Patients with suspected malignancies in other areas of the body. Setting: secondary care, China.
Index tests	Index test: PET. Further details: Technical specifications: Biograph 16 HR PET/CT scanner (Siemens). Performed by: radiologist. Criteria for positive diagnosis: SUVmax > 3.5.
Target condition and reference standard(s)	Target condition: cancerous versus benign. Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		

Hu 2013 (Continued)

		Unclear	High
DOMAIN 2: Index Test Cystic lesion subgroup analysis - Cancerous versus benign - PET			
If a threshold was used, was it pre-specified?	No		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
		High	Low
DOMAIN 2: Index Test Cancerous versus benign - PET (SUV max > 3.5)			
If a threshold was used, was it pre-specified?	No		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
		High	Low
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes		
		Low	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
		Unclear	

Jafarimehr 2010
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: unclear.
Patient characteristics and setting	Sample size: 76. Females: 40 (52.6%). Age: not stated. Presentation: Patients with pancreatic lesions with PET or PET/CT. Setting: secondary care, USA.

Jafarimehr 2010 (Continued)

Index tests	Index test: PET. Further details: Technical specifications: not stated. Performed by: not stated. Criteria for positive diagnosis: not stated.
Target condition and reference standard(s)	Target condition: cancerous versus benign or precancerous. Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.

Comparative

Notes

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
		Unclear	High
DOMAIN 2: Index Test Cancerous versus benign or precancerous - PET			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			

Jafarimehr 2010 (Continued)

Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Unclear	

Jang 2014a

Study characteristics	
Patient sampling	Type of study: retrospective study. Consecutive or random sample: consecutive patients.
Patient characteristics and setting	Sample size: 34. Females: 21 (61.8%). Age: 52 years. Presentation: Patients with neuroendocrine pancreatic lesions who had undergone MRI and surgery. Setting: secondary care, Korea.
Index tests	Index test: MRI. Further details: Technical specifications: Intera Achieva 3.0-T. Performed by: radiologist. Criteria for positive diagnosis: apparent diffusion coefficient: 1.09×10^3 mm ² /s.
Target condition and reference standard(s)	Target condition: precancerous or cancerous versus benign. Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: 7 (20.6%).
Comparative	
Notes	

Methodological quality			
Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		

Jang 2014a (Continued)

Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High
DOMAIN 2: Index Test Precancerous or cancerous versus benign - MRI			
If a threshold was used, was it pre-specified?	No		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
		High	High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
		High	

Jang 2014b
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: consecutive patients.
Patient characteristics and setting	Sample size: 65. Females: 27 (41.5%). Age: not stated. Presentation: Patients with IPMN undergoing MRI and surgery. Setting: secondary care, Korea.
Index tests	Index test: MRI. Further details: Technical specifications: Intera Achieva 3.0-T. Performed by: radiologist.

Jang 2014b (Continued)

Criteria for positive diagnosis: signal intensity of normal pancreatic parenchyma at the mural nodule, septum, cystic wall, ductal wall, and solid lesion of the IPMNs.

Target condition and reference standard(s)	Target condition: cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: 4 (6.2%).
Comparative	
Notes	A second observer with 1 more false positive (with correspondingly 1 less true negative) was also available. The sensitivity and specificity are for combined conventional- and diffusion-weighted scan. The accuracy was lower with conventional scan.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - MRI			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low

Jang 2014b (Continued)

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Unclear

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

High

Jin 2013a
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: unclear.
Patient characteristics and setting	Sample size: 162. Females: 99 (61.1%). Age: 64 years. Presentation: Patients with pancreatic cysts who underwent surgery. Setting: secondary care, further details not available.
Index tests	Index test: EUS-FNA. Further details: Technical specifications: model and manufacturer not stated. Performed by: endoscopist. Criteria for positive diagnosis: cellular atypia.
Target condition and reference standard(s)	Target condition: cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.

Comparative

Notes

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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DOMAIN 1: Patient Selection

Jin 2013a (Continued)

Was a consecutive or random sample of patients enrolled?	Unclear	
Was a case-control design avoided?	Yes	
Did the study avoid inappropriate exclusions?	Unclear	
		Unclear High
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - EUS FNA		
If a threshold was used, was it pre-specified?	Yes	
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear	
		Unclear Low
DOMAIN 3: Reference Standard		
Is the reference standards likely to correctly classify the target condition?	Yes	
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear	
		Unclear Low
DOMAIN 4: Flow and Timing		
Was there an appropriate interval between index test and reference standard?	Unclear	
Did all patients receive the same reference standard?	Yes	
Were all patients included in the analysis?	Unclear	
		Unclear

Jin 2015
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: unclear.
Patient characteristics and setting	Sample size: 86. Females: not stated. Age: not stated. Presentation: Patients with mucinous pancreatic cysts undergoing operative resection. Setting: secondary care, USA.
Index tests	Index test: EUS-FNA.

Jin 2015 (Continued)

 Further details:
 Technical specifications: EUS model not stated; 22-gauge needle.
 Performed by: not stated.
 Criteria for positive diagnosis: not stated.

Target condition and reference standard(s)	Target condition: cancerous (invasive carcinoma) versus precancerous (dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: 1 (1.3%). Number of patients who were excluded from the analysis: 9 (10.6%).
Comparative	
Notes	Results were reported for only 76 out of 77 participants with mucinous cysts. The final results were possible only for these participants.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High
DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS FNA			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	Low
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			

Jin 2015 (Continued)

Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
High	

Kalha 2003
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: neither.
Patient characteristics and setting	Sample size: 24. Females: not stated. Age: not stated. Presentation: Patients undergoing EUS-FNA and surgery for cystic pancreatic lesions. Setting: secondary care, USA.
Index tests	Index test: EUS-FNA. Further details: Technical specifications: EUS model or needle size not stated. Performed by: not stated. Criteria for positive diagnosis: cyst CEA fluid \geq 500 ng/mL.
Target condition and reference standard(s)	Target condition: cancerous versus benign or precancerous. Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	Of 84 participants, 60 who were observed were excluded because the reference standard was not adequate for these participants.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		

Kalha 2003 (Continued)

Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High

DOMAIN 2: Index Test Cancerous versus benign or precancerous - EUS FNA (cytology)

If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	Low

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
		High	

Kamata 2016a
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: neither.
Patient characteristics and setting	Sample size: 70. Females: 39 (55.7%). Age: 62 years. Presentation: Inclusion criteria <ul style="list-style-type: none"> • People with pancreatic cyst. Exclusion criteria

Kamata 2016a (Continued)

- People with multiple cysts.
- People with intraductal pancreatic cancer foci.

Setting: secondary care, Japan.

Index tests	Index test: EUS. Further details: Technical specifications: GF-UCT260; Olympus Medical Systems, Tokyo, Japan. Performed by: endoscopist. Criteria for positive diagnosis: presence of mural nodules.
Target condition and reference standard(s)	Target condition: cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) or benign. Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: 0 (0%). Number of patients who were excluded from the analysis: 419 (85.7%).
Comparative	
Notes	

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) or benign - EUS			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	Low
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		

Kamata 2016a (Continued)

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Unclear
Low
DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Unclear

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

High
Kato 1995
Study characteristics

Patient sampling Type of study: unclear whether prospective or retrospective study.
 Consecutive or random sample: unclear.

Patient characteristics and setting Sample size: 24.
 Females: not stated.
 Age: not stated.
 Presentation:
 Patients with pancreatic masses.
 Setting: secondary care, Japan.

Index tests Index test: PET.
 Further details:
 Technical specifications: HEADTOME-IV (Shimadzu Corporation).
 Performed by: not stated.
 Criteria for positive diagnosis: not stated.

Target condition and reference standard(s) Target condition: cancerous versus benign.
 Reference standard: surgical excision, open laparotomy biopsy or clinical follow-up for at least 3 years.
 Further details:
 Technical specifications: not applicable.
 Performed by: clinicians.
 Criteria for positive diagnosis: not stated.

Flow and timing Number of indeterminates for whom the results of reference standard were available: not stated.
 Number of patients who were excluded from the analysis: not stated.

Comparative

Notes

Methodological quality

Kato 1995 (Continued)

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
		Unclear	High
DOMAIN 2: Index Test Cancerous versus benign - PET			
If a threshold was used, was it pre-specified?	Unclear		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Unclear		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	No		
Were all patients included in the analysis?	Unclear		
		High	

Kim 2015
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: neither.
Patient characteristics and setting	Sample size: 123. Females: not stated. Age: not stated. Presentation:

Kim 2015 (Continued)

Patients with surgically proven and histopathologically confirmed IPMN and who had undergone MRI examinations with diffusion-weighted imaging before surgery.
Setting: secondary care, Korea.

Index tests	<p>Index test: MRI. Further details: Technical specifications: Verio or Trio (Siemens Medical Solutions), Signa HDTx (GE Medical Systems), Achieva (Philips Healthcare). Performed by: radiologist. Criteria for positive diagnosis: signal intensity of normal pancreatic parenchyma at the mural nodule, septum, cystic wall, ductal wall, and solid lesion of the IPMNs.</p>
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Target condition and reference standard(s)	<p>Target condition: cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.</p>
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Flow and timing	<p>Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: 30 (24.4%).</p>
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Comparative

Notes	<p>25 participants were excluded due to lack of diffusion-weighted MRI or subquality MRI. The sensitivities and specificities reported by other radiologists were lower.</p>
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Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - MRI			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
		Low	Low

DOMAIN 3: Reference Standard

Kim 2015 (Continued)

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Unclear

Low

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Unclear

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

High

Klau 2011
Study characteristics

Patient sampling

Type of study: retrospective study.
 Consecutive or random sample: consecutive patients.

Patient characteristics and setting

Sample size: 29.
 Females: 10 (34.5%).
 Age: 61 years.
 Presentation:
 Patients with solid focal pancreatic lesions who had undergone surgery.
 Setting: secondary care, Germany.

Index tests

Index test: MRI.
 Further details:
 Technical specifications: 1.5 T Magnetom Avanto, Siemens.
 Performed by: radiologist.
 Criteria for positive diagnosis: perfusion fraction < 0.1105.

Target condition and reference standard(s)

Target condition: cancerous versus benign.
 Reference standard: surgical excision.
 Further details:
 Technical specifications: not applicable.
 Performed by: clinicians.
 Criteria for positive diagnosis: not stated.

Flow and timing

Number of indeterminates for whom the results of reference standard were available: not stated.
 Number of patients who were excluded from the analysis: not stated.

Comparative

Notes

Sensitivities and specificities for other cut-off values were lower.

Klau 2011 (Continued)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
		Low	High
DOMAIN 2: Index Test Cancerous versus benign - MRI			
If a threshold was used, was it pre-specified?	No		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		High	High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
		Unclear	

Kobayashi 2012
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: neither.
Patient characteristics and setting	Sample size: 36. Females: 15 (41.7%).

Imaging modalities for characterising focal pancreatic lesions (Review)

Kobayashi 2012 (Continued)

Age: 66 years.
Presentation:
Patients with IPMN who had undergone surgical resection.
Setting: secondary care, Japan.

Index tests	Index test: EUS. Further details: Technical specifications: UM20, UM2000; Olympus. Performed by: endoscopists. Criteria for positive diagnosis: lateral spread of the nodule > 15 mm.
Target condition and reference standard(s)	Target condition: cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	Of 238 participants with IPMN, only 46 who had undergone surgical resection were included in the analysis; another criterion for diagnosis with lower diagnostic test accuracy was also available.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - EUS			
If a threshold was used, was it pre-specified?	Unclear		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	High
DOMAIN 3: Reference Standard			

Kobayashi 2012 (Continued)

Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Unclear Low	
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
High	

Kubo 2001
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: unclear.
Patient characteristics and setting	Sample size: 51. Females: 19 (37.3%). Age: 67 years. Presentation: Patients with IPMN who had undergone surgical resection. Setting: secondary care, Japan.
Index tests	Index test: EUS. Further details: Technical specifications: GF-UM2, UM3, UM20; Olympus. Performed by: endoscopists. Criteria for positive diagnosis: <ul style="list-style-type: none"> • in main duct type, tumour > 10 mm dilated MPD; • in branch duct type, large cystic tumour (> 40 mm) with irregular thick septum; or • large mural nodule (> 10 mm).
Target condition and reference standard(s)	Target condition: cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated.

Kubo 2001 (Continued)

Number of patients who were excluded from the analysis: not stated.

Comparative

Notes

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
		Unclear	High
DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (low grade dysplasia) - EUS			
If a threshold was used, was it pre-specified?	Unclear		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
		Low	Low
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
		Unclear	

Kucera 2012
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: neither.
Patient characteristics and setting	Sample size: 47. Females: 15 (31.9%). Age: 66 years. Presentation: Patients with IPMN who had undergone EUS-FNA with cyst fluid analysis and surgical resection. Setting: secondary care, USA.
Index tests	Index test: EUS-FNA. Further details: Technical specifications: GF-UC30P and GF-UC140P, Olympus. Performed by: endoscopist and cytologist. Criteria for positive diagnosis: CEA > 200 ng/mL.
Target condition and reference standard(s)	Target condition: cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	Of 87 participants who had undergone surgical resection for IPMN, 40 were excluded because they had not undergone EUS-FNA.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - EUS FNA (CEA > 200 ng/ml)			
If a threshold was used, was it pre-specified?	Unclear		

Kucera 2012 (Continued)

Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
		High	

Le Baleur 2011a
Study characteristics

Patient sampling	Type of study: unclear whether prospective or retrospective study. Consecutive or random sample: unclear.
Patient characteristics and setting	Sample size: 60. Females: 59 (98.3%). Age: 43 years. Presentation: Patients with MCN who had undergone surgical resection. Setting: secondary care, France.
Index tests	Index test: CT. Further details: Technical specifications: not stated. Performed by: not stated. Criteria for positive diagnosis: presence of mural nodule.
Target condition and reference standard(s)	Target condition: pre-malignant (low- or intermediate-grade dysplasia) versus malignant (high-grade dysplasia or invasive carcinoma). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians.

Le Baleur 2011a (Continued)

Criteria for positive diagnosis: not stated.

Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	Sensitivity and specificity for other parameters related to size of tumour were available and were lower.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
		Unclear	High
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - CT			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	Low
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		

Le Baleur 2011a (Continued)

Unclear

Lee 2014
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: unclear.
Patient characteristics and setting	Sample size: 84. Females: 29 (34.5%). Age: 65 years. Presentation: Patients with branch duct IPMN who had undergone surgical resection. Setting: secondary care, Korea.
Index tests	Index test: EUS. Further details: Technical specifications: not stated. Performed by: endoscopists. Criteria for positive diagnosis: an EUS score composed of cyst size, mural nodule height, associated main pancreatic duct dilation, thick septum, and patulous papilla ≥ 7 .
Target condition and reference standard(s)	Target condition: cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High

Lee 2014 (Continued)

DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - EUS

If a threshold was used, was it pre-specified?	No		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		High	High

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	No		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
		High	

Maire 2008
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: unclear.
Patient characteristics and setting	Sample size: 41. Females: 27 (65.9%). Age: 64 years. Presentation: Patients with IPMN who had undergone surgical resection. Setting: secondary care, France.
Index tests	Index test: EUS-FNA. Further details: Technical specifications: Pentax-FG 32 UA 120°. Performed by: endoscopists. Criteria for positive diagnosis: CEA > 200 ng/mL. Second criteria for positive diagnosis: carbohydrate antigen 19-9 > 1000 U/mL.
Target condition and reference standard(s)	Target conditions:

Maire 2008 (Continued)

1. Cancerous (invasive carcinoma) versus precancerous (dysplasia).
2. Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia)

Reference standard: surgical excision.

Further details:

Technical specifications: not applicable.

Performed by: clinicians.

Criteria for positive diagnosis: not stated.

Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	6 different criteria for diagnosis were used. All 6 are listed.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
		Unclear	High
DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS FNA (CEA > 200 ng/ml)			
If a threshold was used, was it pre-specified?	No		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		High	High
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - EUS FNA (CEA > 200 ng/ml)			
If a threshold was used, was it pre-specified?	No		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		High	High
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - EUS FNA (Ca 19.9 > 1000 U/ml)			
If a threshold was used, was it pre-specified?	No		

Maire 2008 (Continued)

Were the index test results interpreted without knowledge of the results of the reference standard? Unclear

High
High
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Unclear
Low
DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Unclear

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Unclear
McHenry 2002
Study characteristics

Patient sampling Type of study: retrospective study.
 Consecutive or random sample: unclear.

Patient characteristics and setting Sample size: 45.
 Females: not stated.
 Age: not stated.
 Presentation:
 Patients with cystic pancreatic lesion who had undergone surgical resection.
 Setting: secondary care, USA.

Index tests Index test: EUS-FNA.
 Further details:
 Technical specifications: Pentax echoendoscope.
 Performed by: not stated.
 Criteria for positive diagnosis: not stated.

Target condition and reference standard(s) Target condition: precancerous or cancerous versus benign.
 Reference standard: surgical excision.
 Further details:
 Technical specifications: not applicable.
 Performed by: clinicians.
 Criteria for positive diagnosis: not stated.

Flow and timing Number of indeterminates for whom the results of reference standard were available: not stated.

McHenry 2002 (Continued)

Number of patients who were excluded from the analysis: not stated.

Comparative

Notes

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
		Unclear	High
DOMAIN 2: Index Test Cystic lesion subgroup analysis - Precancerous or cancerous versus benign - EUS FNA			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		
		Unclear	

Nakagawa 2009
Study characteristics
Imaging modalities for characterising focal pancreatic lesions (Review)

Nakagawa 2009 (Continued)

Patient sampling	Type of study: retrospective study. Consecutive or random sample: neither.
Patient characteristics and setting	Sample size: 34. Females: not stated. Age: not stated. Presentation: Patients with cystic pancreatic lesion who had undergone surgical resection and EUS. Setting: secondary care, Japan.
Index tests	Index test: EUS. Further details: Technical specifications: GF-UMP230 or GF-UC2000P (Olympus). Performed by: endoscopists. Criteria for positive diagnosis: height of protruding lesion > 4.1 mm. Index test: CT. Further details: Technical specifications: GE LightSpeed Ultra, GE LightSpeed 16; GE Medical Systems. Performed by: radiologists. Criteria for positive diagnosis: height of protruding lesion > 4.1 mm.
Target condition and reference standard(s)	Target condition: cancerous (invasive carcinoma) versus precancerous (dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High

DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS

Nakagawa 2009 *(Continued)*

If a threshold was used, was it pre-specified?	No		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		High	High

DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (dysplasia) - CT

If a threshold was used, was it pre-specified?	No		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
		High	High

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
		High	

Nara 2009
Study characteristics

Patient sampling	Type of study: unclear whether prospective or retrospective study. Consecutive or random sample: consecutive patients.
Patient characteristics and setting	Sample size: 123. Females: 53 (43.1%). Age: 65 years. Presentation: Patients with IPMN who had undergone surgical resection. Setting: secondary care, Japan.
Index tests	Index test: CT. Further details: Technical specifications: single-slice helical CT or MDCT. Performed by: radiologist.

Nara 2009 (Continued)

Criteria for positive diagnosis: irregularly shaped hypoattenuating solid mass detected adjacent to or surrounding an IPMN on contrast-enhanced CT.

Target condition and reference standard(s)	Target condition: cancerous (invasive carcinoma) versus precancerous (dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
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Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
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Comparative

Notes

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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DOMAIN 1: Patient Selection

Was a consecutive or random sample of patients enrolled?	Yes		
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Was a case-control design avoided?	Yes		
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Did the study avoid inappropriate exclusions?	Yes		
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Low

High

DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (dysplasia) - CT

If a threshold was used, was it pre-specified?	Yes		
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Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
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Low

Low

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	Yes		
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Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
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Unclear

Low

DOMAIN 4: Flow and Timing

Nara 2009 (Continued)

Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Unclear	

Ogawa 2008
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: consecutive patients.
Patient characteristics and setting	Sample size: 64. Females: 20 (31.3%). Age: 65 years. Presentation: Patients with surgically proven and histopathologically confirmed IPMN. Setting: secondary care, Japan.
Index tests	Index test: CT. Further details: Technical specifications: Aquilion; Toshiba. Performed by: radiologist. Criteria for positive diagnosis: main pancreatic duct - the maximum diameter, the presence of a septum, and the presence of a mural nodule and its maximum size (length of major axis); the type (unilocular or multilocular) of lesion, the maximum size of the lesion, the presence of wall thickness.
Target condition and reference standard(s)	Target conditions: <ol style="list-style-type: none">Cancerous (invasive carcinoma) versus precancerous (dysplasia).Precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: 5 (7.8%).
Comparative	
Notes	Only analysis at lesion level was available.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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Ogawa 2008 (Continued)

DOMAIN 1: Patient Selection

Was a consecutive or random sample of patients enrolled?	Yes
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Was a case-control design avoided?	Yes
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Did the study avoid inappropriate exclusions?	No
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High
High
DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (dysplasia) - CT

If a threshold was used, was it pre-specified?	Unclear
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Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
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Unclear
Low
DOMAIN 2: Index Test Precancerous or cancerous (intermediate or high grade dysplasia or invasive carcinoma) versus precancerous (low grade dysplasia) - CT

If a threshold was used, was it pre-specified?	Unclear
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Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
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Unclear
Low
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	Yes
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Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
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Unclear
Low
DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	No
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Did all patients receive the same reference standard?	Yes
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Were all patients included in the analysis?	No
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High

Ogawa 2014
Study characteristics

Patient sampling	Type of study: unclear whether prospective or retrospective study. Consecutive or random sample: consecutive patients.
Patient characteristics and setting	Sample size: 38. Females: 12 (31.6%). Age: 68 years. Presentation: Patients with IPMN undergoing surgery and MRI. Setting: secondary care, Japan.
Index tests	Index test: MRI. Further details: Technical specifications: EXCELART Vantage, Toshiba. Performed by: radiologist. Criteria for positive diagnosis: presence of positive signal in diffusion-weighted imaging.
Target condition and reference standard(s)	Target condition: cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: 3 (7.9%).
Comparative	
Notes	

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - MRI			
If a threshold was used, was it pre-specified?	Yes		

Ogawa 2014 (Continued)

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

Low
Low
DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Unclear
Low
DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Unclear

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No

High
Otomi 2014
Study characteristics

Patient sampling Type of study: retrospective study.
Consecutive or random sample: consecutive patients.

Patient characteristics and setting Sample size: 32.
Females: 17 (53.1%).
Age: 63 years.
Presentation:
Patients with pancreatic lesions undergoing PET/CT prior to surgery other than pancreatic adenocarcinoma.
Setting: secondary care, Japan.

Index tests Index test: PET.
Further details:
Technical specifications: F100 & CYPRIS (Sumitomo Heavy Industries) and Aquido (Toshiba) CT scanner.
Performed by: radiologist.
Criteria for positive diagnosis: SUVmax > 2.4.

Target condition and reference standard(s) Target condition: precancerous or cancerous versus benign.
Reference standard: surgical excision.
Further details:
Technical specifications: not applicable.
Performed by: clinicians.
Criteria for positive diagnosis: not stated.

Otomi 2014 (Continued)

Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
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Comparative

Notes	Sensitivity and specificity for other parameters such as visualisation and SUVmean were available.
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Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
		Low	High
DOMAIN 2: Index Test Precancerous or cancerous versus benign - PET (SUV max > 2.4)			
If a threshold was used, was it pre-specified?	No		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		High	High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
		Unclear	

Pais 2007
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: unclear.
Patient characteristics and setting	Sample size: 74. Females: 36 (48.6%). Age: 65 years. Presentation: Patients with IPMN undergoing surgery and EUS-FNA. Setting: secondary care, USA.
Index tests	Index test: EUS-FNA. Further details: Technical specifications: Olympus GF-UM20, GF-UM130, or GF-UM160; 22-gauge needle. Performed by: endoscopist and cytologist. Criteria for positive diagnosis: presence of hyperchromasia, nuclear crowding, and loss of nuclear uniformity, nucleolar prominence, or chromatin abnormalities.
Target condition and reference standard(s)	Target condition: cancerous (invasive carcinoma) versus precancerous (dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
		Unclear	High
DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS FNA			

Pais 2007 (Continued)

If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
		Unclear	Low
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	No		
		High	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	No		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
		High	

Sahani 2006
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: unclear.
Patient characteristics and setting	Sample size: 25. Females: 12 (48.0%). Age: 69 years. Presentation: Patients with IPMN undergoing surgery. Setting: secondary care, USA.
Index tests	<p>Index test: CT. Further details: Technical specifications: LightSpeed QX/I (GE Medical Systems). Performed by: radiologist. Criteria for positive diagnosis: presence of mural nodules, papillary projections, or a solid mass in the dilated duct or within the cystic lesion.</p> <p>Index test: MRI. Further details: Technical specifications: 1.5-T system Signa (GE Medical Systems). Performed by: radiologist. Criteria for positive diagnosis: presence of mural nodules, papillary projections, or a solid mass in the dilated duct or within the cystic lesion.</p>

Sahani 2006 (Continued)

Target condition and reference standard(s)	Target condition: precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
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Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
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Comparative	
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Notes	
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Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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DOMAIN 1: Patient Selection

Was a consecutive or random sample of patients enrolled?	Unclear		
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Was a case-control design avoided?	Yes		
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Did the study avoid inappropriate exclusions?	Unclear		
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		Unclear	High
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DOMAIN 2: Index Test Precancerous or cancerous (intermediate or high grade dysplasia or invasive carcinoma) versus precancerous (low grade dysplasia) - CT

If a threshold was used, was it pre-specified?	No		
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Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
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		High	Low
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DOMAIN 2: Index Test Precancerous or cancerous (intermediate or high grade dysplasia or invasive carcinoma) versus precancerous (low grade dysplasia) - MRI

If a threshold was used, was it pre-specified?	No		
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Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
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		High	Low
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DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	Yes		
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Sahani 2006 (Continued)

Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Unclear
Low
DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? Unclear

Unclear
Saito 2013
Study characteristics

Patient sampling Type of study: retrospective study.
 Consecutive or random sample: consecutive patients.

Patient characteristics and setting Sample size: 48.
 Females: 16 (33.3%).
 Age: 69 years.
 Presentation:
 Patients with IPMN who had undergone surgical resection.
 Setting: secondary care, Japan.

Index tests Index test: PET.
 Further details:
 Technical specifications: Aquiduo (Toshiba Medical Systems), Advance NXi (GE Healthcare), and Discovery ST (GE Healthcare).
 Performed by: radiologist.
 Criteria for positive diagnosis: SUVmax > 2 and retention index < -10.

Target condition and reference standard(s) Target condition: cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia).
 Reference standard: surgical excision.
 Further details:
 Technical specifications: not applicable.
 Performed by: clinicians.
 Criteria for positive diagnosis: not stated.

Flow and timing Number of indeterminates for whom the results of reference standard were available: not stated.
 Number of patients who were excluded from the analysis: not stated.

Comparative

Notes Sensitivity and specificity for SUVmax > 2 are also available.

Saito 2013 (Continued)

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
		Low	High
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - PET (SUV max 2-2.5)			
If a threshold was used, was it pre-specified?	No		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		High	High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Yes		
		Unclear	

Salla 2007
Study characteristics

Patient sampling	Type of study: retrospective study.
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Salla 2007 (Continued)

Consecutive or random sample: consecutive patients.

Patient characteristics and setting

Sample size: 8.
Females: 3 (37.5%).
Age: 63 years.
Presentation:
Patients with IPMN who had undergone surgical resection.
Setting: secondary care, Greece.

Index tests

Index test: EUS-FNA.
Further details:
Technical specifications: equipment not stated; 22-gauge needle.
Performed by: endoscopist.
Criteria for positive diagnosis: not stated.

Target condition and reference standard(s)

Target condition: cancerous (invasive carcinoma) versus precancerous (dysplasia).
Reference standard: surgical excision.
Further details:
Technical specifications: not applicable.
Performed by: clinicians.
Criteria for positive diagnosis: not stated.

Flow and timing

Number of indeterminates for whom the results of reference standard were available: not stated.
Number of patients who were excluded from the analysis: not stated.

Comparative

Notes

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Yes		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Yes		
		Low	High
DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS FNA			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	High
DOMAIN 3: Reference Standard			

Salla 2007 (Continued)

Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Unclear Low	
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
Unclear	

Sedlack 2002
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: neither.
Patient characteristics and setting	Sample size: 34. Females: 18 (52.9%). Age: 55 years. Presentation: Patients with cystic lesions of pancreas who had undergone EUS and surgical resection. Setting: secondary care, USA.
Index tests	Index test: EUS. Further details: Technical specifications: GFU-130, Olympus. Performed by: endoscopist. Criteria for positive diagnosis: If 1 or more of the following EUS criteria were met. <ul style="list-style-type: none"> • Wall thickness of 3 mm or greater, macroseptation (all cyst compartments > 10 mm diameter). • Presence of a mass or intramural growth. • Cystic dilation of the main pancreatic duct. Index test: EUS-FNA. Further details: Technical specifications: GFUC-30P, Olympus; 22-gauge needle. Performed by: endoscopist. Criteria for positive diagnosis: CEA \geq 50 ng/mL. Second criteria for positive diagnosis: not stated.

Sedlack 2002 (Continued)

Target condition and reference standard(s)	Target condition: precancerous or cancerous versus benign. Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.

Comparative

Notes

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High
DOMAIN 2: Index Test Precancerous or cancerous versus benign - EUS			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	Low
DOMAIN 2: Index Test Precancerous or cancerous versus benign - EUS FNA			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	Low
DOMAIN 2: Index Test Precancerous or cancerous versus benign - EUS FNA (CEA > 50 ng/ml)			
If a threshold was used, was it pre-specified?	Unclear		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	High

Sedlack 2002 (Continued)

DOMAIN 2: Index Test Cystic lesion subgroup analysis - Precancerous or cancerous versus benign - EUS FNA

If a threshold was used, was it pre-specified?	Unclear
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear
	Unclear Low

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
	Unclear Low

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
	High

Smith 2016
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: neither.
Patient characteristics and setting	Sample size: 138. Females: 99 (71.7%). Age: 62 years. Presentation: Patients with IPMN or MCN. Setting: secondary care, USA.
Index tests	Index test: EUS-FNA. Further details: Technical specifications: not stated. Performed by: not stated. Criteria for positive diagnosis: high-grade atypia or worse. Second criteria for positive diagnosis: abnormal cytology.
Target condition and reference standard(s)	Target condition: cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia). Reference standard: surgical excision. Further details:

Smith 2016 (Continued)

Technical specifications: not applicable.
 Performed by: clinicians.
 Criteria for positive diagnosis: not stated.

Flow and timing

Number of indeterminates for whom the results of reference standard were available: 0 (0%).
 Number of patients who were excluded from the analysis: 11 (8%).

Comparative

Notes

Diagnostic accuracy was also available for another threshold (abnormal cytology) with lower diagnostic accuracy.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - EUS FNA			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
		Unclear	Low
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	No		
Did all patients receive the same reference standard?	Yes		

Smith 2016 (Continued)

Were all patients included in the analysis? No

High

Takanami 2011
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: neither.
Patient characteristics and setting	Sample size: 59. Females: 3 (5.1%). Age: 66 years. Presentation: Patients with IPMN with mural nodules who had undergone PET/CT and surgical resection. Setting: secondary care, Japan.
Index tests	Index test: PET. Further details: Technical specifications: Biograph LSO DUO PET/CT scanner, Siemens. Performed by: radiologist. Criteria for positive diagnosis: SUVmax > 2.3.
Target condition and reference standard(s)	Target condition: cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: 43 (72.9%).
Comparative	
Notes	Only 16 of 43 people with IPMN were included in the analysis. Sensitivity was also available for SUVmax 2.0 and 2.5.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		

Takanami 2011 (Continued)

		High	High
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - PET (SUV max 2-2.5)			
If a threshold was used, was it pre-specified?	No		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
		High	High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
		High	

Takeshita 2008
Study characteristics

Patient sampling	Type of study: unclear whether prospective or retrospective study. Consecutive or random sample: unclear.
Patient characteristics and setting	Sample size: 53. Females: 25 (47.2%). Age: 65 years. Presentation: Patients with IPMN who had undergone surgery. Setting: secondary care, Japan.
Index tests	Index test: CT. Further details: Technical specifications: LightSpeed QX/I; GE Medical Systems. Performed by: radiologist.

Takeshita 2008 (Continued)

Criteria for positive diagnosis: presence of mural nodule and main ductal dilatation (> 5 mm) or presence of mural nodule and cystic tumour size > 3 cm.

Target condition and reference standard(s)	Target condition: cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: 7 (13.2%).
Comparative	
Notes	Sensitivity and specificity for other parameters were available.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
		Unclear	High
DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (low grade dysplasia) - CT			
If a threshold was used, was it pre-specified?	No		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		High	High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			

Takeshita 2008 (Continued)

Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Unclear	

Tan 2009
Study characteristics

Patient sampling	Type of study: unclear whether prospective or retrospective study. Consecutive or random sample: neither.
Patient characteristics and setting	Sample size: 20. Females: 9 (45.0%). Age: 62 years. Presentation: Patients with IPMN who had undergone surgical resection. Setting: secondary care, China.
Index tests	Index test: CT. Further details: Technical specifications: LightSpeed QX/I or LightSpeed 16; GE Medical Systems. Performed by: radiologist. Criteria for positive diagnosis: not stated.
Target condition and reference standard(s)	Target condition: precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
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DOMAIN 1: Patient Selection

Tan 2009 (Continued)

Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High
DOMAIN 2: Index Test Precancerous or cancerous (intermediate or high grade dysplasia or invasive carcinoma) versus precancerous (low grade dysplasia) - CT			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
		Low	High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Yes		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
		High	

Taouli 2000
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: neither.
Patient characteristics and setting	Sample size: 36. Females: 17 (47.2%). Age: 61 years. Presentation: Patients with IPMN who had undergone surgical resection. Setting: secondary care, France.
Index tests	Index test: CT.

Taouli 2000 (Continued)

Further details:
 Technical specifications: Elscint CT Twin; Elscint.
 Performed by: radiologist.
 Criteria for positive diagnosis: dilatation of MPD > 10 mm.

Target condition and reference standard(s)	Target condition: cancerous (invasive carcinoma) versus precancerous (dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	Sensitivity and specificity for other parameters were available.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High
DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (dysplasia) - CT			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes		
		Low	High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			

Taouli 2000 (Continued)

Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
High	

Tomimaru 2010
Study characteristics

Patient sampling	Type of study: unclear whether prospective or retrospective study. Consecutive or random sample: neither.
Patient characteristics and setting	Sample size: 29. Females: 13 (44.8%). Age: 65 years. Presentation: Patients with IPMN who had undergone surgical resection. Setting: secondary care, Japan.
Index tests	Index test: PET. Further details: Technical specifications: Headtome/Set 2400W; Shimadzu Corporation. Performed by: radiologist. Criteria for positive diagnosis: SUVmax > 2.5.
Target condition and reference standard(s)	Target condition: cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.

Comparative

Notes

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		

Tomimaru 2010 (Continued)

Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High

DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - PET (SUV max 2-2.5)

If a threshold was used, was it pre-specified?	No		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		High	High

DOMAIN 3: Reference Standard

Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low

DOMAIN 4: Flow and Timing

Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
		High	

Yamao 2001
Study characteristics

Patient sampling	Type of study: unclear whether prospective or retrospective study. Consecutive or random sample: neither.
Patient characteristics and setting	Sample size: 49. Females: 18 (36.7%). Age: 63 years. Presentation: Patients with IPMN undergoing surgical resection. Setting: secondary care, Japan.
Index tests	Index test: CT. Further details: Technical specifications: CT9200 (Yokogawa), HiSpeed Advantage (GE). Performed by: radiologist.

Yamao 2001 (Continued)

Criteria for positive diagnosis: wall-thickening, presence of nodule, and heterogenous pattern.

Index test: EUS.

Further details:

Technical specifications: JF-UM20 and GF-UM240 (Olympus).

Performed by: endoscopist.

Criteria for positive diagnosis: wall-thickening, presence of nodule, and heterogenous pattern.

Target condition and reference standard(s)	Target conditions: <ol style="list-style-type: none"> 1. Cancerous (invasive carcinoma) versus precancerous (dysplasia). 2. Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: 1 (2%). Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	The study reported 3 x 3 table for CT scan and EUS. 1 patient was excluded from analysis, but this differed between CT and EUS.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	No		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	No		
		High	High
DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	Low
DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (dysplasia) - CT			

Yamao 2001 *(Continued)*

If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	Low
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - EUS			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	Low
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - CT			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	Low
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	No		
		High	

Zhan 2011
Study characteristics

Patient sampling	Type of study: retrospective study. Consecutive or random sample: unclear.
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Zhan 2011 (Continued)

Patient characteristics and setting	Sample size: 21. Females: 3 (14.3%). Age: not stated. Presentation: Patients with MCN undergoing operative resection. Setting: secondary care, China.
Index tests	Index test: EUS. Further details: Technical specifications: model and manufacturer not stated. Performed by: endoscopist. Criteria for positive diagnosis: different criteria were reported for IPMN and MCN without any information on how these were distinguished prior to FNA.
Target condition and reference standard(s)	Target condition: cancerous (invasive carcinoma) versus precancerous (dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	
Notes	Other criteria with lower sensitivity and specificity were available.

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
		Unclear	High
DOMAIN 2: Index Test Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	High
DOMAIN 3: Reference Standard			

Zhan 2011 *(Continued)*

Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Unclear Low	
DOMAIN 4: Flow and Timing	
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Unclear
Unclear	

Zhan 2013

Study characteristics	
Patient sampling	Type of study: retrospective study. Consecutive or random sample: unclear.
Patient characteristics and setting	Sample size: 20. Females: 6 (30.0%). Age: 59 years. Presentation: Patients with MCN undergoing operative resection. Setting: secondary care, China.
Index tests	Index test: EUS-FNA. Further details: Technical specifications: GF-UCT-2000-OL5 (Olympus). Performed by: endoscopist. Criteria for positive diagnosis: cytology Second criteria for positive diagnosis: CEA > 692.8 ng/mL.
Target condition and reference standard(s)	Target condition: cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia). Reference standard: surgical excision. Further details: Technical specifications: not applicable. Performed by: clinicians. Criteria for positive diagnosis: not stated.
Flow and timing	Number of indeterminates for whom the results of reference standard were available: not stated. Number of patients who were excluded from the analysis: not stated.
Comparative	

Zhan 2013 (Continued)

Notes

Methodological quality

Item	Authors' judgement	Risk of bias	Applicability concerns
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear		
Was a case-control design avoided?	Yes		
Did the study avoid inappropriate exclusions?	Unclear		
		Unclear	High
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - EUS FNA			
If a threshold was used, was it pre-specified?	Yes		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		Unclear	Low
DOMAIN 2: Index Test Cancerous (high grade dysplasia or invasive carcinoma) versus precancerous (low or intermediate grade dysplasia) - EUS FNA (CEA > 692.8 ng/ml)			
If a threshold was used, was it pre-specified?	No		
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear		
		High	High
DOMAIN 3: Reference Standard			
Is the reference standards likely to correctly classify the target condition?	Yes		
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear		
		Unclear	Low
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear		
Did all patients receive the same reference standard?	Yes		
Were all patients included in the analysis?	Unclear		

Zhan 2013 (Continued)

Unclear

CEA: carcinoembryonic antigen
 CT: computed tomography
 EUS: endoscopic ultrasound
 FNA: fine-needle aspiration
 IPMN: intraductal pancreatic mucinous neoplasm
 MCN: mucinous cystic neoplasm
 MDCT: multidetector computed tomography
 MPD: main pancreatic duct
 MRI: magnetic resonance imaging
 PET: positron emission tomography
 SUV: standard uptake value

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Aburime 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Adamek 2000	This study was not included as no pancreatic mass was present in the patient(s) tested.
Adimoolam 2011	There was no comparison of whether cancer was present or not.
Afify 2003	There was no comparison of whether cancer was present or not.
Agarwal 2004	This study was not included as no pancreatic mass was present in the patient(s) tested.
Agarwal 2008a	This study was not included as no pancreatic mass was present in the patient(s) tested.
Agarwal 2008b	This study was not included as no pancreatic mass was present in the patient(s) tested.
Agarwal 2008c	This study was not included as no pancreatic mass was present in the patient(s) tested.
Aguilar-Saavedra 2011	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Ahmad 2001	There was no comparison of whether cancer was present or not.
Ahmad 2003	There was no comparison of whether cancer was present or not.
Ainsworth 2010	There was no comparison of whether cancer was present or not.
Aithal 2001	There was no comparison of whether cancer was present or not.
Aithal 2002	There was no comparison of whether cancer was present or not.
Akahoshi 1998	This study was not included as no pancreatic mass was present in the patient(s) tested.
Akwei 2011	There was no comparison of whether cancer was present or not.

Study	Reason for exclusion
Al-Haddad 2007	There was no comparison of whether cancer was present or not.
Al-Haddad 2010a	This study was not included as no pancreatic mass was present in the patient(s) tested.
Al-Haddad 2010b	There was no comparison of whether cancer was present or not.
Al-Haddad 2014	There was no comparison of whether cancer was present or not.
Al-Jebreen 2004	There was no comparison of whether cancer was present or not.
Al-Najami 2015	This study was not included as no pancreatic mass was present in the patient(s) tested.
Alizadeh 2014	There was no comparison of whether cancer was present or not.
Aljebreen 2007	Inadequate reference standard (nature of follow-up not stated)
Alsohaibani 2008	This study was not included as no pancreatic mass was present in the patient(s) tested.
Alsohaibani 2009	This study was not included as no pancreatic mass was present in the patient(s) tested.
Alston 2014	There was no comparison of whether cancer was present or not.
Amin 2006	This study was not included as no pancreatic mass was present in the patient(s) tested.
Andersen 1994	This study was not included as no pancreatic mass was present in the patient(s) tested.
Antonini 2015	There was no comparison of whether cancer was present or not.
Arabul 2012	There was no comparison of whether cancer was present or not.
Ardengh 2007a	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities were used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Ardengh 2007b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Ardengh 2008a	There was no comparison of whether cancer was present or not.
Ardengh 2008b	There was no comparison of whether cancer was present or not.
Ardengh 2013	Inadequate reference standards
Argimak 2009	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Arikawa 2007	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.

Study	Reason for exclusion
Arlt 2013	The study was not classed as primary research (i.e. not a review or editorial or comment).
Asagi 2013	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Aslanian 2011	This study was not included as no pancreatic mass was present in the patient(s) tested.
Asnacios 2003	There was no comparison of whether cancer was present or not.
Atef 2013	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Attasaranya 2007	There was no comparison of whether cancer was present or not.
Awadallah 2008	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Azizi 2014	This study was not included as no pancreatic mass was present in the patient(s) tested.
Baba 2004	Although this study provides diagnostic accuracy data for pancreatic lesions, it presents information on branch type and non-branch type first, then presents the diagnostic test accuracy only for branch type and not for the overall cohort. This is therefore not a representative population.
Baek 2015	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Baghbanian 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Baiocchi 2008	Overlap with Baiocchi 2012
Baiocchi 2010	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Baiocchi 2012	Inadequate reference standard (criteria for diagnosing malignancy during clinical follow-up not stated)
Bali 2011	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Bang 2012a	There was no comparison of whether cancer was present or not.
Bang 2012b	There was no comparison of whether cancer was present or not.
Bang 2013a	There was no comparison of whether cancer was present or not.
Bang 2013b	The study was not classed as primary research (i.e. not a review or editorial or comment).

Study	Reason for exclusion
Bang 2015	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Barber 2011	There was no comparison of whether cancer was present or not.
Bares 1994	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Barkin 1977	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Baron 1997	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Barral 2013a	There was no comparison of whether cancer was present or not.
Barral 2013b	There was no comparison of whether cancer was present or not.
Barresi 2014	There was no comparison of whether cancer was present or not.
Barron 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Bartsch 1998	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Basir 2003	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Bassi 2003	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Beal 2015a	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test pos-

Study	Reason for exclusion
	itive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Beal 2015b	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Becker 2001	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Beliao 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Bentz 1998	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Bergeron 2015	There was no comparison of whether cancer was present or not.
Bernstein 2013	There was no comparison of whether cancer was present or not.
Berzosa 2015	There was no comparison of whether cancer was present or not.
Bhutani 1995	There was no comparison of whether cancer was present or not.
Bhutani 1997	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Bick 2015	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Bigli 1989	This study was not included as no pancreatic mass was present in the patient(s) tested.
Binmoeller 1998a	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless

Study	Reason for exclusion
	all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Binmoeller 1998b	This study was not included as no pancreatic mass was present in the patient(s) tested.
Bluen 2012	This study was not included as no pancreatic mass was present in the patient(s) tested.
Bournet 2007	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Bournet 2009	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Bournet 2012	There was no comparison of whether cancer was present or not.
Bournet 2015	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Boutros 2010	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Brand 2002	This study was not included as no pancreatic mass was present in the patient(s) tested.
Brand 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Brenin 1995	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Brimiène 2011	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless

Study	Reason for exclusion
	all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Brugge 2000	The study was not classed as primary research (i.e. not a review or editorial or comment).
Brugge 2004a	The study was not classed as primary research (i.e. not a review or editorial or comment).
Brugge 2004b	There was no comparison of whether cancer was present or not.
Bruno 2009	This study was not included as no pancreatic mass was present in the patient(s) tested.
Buchholz 2005	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Buchs 2011	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Butt 2015a	There was no comparison of whether cancer was present or not.
Butt 2015b	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Caglar 2013	There was no comparison of whether cancer was present or not.
Cahn 1996	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Caldelari 2011	There was no comparison of whether cancer was present or not.
Camellini 2011	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Cantley 2014	There was no comparison of whether cancer was present or not.
Carbognin 2006	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Carlinfante 2014	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.

Study	Reason for exclusion
Carroll 1997	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Casneuf 2007	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Catanzaro 2003	There was no comparison of whether cancer was present or not.
Catanzaro 2013	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Cermak 2012	There was no comparison of whether cancer was present or not.
Chai 2013	There was no comparison of whether cancer was present or not.
Chang 1994	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Chang 1997	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Chang 2009	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Chaudhari 2007	There was no comparison of whether cancer was present or not.
Chaudhari 2008	There was no comparison of whether cancer was present or not.

Study	Reason for exclusion
Chaya 2006	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Chebib 2014	There was no comparison of whether cancer was present or not.
Chen 2001	There was no comparison of whether cancer was present or not.
Chen 2003	There was no comparison of whether cancer was present or not.
Chen 2007	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Chen 2014	There was no comparison of whether cancer was present or not.
Cheng 2012	This study was not included as no pancreatic mass was present in the patient(s) tested.
Cheng 2013	This study was not included as no pancreatic mass was present in the patient(s) tested.
Chiu 2005	This study was not included as no pancreatic mass was present in the patient(s) tested.
Chiu 2006	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Cho 2005	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Cho 2013	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Choi 2011	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Choi 2013	There was no comparison of whether cancer was present or not.
Choi 2016	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Chung 2009	Inappropriate index test
Cizginer 2011	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Clave 1999	This study was not included as no pancreatic mass was present in the patient(s) tested.

Study	Reason for exclusion
Cocieru 2011	There was no comparison of whether cancer was present or not.
Collins 2007	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Collins 2013	There was no comparison of whether cancer was present or not.
Collins 2015	There was no comparison of whether cancer was present or not.
Cone 2011	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Corominas-Cishek 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Cosgrove 2015	The study was not classed as primary research (i.e. not a review or editorial or comment).
Crippa 2010	The study was not classed as primary research (i.e. not a review or editorial or comment).
Cuillerier 1996	There was no comparison of whether cancer was present or not.
D'Onofrio 2007	There was no comparison of whether cancer was present or not.
D'Onofrio 2013	This study was not included as no pancreatic mass was present in the patient(s) tested.
Dadabhai 2005	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Dadds 2012	There was no comparison of whether cancer was present or not.
Dani 2000	There was no comparison of whether cancer was present or not.
Dawwas 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biop-

Study	Reason for exclusion
	sy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Dawwas 2013	The study was not classed as primary research (i.e. not a review or editorial or comment).
De Jong 2010	Should be included under de Jong 2012
de Jong 2011	There was no comparison of whether cancer was present or not.
De Tejada 2008	There was no comparison of whether cancer was present or not.
Decalan 1995	There was no comparison of whether cancer was present or not.
Del Vecchio 2016	Inadequate reference standards
Delbeke 1999	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
DelMaschio 1991	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Deng 2008	This study was not included as no pancreatic mass was present in the patient(s) tested.
Deshpande 2008	There was no comparison of whether cancer was present or not.
DeWitt 2004	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
DeWitt 2005	The study was not classed as primary research (i.e. not a review or editorial or comment).
DeWitt 2008	This study was not included as no pancreatic mass was present in the patient(s) tested.
Di Cataldo 2014	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Diederichs 2000	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Diehl 1999	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biop-

Study	Reason for exclusion
	sy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Dietrich 2008	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Dim 2014	This study was not included as no pancreatic mass was present in the patient(s) tested.
DiMagno 1977	This study was not included as no pancreatic mass was present in the patient(s) tested.
Dinkel 1990	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Do 2014	There was no comparison of whether cancer was present or not.
Draganov 2010	This study was not included as no pancreatic mass was present in the patient(s) tested.
Eguia 2013	There was no comparison of whether cancer was present or not.
Elmas 1996	Inadequate reference standards
Eloubeidi 2002	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Eloubeidi 2003a	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Eloubeidi 2003b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Eloubeidi 2005	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Eloubeidi 2006a	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biop-

Study	Reason for exclusion
	sy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Eloubeidi 2006b	This study was not included as no pancreatic mass was present in the patient(s) tested.
Eloubeidi 2006c	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Eloubeidi 2007	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Eloubeidi 2008a	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Eloubeidi 2008b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Eloubeidi 2013	This study was not included as no pancreatic mass was present in the patient(s) tested.
Ergul 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Erickson 1997	This study was not included as no pancreatic mass was present in the patient(s) tested.
Erickson 2000	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Erickson 2001	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Ernst 1998	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biop-

Study	Reason for exclusion
	sy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Erturk 2006a	The study was not classed as primary research (i.e. not a review or editorial or comment).
Erturk 2006b	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Fabbri 2013	There was no comparison of whether cancer was present or not.
Fabbri 2015a	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Fabbri 2015b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Faigel 1997	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Fan 2013	There was no comparison of whether cancer was present or not.
Fan 2015	There was no comparison of whether cancer was present or not.
Fanning 2010	This study was not included as no pancreatic mass was present in the patient(s) tested.
Faravelli 1990	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Felgueroso 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Fernandez-Esparrach 2007a	There was no comparison of whether cancer was present or not.
Fernandez-Esparrach 2007b	There was no comparison of whether cancer was present or not.
Figueiredo 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient).

Study	Reason for exclusion
	Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Fischer 2002	This study was not included as no pancreatic mass was present in the patient(s) tested.
Fischer 2009	There was no comparison of whether cancer was present or not.
Fisher 2009	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Fisher 2011	There was no comparison of whether cancer was present or not.
Frampton 2013	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Friess 1995	This study was not included as no pancreatic mass was present in the patient(s) tested.
Fritscher-Ravens 1998	This study was not included as no pancreatic mass was present in the patient(s) tested.
Fritscher-Ravens 1999	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Fritscher-Ravens 2000	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Fritscher-Ravens 2001a	This study was not included as no pancreatic mass was present in the patient(s) tested.
Fritscher-Ravens 2001b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Fritscher-Ravens 2002	This study was not included as no pancreatic mass was present in the patient(s) tested.

Study	Reason for exclusion
Frossard 2003	There was no comparison of whether cancer was present or not.
Fugazzola 1991	There was no comparison of whether cancer was present or not.
Furuhashi 2015	There was no comparison of whether cancer was present or not.
Furuhata 2012	There was no comparison of whether cancer was present or not.
Fusari 2010	There was no comparison of whether cancer was present or not.
Fusaroli 2010	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Fusaroli 2014	The study was not classed as primary research (i.e. not a review or editorial or comment).
Gaa 1999	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Gambitta 2014	This study was not included as no pancreatic mass was present in the patient(s) tested.
Ganc 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Ganc 2015	Inadequate reference standards
Gaspar 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Gill 2008	The study was not classed as primary research (i.e. not a review or editorial or comment).
Gimeno-Garcia 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Giorgetti 2010	Inadequate reference standard (nature of follow-up not stated)
Giovannini 1995	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless

Study	Reason for exclusion
	all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Giovannini 2009	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Glasbrenner 2000	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Goh 2006a	The study was not classed as primary research (i.e. not a review or editorial or comment).
Goh 2008	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Gomez 2006	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Gomez 2008	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Gong 2004	This study was not included as no pancreatic mass was present in the patient(s) tested.
Gordon 2014	Inadequate reference standards
Gowland 1981	This study was not included as no pancreatic mass was present in the patient(s) tested.
Green 2002	The study was not classed as primary research (i.e. not a review or editorial or comment).
Grenacher 2004	This study was not included as no pancreatic mass was present in the patient(s) tested.
Gress 1997	This study was not included as no pancreatic mass was present in the patient(s) tested.
Gress 2001	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Grieser 2013	There was no comparison of whether cancer was present or not.
Guo 2008	There was no comparison of whether cancer was present or not.
Gupta 1995	This study was not included as no pancreatic mass was present in the patient(s) tested.
Gupta 2008	There was no comparison of whether cancer was present or not.

Study	Reason for exclusion
Haba 2011	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Haba 2013	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Hammel 1995	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Hammel 1998	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Han 2016	Inadequate reference standards
Hanada 2009	There was no comparison of whether cancer was present or not.
Hanninen 2002	This study was not included as no pancreatic mass was present in the patient(s) tested.
Hanninen 2005	This study was not included as no pancreatic mass was present in the patient(s) tested.
Harewood 2001a	The study was not classed as primary research (i.e. not a review or editorial or comment).
Harewood 2001b	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Harewood 2002	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Hasan 2014	This study was not included as no pancreatic mass was present in the patient(s) tested.
Hasenberg 2009	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Hasyagar 2004	There was no comparison of whether cancer was present or not.
Hayashi 2013	There was no comparison of whether cancer was present or not.
Hebert-Magee 2015	The study was not classed as primary research (i.e. not a review or editorial or comment).

Study	Reason for exclusion
Heinrich 2005	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Henkes 2013	This study was not included as no pancreatic mass was present in the patient(s) tested.
Heo 2013	This study was not included as no pancreatic mass was present in the patient(s) tested.
Herman-Sucharska 1999	This study was not included as no pancreatic mass was present in the patient(s) tested.
Hernandez 2002	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Herrmann 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Higashi 2002a	The study was not classed as primary research (i.e. not a review or editorial or comment).
Higashi 2002b	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Higashi 2003	The study was not classed as primary research (i.e. not a review or editorial or comment).
Hijioka 2014	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Hikichi 2009	Inadequate reference standard (details of clinical follow-up not stated)
Hilendarov 2010	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Hilendarov 2011	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient).

Study	Reason for exclusion
	Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Hilendarov 2012	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Hilendarov 2013	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Ho 1996	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Ho 2004	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Hocke 2006	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Hocke 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Hollerbach 2004	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Holt 2008	There was no comparison of whether cancer was present or not.
Holt 2014	The study was not classed as primary research (i.e. not a review or editorial or comment).
Hong 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.

Study	Reason for exclusion
Honselmann 2016	Inadequate reference standards
Horatagis 2003	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Horwhat 2004	This study was not included as no pancreatic mass was present in the patient(s) tested.
Horwhat 2006	This study was not included as no pancreatic mass was present in the patient(s) tested.
Hou 2015	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Hu 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Huang 2010	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Huang 2011	This study was not included as no pancreatic mass was present in the patient(s) tested.
Hunt 2009	There was no comparison of whether cancer was present or not.
Hussain 2009	This study was not included as no pancreatic mass was present in the patient(s) tested.
Hwang 2009	This study was not included as no pancreatic mass was present in the patient(s) tested.
Hwang 2011	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Ibrahim 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Ichikawa 2001	There was no comparison of whether cancer was present or not.
Iftimia 2012	The study was not classed as primary research (i.e. not a review or editorial or comment).

Study	Reason for exclusion
Iglesias 2013	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Iglesias-Garcia 2007	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Iglesias-Garcia 2008	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Iglesias-Garcia 2009a	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Iglesias-Garcia 2009b	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Iglesias-Garcia 2010	<p>There was no comparison of whether cancer was present or not.</p>
Iglesias-Garcia 2011	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Iglesias-Garcia 2013a	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>

Study	Reason for exclusion
Iglesias-Garcia 2013b	The study was not classed as primary research (i.e. not a review or editorial or comment).
Iguchi 2010	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Ikeura 2014	This study was not included as no pancreatic mass was present in the patient(s) tested.
Ikeura 2015a	This study was not included as no pancreatic mass was present in the patient(s) tested.
Ikeura 2015b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Imazu 2009	This study was not included as no pancreatic mass was present in the patient(s) tested.
Imdahl 1999	This study was not included as no pancreatic mass was present in the patient(s) tested.
Inokuma 1995	This study was not included as no pancreatic mass was present in the patient(s) tested.
Iordache 2016	Inadequate reference standards
Ippolito 2015	There was no comparison of whether cancer was present or not.
Irie 2002	There was no comparison of whether cancer was present or not.
Ironside 2010	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Ishigami 2010	This study was not included as no pancreatic mass was present in the patient(s) tested.
Ishii 2012	There was no comparison of whether cancer was present or not.
Ishikawa 2010	This study was not included as no pancreatic mass was present in the patient(s) tested.
Itoh 2005	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Itoi 2005a	This study was not included as no pancreatic mass was present in the patient(s) tested.

Study	Reason for exclusion
Itoi 2005b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Itoi 2011	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Itokawa 2010	This study was not included as no pancreatic mass was present in the patient(s) tested.
Itokawa 2011	This study was not included as no pancreatic mass was present in the patient(s) tested.
Iwashita 2013	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Iwashita 2015	This study was not included as no pancreatic mass was present in the patient(s) tested.
Izuishi 2010	This study was not included as no pancreatic mass was present in the patient(s) tested.
Jabbar 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Jadvar 2001	This study was not included as no pancreatic mass was present in the patient(s) tested.
Jahng 2010	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Jahromi 2014	There was no comparison of whether cancer was present or not.
Jang 2012	There was no comparison of whether cancer was present or not.
Jang 2015	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test pos-

Study	Reason for exclusion
	itive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Jani 2006	The study was not classed as primary research (i.e. not a review or editorial or comment).
Jani 2008	There was no comparison of whether cancer was present or not.
Janssen 2007	This study was not included as no pancreatic mass was present in the patient(s) tested.
Jayasekeran 2012	This study was not included as no pancreatic mass was present in the patient(s) tested.
Jeong 2012	This study was not included as no pancreatic mass was present in the patient(s) tested.
Jhala 2007	This study was not included as no pancreatic mass was present in the patient(s) tested.
Jin 2013b	This study was not included as no pancreatic mass was present in the patient(s) tested.
Jing 2009	This study was not included as no pancreatic mass was present in the patient(s) tested.
Johnson 1999	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Kadayifci 2014	The study was not classed as primary research (i.e. not a review or editorial or comment).
Kadayifci 2016	Inadequate reference standards
Kaffes 2012	This study was not included as no pancreatic mass was present in the patient(s) tested.
Kaimakliotis 2015	Inappropriate index test
Kalb 2013	There was no comparison of whether cancer was present or not.
Kalra 2003	The study was not classed as primary research (i.e. not a review or editorial or comment).
Kamata 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Kamata 2016b	Inadequate reference standards
Kamin 1980	This study was not included as no pancreatic mass was present in the patient(s) tested.
Kamisawa 2008	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient).

Study	Reason for exclusion
	Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Kanazawa 2012	This study was not included as no pancreatic mass was present in the patient(s) tested.
Kang 2013	Reference to be included under Kim 2015 .
Kang 2014	There was no comparison of whether cancer was present or not.
Kang 2016	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Katanuma 2013	There was no comparison of whether cancer was present or not.
Katz 2007	The study was not classed as primary research (i.e. not a review or editorial or comment).
Kauhanen 2009a	This study was not included as no pancreatic mass was present in the patient(s) tested.
Kauhanen 2009b	This study was not included as no pancreatic mass was present in the patient(s) tested.
Kauhanen 2015	Inadequate reference standards
Kawada 2012	There was no comparison of whether cancer was present or not.
Kawada 2014	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Kawada 2015	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Kawada 2016	Inappropriate target condition
Kawamoto 2006	There was no comparison of whether cancer was present or not.
Keil 2008	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Keswani 2014	This study was not included as no pancreatic mass was present in the patient(s) tested.
Khalid 2005	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.

Study	Reason for exclusion
Khalid 2006	Same as Kim 2015
Khan 2010	There was no comparison of whether cancer was present or not.
Khashab 2010	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Khashab 2013	There was no comparison of whether cancer was present or not.
Khodadadian 2001	This study was not included as no pancreatic mass was present in the patient(s) tested.
Khurana 2012	This study was not included as no pancreatic mass was present in the patient(s) tested.
Khurana 2014	There was no comparison of whether cancer was present or not.
Kida 2011	This study was not included as no pancreatic mass was present in the patient(s) tested.
Kim 2007	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Kim 2009	There was no comparison of whether cancer was present or not.
Kim 2010	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Kim 2012a	There was no comparison of whether cancer was present or not.
Kim 2012b	There was no comparison of whether cancer was present or not.
Kim 2012c	This study was not included as no pancreatic mass was present in the patient(s) tested.
Kim 2013a	There was no comparison of whether cancer was present or not.
Kim 2013b	This study was not included as no pancreatic mass was present in the patient(s) tested.
Kim 2013c	This study was not included as no pancreatic mass was present in the patient(s) tested.
Kim 2013d	There was no comparison of whether cancer was present or not.
Kim 2014a	This study was not included as no pancreatic mass was present in the patient(s) tested.

Study	Reason for exclusion
Kim 2014b	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Kim 2014c	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Kim 2014d	There was no comparison of whether cancer was present or not.
Kim 2015a	Inappropriate index test
Kin 2015	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Kitano 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Klapman 2003	This study was not included as no pancreatic mass was present in the patient(s) tested.
Klapman 2004	This study was not included as no pancreatic mass was present in the patient(s) tested.
Klapman 2005	This study was not included as no pancreatic mass was present in the patient(s) tested.
Kliment 2010	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Kliment 2013	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Kokhanenko 2001	This study was not included as no pancreatic mass was present in the patient(s) tested.
Kongkam 2015	Inadequate reference standards
Kopelman 2011	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.

Study	Reason for exclusion
Koranda 2010	This study was not included as no pancreatic mass was present in the patient(s) tested.
Korenblit 2016	Inadequate reference standards
Koyama 2001	This study was not included as no pancreatic mass was present in the patient(s) tested.
Kriger 2011	This study was not included as the index test was not performed to distinguish between cancerous, precancerous, and benign lesions.
Krishna 2009a	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Krishna 2009b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Krishna 2009c	This study was not included as no pancreatic mass was present in the patient(s) tested.
Krishna 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Krishna 2013	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Krishna 2015	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Krishnan 2013	This study was not included as no pancreatic mass was present in the patient(s) tested.
Kubiliun 2011	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient).

Study	Reason for exclusion
	Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Kubo 2009	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Kudo 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Kula 2008	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Kumon 2009	This study was not included as no pancreatic mass was present in the patient(s) tested.
Kumon 2010	This study was not included as no pancreatic mass was present in the patient(s) tested.
Kumon 2012	This study was not included as no pancreatic mass was present in the patient(s) tested.
Kung 2014	This study was not included as no pancreatic mass was present in the patient(s) tested.
Kursawa 1991	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Kwong 2015	Inadequate reference standards
Kyokane 1996	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Kysucan 2010	This study was not included as no pancreatic mass was present in the patient(s) tested.
Lackner 1980	The study was not classed as primary research (i.e. not a review or editorial or comment).
Larghi 2013	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless

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	<p>all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Larino-Noia 2013	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Le Baleur 2009	<p>There was no comparison of whether cancer was present or not.</p>
Le Baleur 2011b	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
LeBlanc 2004	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
LeBlanc 2010	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Lee 2005a	<p>There was no comparison of whether cancer was present or not.</p>
Lee 2005b	<p>This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.</p>
Lee 2006	<p>There was no comparison of whether cancer was present or not.</p>
Lee 2007	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Lee 2008a	<p>There was no comparison of whether cancer was present or not.</p>
Lee 2008b	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless</p>

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	all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Lee 2009	This study was not included as no pancreatic mass was present in the patient(s) tested.
Lee 2010a	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Lee 2010b	This study was not included as no pancreatic mass was present in the patient(s) tested.
Lee 2011	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Lee 2013a	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Lee 2013b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Lee 2013c	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Lee 2013d	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Lee 2014b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.

Study	Reason for exclusion
Lee 2014c	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Lee 2014d	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Leeds 2013	There was no comparison of whether cancer was present or not.
Legmann 1998	This study was not included as no pancreatic mass was present in the patient(s) tested.
Lehmann 1998	This study was not included as no pancreatic mass was present in the patient(s) tested.
Lemke 2004	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Levy 1995	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Levy 2005	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Levy 2007	This study was not included as no pancreatic mass was present in the patient(s) tested.
Levy 2012	This study was not included as no pancreatic mass was present in the patient(s) tested.
Lightdale 1994	The study was not classed as primary research (i.e. not a review or editorial or comment).
Lim 2005	There was no comparison of whether cancer was present or not.
Lim 2013	There was no comparison of whether cancer was present or not.

Study	Reason for exclusion
Lin 2003	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Lin 2011	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Lin 2014	<p>This study was not included as no pancreatic mass was present in the patient(s) tested.</p>
Linder 2006	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Liu 2010a	<p>Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.</p>
Liu 2010b	<p>This study was not included as no pancreatic mass was present in the patient(s) tested.</p>
Liu 2014	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Lopez 2002	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Lozano 2011	<p>There was no comparison of whether cancer was present or not.</p>
Lu 2013	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient).</p>

Study	Reason for exclusion
	Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Lu 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Lytras 2005	This study was not included as no pancreatic mass was present in the patient(s) tested.
Mackie 1979	This study was not included as no pancreatic mass was present in the patient(s) tested.
Madan 2012	There was no comparison of whether cancer was present or not.
Madura 1997	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Maguchi 2006	The study was not classed as primary research (i.e. not a review or editorial or comment).
Maire 2003	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Makaiova 2005	This study was not included as no pancreatic mass was present in the patient(s) tested.
Malak 2016	Inadequate reference standards
Malleo 2012	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Mallery 2002	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Maluf 2005	There was no comparison of whether cancer was present or not.
Maluf-Filho 2007	There was no comparison of whether cancer was present or not.
Mamoon 2011	This study was not included as no pancreatic mass was present in the patient(s) tested.
Manfredi 2009	There was no comparison of whether cancer was present or not.
Mansoor 2012	There was no comparison of whether cancer was present or not.
Mansour 2006	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Mao 2011	This study was not included as no pancreatic mass was present in the patient(s) tested.

Study	Reason for exclusion
Marchevsky 2003	This study was not included as no pancreatic mass was present in the patient(s) tested.
Marotta 1991	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Martin 1998	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Martinez 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Marzioni 2015	Inadequate reference standards; details of clinical follow-up not available
Matsubara 2011	This study was not included as no pancreatic mass was present in the patient(s) tested.
Matsubayashi 2015	The study was not classed as primary research (i.e. not a review or editorial or comment).
Matsuda 2012	There was no comparison of whether cancer was present or not.
Matsumoto 2012	This study was not included as no pancreatic mass was present in the patient(s) tested.
Matsumoto 2013	This study was not included as no pancreatic mass was present in the patient(s) tested.
Matsumoto 2014	This study was not included as no pancreatic mass was present in the patient(s) tested.
Maurea 2009	This study was not included as no pancreatic mass was present in the patient(s) tested.
Mavrogenis 2015	This study was not included as no pancreatic mass was present in the patient(s) tested.
Mayerle 2016	Inadequate reference standards
McClellan 2003	This study was not included as no pancreatic mass was present in the patient(s) tested.
McDowell 1997	There was no comparison of whether cancer was present or not.
Mehan 2009	There was no comparison of whether cancer was present or not.
Mehmood 2015	This study was not included as no pancreatic mass was present in the patient(s) tested.
Meijer 2009	This study was not included as no pancreatic mass was present in the patient(s) tested.
Meijer 2010	This study was not included as no pancreatic mass was present in the patient(s) tested.
Mera 1999	There was no comparison of whether cancer was present or not.
Mertz 2000	This study was not included as no pancreatic mass was present in the patient(s) tested.
Mesihovic 2005	This study was not included as no pancreatic mass was present in the patient(s) tested.
Micames 2007	The study was not classed as primary research (i.e. not a review or editorial or comment).
Michaels 2006	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.

Study	Reason for exclusion
Midwinter 1999	This study was not included as no pancreatic mass was present in the patient(s) tested.
Mishra 2006	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Mitsuhashi 2006	There was no comparison of whether cancer was present or not.
Miyabe 2015	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Moehler 2011	This study was not included as no pancreatic mass was present in the patient(s) tested.
Moparty 2007	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Moris 2016	Inappropriate target population
Morozova 2014	There was no comparison of whether cancer was present or not.
Morozova 2015	Inappropriate target population
Murayama 2011	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Nadig 2012	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Nagamachi 2013	Inadequate reference standards
Nagula 2010	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Nakai 2015	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Nakamoto 2000	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Nakamoto 2003	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient).

Study	Reason for exclusion
	Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Napoleon 2010a	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Napoleon 2010b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Napoleon 2015	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Nattermann 1995	There was no comparison of whether cancer was present or not.
Nayar 2011	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Nayar 2013	This study was not included as no pancreatic mass was present in the patient(s) tested.
Nguyen 1998	This study was not included as no pancreatic mass was present in the patient(s) tested.
Nguyen 2007	This study was not included as no pancreatic mass was present in the patient(s) tested.
Nguyen 2008	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Nicaud 2010	This study was not included as no pancreatic mass was present in the patient(s) tested.
Nieto 2007	Details of clinical follow-up not available
Nijhawan 2014	This study was not included as no pancreatic mass was present in the patient(s) tested.

Study	Reason for exclusion
Nikiforova 2013	There was no comparison of whether cancer was present or not.
Nishihara 1996	Inappropriate target condition
Nitzsche 2002	This study was not included as no pancreatic mass was present in the patient(s) tested.
Nobrega 1994	This study was not included as no pancreatic mass was present in the patient(s) tested.
Noda 2010	This study was not included as no pancreatic mass was present in the patient(s) tested.
Noma 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Noone 2004	This study was not included as no pancreatic mass was present in the patient(s) tested.
Norton 2001	This study was not included as no pancreatic mass was present in the patient(s) tested.
Nougaret 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
O'Toole 2004	There was no comparison of whether cancer was present or not.
Ogawa 2008b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Ogura 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Oguz 2013	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Ohno 2009	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.

Study	Reason for exclusion
Ohta 2012	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Ohtsuka 2013	This study was not included as no pancreatic mass was present in the patient(s) tested.
Okada 1979	This study was not included as no pancreatic mass was present in the patient(s) tested.
Okada 1981	This study was not included as no pancreatic mass was present in the patient(s) tested.
Okasha 2013	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Okasha 2015	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Olson 2012	This study was not included as no pancreatic mass was present in the patient(s) tested.
Ooi 1998	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Ootaki 2012	There was no comparison of whether cancer was present or not.
Opacic 2015	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Oppong 2015	Inadequate reference standards
Osman 2016	Inadequate reference standards
Othman 2011	The study was not classed as primary research (i.e. not a review or editorial or comment).
Ozkan 2016	Inadequate reference standards
Paik 2015	This study was not included as no pancreatic mass was present in the patient(s) tested.
Palacios-Gerona 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Palaniappan 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless

Study	Reason for exclusion
	all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Palazzo 1993	This study was not included as no pancreatic mass was present in the patient(s) tested.
Palazzo 2011	The study was not classed as primary research (i.e. not a review or editorial or comment).
Pan 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Panaro 1978	This study was not included as no pancreatic mass was present in the patient(s) tested.
Papanikolaou 2008	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Papos 1999	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Papos 2002a	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Papos 2002b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Park 2014a	There was no comparison of whether cancer was present or not.
Park 2014b	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Park 2016a	Inadequate reference standards

Study	Reason for exclusion
Park 2016b	Inadequate reference standards
Pasanen 1992	This study was not included as no pancreatic mass was present in the patient(s) tested.
Pasanen 1993	This study was not included as no pancreatic mass was present in the patient(s) tested.
Patoureaux 2013	There was no comparison of whether cancer was present or not.
Paye 2000	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Pedrazzoli 2005	The study was not classed as primary research (i.e. not a review or editorial or comment).
Pellise 2003	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Perri 2012	The study was not classed as primary research (i.e. not a review or editorial or comment).
Perrone 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Petrone 2012	There was no comparison of whether cancer was present or not.
Pezzilli 2013	There was no comparison of whether cancer was present or not.
Pitman 2010	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Pitman 2013a	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Pitman 2013b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.

Study	Reason for exclusion
Pitman 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Pomerri 1991	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Pongpornsup 2011	There was no comparison of whether cancer was present or not.
Qian 2003	There was no comparison of whether cancer was present or not.
Qian 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Qin 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Quentin 2005	There was no comparison of whether cancer was present or not.
Qureshi 2013	There was no comparison of whether cancer was present or not.
Raddaoui 2011	This study was not included as no pancreatic mass was present in the patient(s) tested.
Rajput 1998	This study was not included as no pancreatic mass was present in the patient(s) tested.
Raman 2013	There was no comparison of whether cancer was present or not.
Ramesh 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Ramesh 2015	There was no comparison of whether cancer was present or not.
Ramesh 2016	Inadequate reference standards

Study	Reason for exclusion
Ramirez-Luna 2008	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Rana 2011	There was no comparison of whether cancer was present or not.
Ranney 2012	There was no comparison of whether cancer was present or not.
Rao 2011	There was no comparison of whether cancer was present or not.
Rasmussen 2001	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Rasmussen 2004	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Raut 2002	This study was not included as no pancreatic mass was present in the patient(s) tested.
Raut 2003	This study was not included as no pancreatic mass was present in the patient(s) tested.
Redelman 2014	This study was not included as no pancreatic mass was present in the patient(s) tested.
Reicher 2011	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Repak 2009	There was no comparison of whether cancer was present or not.
Ribeiro 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Richter 1996	This study was not included as no pancreatic mass was present in the patient(s) tested.
Richter 2001	This study was not included as no pancreatic mass was present in the patient(s) tested.

Study	Reason for exclusion
Ridtitid 2015	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Rocca 2007	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Roch 2014	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Rodriguez 2007	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Rodriguez 2010	This study was not included as no pancreatic mass was present in the patient(s) tested.
Rodriguez-D'Jesus 2013	There was no comparison of whether cancer was present or not.
Rogart 2011	There was no comparison of whether cancer was present or not.
Romagnuolo 2011	This study was not included as no pancreatic mass was present in the patient(s) tested.
Rong 2012	There was no comparison of whether cancer was present or not.
Rosch 1990a	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Rosch 1990b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Rosch 1991a	There was no comparison of whether cancer was present or not.
Rosch 1991b	This study was not included as no pancreatic mass was present in the patient(s) tested.
Rosch 2000	This study was not included as no pancreatic mass was present in the patient(s) tested.
Rose 1999	This study was not included as no pancreatic mass was present in the patient(s) tested.

Study	Reason for exclusion
Rosique 2002	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Rudolph 2001	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Ruf 2006	<p>This study was not included as no pancreatic mass was present in the patient(s) tested.</p>
Ryozawa 2005	<p>This study was not included as no pancreatic mass was present in the patient(s) tested.</p>
Saftoiu 2006	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Saftoiu 2008	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Saftoiu 2010a	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Saftoiu 2010b	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Saftoiu 2011	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient).</p>

Study	Reason for exclusion
	Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Saftoiu 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Saftoiu 2013	The study was not classed as primary research (i.e. not a review or editorial or comment).
Saftoiu 2015	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Sahai 2012	The study was not classed as primary research (i.e. not a review or editorial or comment).
Sahani 2006b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Sahani 2011	There was no comparison of whether cancer was present or not.
Sai 2003	There was no comparison of whether cancer was present or not.
Sakamoto 2008	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Sakamoto 2009	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Salvia 2012	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Sandrasegaran 2011	There was no comparison of whether cancer was present or not.
Santhosh 2013	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless

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	<p>all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Sarbia 2007	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Sariya 2003	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Savides 2006	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Savides 2007	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Savoy 2007	<p>This study was not included as no pancreatic mass was present in the patient(s) tested.</p>
Saxena 2014	<p>There was no comparison of whether cancer was present or not.</p>
Schick 2008	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Schima 2002	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>

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Schmidt 2015	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Schneider 2015	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Schrader 2012	This study was not included as no pancreatic mass was present in the patient(s) tested.
Schraibman 2011	There was no comparison of whether cancer was present or not.
Scott 2000	There was no comparison of whether cancer was present or not.
Seicean 2010	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Seicean 2016	Inadequate reference standards
Sendino 2010	There was no comparison of whether cancer was present or not.
Sendler 2000	Inadequate reference standards
Serikawa 2006	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Shah 2008	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Shen 2013	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Shimizu 2010	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Shimizu 2013a	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Shimizu 2013b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient).

Study	Reason for exclusion
	Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Shimizu 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Shimizu 2015	Inappropriate index test
Shin 2002	This study was not included as no pancreatic mass was present in the patient(s) tested.
Shin 2010	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Siddiqui 2009	There was no comparison of whether cancer was present or not.
Siddiqui 2010	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Siddiqui 2011	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Siddiqui 2012	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Siddiqui 2013	There was no comparison of whether cancer was present or not.
Siech 1998	There was no comparison of whether cancer was present or not.
Simon 2009	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Sina 2014	The study was not classed as primary research (i.e. not a review or editorial or comment).
Singer 2007	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Singhi 2014	There was no comparison of whether cancer was present or not.
Singhi 2016	Inadequate reference standards

Study	Reason for exclusion
Singu 2008	There was no comparison of whether cancer was present or not.
Soares 2015a	Inadequate reference standards
Soares 2015b	Inadequate reference standards
Sole 2005	There was no comparison of whether cancer was present or not.
Song 2007	There was no comparison of whether cancer was present or not.
Song 2010	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Sperti 1994	There was no comparison of whether cancer was present or not.
Sperti 2001	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Sperti 2005	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Sperti 2007	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Sreenarasimhaiah 2008	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.</p>
Sreenarasimhaiah 2009	<p>This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient).</p>

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	Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Sreenarasimhaiah 2013	The study was not classed as primary research (i.e. not a review or editorial or comment).
Sreenarasimhaiah 2015	There was no comparison of whether cancer was present or not.
Staib 1997	This study was not included as no pancreatic mass was present in the patient(s) tested.
Starkov 2008	This study was not included as no pancreatic mass was present in the patient(s) tested.
Stelow 2003	There was no comparison of whether cancer was present or not.
Storch 2006	This study was not included as no pancreatic mass was present in the patient(s) tested.
Storch 2007	This study was not included as no pancreatic mass was present in the patient(s) tested.
Story 2009	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Strand 2014	There was no comparison of whether cancer was present or not.
Strauss 2016	Inadequate reference standards
Strobel 2013	The study was not classed as primary research (i.e. not a review or editorial or comment).
Strohms 1984	This study was not included as no pancreatic mass was present in the patient(s) tested.
Su 2007	There was no comparison of whether cancer was present or not.
Sugimoto 2015	Inadequate reference standards
Sugiyama 2012	This study was not included as no pancreatic mass was present in the patient(s) tested.
Suits 1999	This study was not included as no pancreatic mass was present in the patient(s) tested.
Sun 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Sur 2015	Inadequate reference standards
Suzuki 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient).

Study	Reason for exclusion
	Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Suzuki 2013	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Sverko 2011	This study was not included as no pancreatic mass was present in the patient(s) tested.
Swobodnik 1983	This study was not included as no pancreatic mass was present in the patient(s) tested.
Szafranska 2008	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Tada 2002	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Tadic 2008	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Takahashi 2005	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Talar-Wojnarowska 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Tallini 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless

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	all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Taouli 2002	The study was not classed as primary research (i.e. not a review or editorial or comment).
Tarantino 2014a	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Tarantino 2014b	There was no comparison of whether cancer was present or not.
Tarantino 2014c	There was no comparison of whether cancer was present or not.
Tatsumi 2011	This study was not included as no pancreatic mass was present in the patient(s) tested.
Tatsuta 1985	This study was not included as no pancreatic mass was present in the patient(s) tested.
Taylor 2007	The study was not classed as primary research (i.e. not a review or editorial or comment).
Tervahartiala 1997	This study was not included as no pancreatic mass was present in the patient(s) tested.
Tessler 2006	This study was not included as no pancreatic mass was present in the patient(s) tested.
Theruvath 2010	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Thomas 2009	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Thomas 2010a	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Thomas 2010b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Tlostanova 2008	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless

Study	Reason for exclusion
	all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Togliani 2015	This study was not included as no pancreatic mass was present in the patient(s) tested.
Touchefeu 2009	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Trifunovic 2004	This study was not included as no pancreatic mass was present in the patient(s) tested.
Tummala 2013	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Turowska 2007	This study was not included as no pancreatic mass was present in the patient(s) tested.
Uehara 2011	This study was not included as no pancreatic mass was present in the patient(s) tested.
Uehara 2015	Inadequate reference standards
Uekitani 2016	Inadequate reference standards
Valinas 2002	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
van Gulik 1999	This study was not included as no pancreatic mass was present in the patient(s) tested.
van Kouwen 2004	The study was not classed as primary research (i.e. not a review or editorial or comment).
van Kouwen 2005	This study was not included as no pancreatic mass was present in the patient(s) tested.
Vanbiervliet 2014	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Varadarajulu 2004a	There was no comparison of whether cancer was present or not.

Study	Reason for exclusion
Varadarajulu 2004b	This study was not included as no pancreatic mass was present in the patient(s) tested.
Varadarajulu 2014a	There was no comparison of whether cancer was present or not.
Varadarajulu 2014b	There was no comparison of whether cancer was present or not.
Vasile 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Verzola 2000	This study was not included as no pancreatic mass was present in the patient(s) tested.
Vilgrain 1989	There was no comparison of whether cancer was present or not.
Vilgrain 1995	There was no comparison of whether cancer was present or not.
Vilmann 1995	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Virtue 2008	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Visser 2007	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Visser 2008	There was no comparison of whether cancer was present or not.
Voss 2000	There was no comparison of whether cancer was present or not.
Votrubova 2005	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Vullierme 2007	There was no comparison of whether cancer was present or not.

Study	Reason for exclusion
Wachs 2010	There was no comparison of whether cancer was present or not.
Wakabayashi 2008	This study was not included as no pancreatic mass was present in the patient(s) tested.
Wakatsuki 2004	There was no comparison of whether cancer was present or not.
Wakatsuki 2005	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Walter 2015	Inadequate reference standards
Wang 2005	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Wang 2007a	There was no comparison of whether cancer was present or not.
Wang 2007b	This study was not included as no pancreatic mass was present in the patient(s) tested.
Wang 2009	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Wang 2011a	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Wang 2011b	This study was not included as no pancreatic mass was present in the patient(s) tested.
Wang 2012	There was no comparison of whether cancer was present or not.
Wani 2011	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Wani 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Warda 2015	Inadequate reference standards
Watanabe 2012	This study was not included as no pancreatic mass was present in the patient(s) tested.

Study	Reason for exclusion
Waters 2008	There was no comparison of whether cancer was present or not.
Waxman 2001	The study was not classed as primary research (i.e. not a review or editorial or comment).
Wegener 1995	There was no comparison of whether cancer was present or not.
Wiersema 1994	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Wiersema 2002	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Wiesenauer 2003	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Will 2007	This study was not included as no pancreatic mass was present in the patient(s) tested.
Will 2008	This study was not included as no pancreatic mass was present in the patient(s) tested.
Will 2010	This study was not included as no pancreatic mass was present in the patient(s) tested.
Williams 1999	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Wilson 2009	This study was not included as no pancreatic mass was present in the patient(s) tested.
Winner 2015	There was no comparison of whether cancer was present or not.
Wittmann 2006	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Woolf 2013	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.

Study	Reason for exclusion
Wright 2014	There was no comparison of whether cancer was present or not.
Wu 2007a	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Wu 2007b	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Wu 2013	This study was not included as no pancreatic mass was present in the patient(s) tested.
Wu 2014	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Wyse 2009	This study was not included as no pancreatic mass was present in the patient(s) tested.
Xiao 2009	There was no comparison of whether cancer was present or not.
Xu 2012	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Xu 2013	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Xu 2014	There was no comparison of whether cancer was present or not.
Yamada 2010a	There was no comparison of whether cancer was present or not.
Yamada 2010b	This study was not included as no pancreatic mass was present in the patient(s) tested.
Yamaguchi 1990	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Yamao 2003	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.

Study	Reason for exclusion
Yamashita 2015	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Yan 2014	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Yang 2014	There was no comparison of whether cancer was present or not.
Yang 2015a	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Yang 2015b	Inadequate reference standards
Yantiss 2008	There was no comparison of whether cancer was present or not.
Yao 2012	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Yeh 1999	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Yim 2005	There was no comparison of whether cancer was present or not.
Yin 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Yin 2015	Inadequate reference standards
Ylagan 2002	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Yoshioka 2015	There was no comparison of whether cancer was present or not.
Yuan 2007	There was no comparison of whether cancer was present or not.

Study	Reason for exclusion
Yun 2007	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Yusuf 2009	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Zamboni 2012	This study was not included as no pancreatic mass was present in the patient(s) tested.
Zaruba 2013	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Zdanyte 2004	There was no comparison of whether cancer was present or not.
Zeiderman 1991	This study did not use an index test such as CT, MRI, PET, EUS-FNA, and EUS elastography.
Zhang 2010a	There was no comparison of whether cancer was present or not.
Zhang 2010b	This study was not included as no pancreatic mass was present in the patient(s) tested.
Zhang 2010c	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Zhang 2010d	There was no comparison of whether cancer was present or not.
Zhang 2011	Diagnostic accuracy data were not available for this study. We classed any of the following as acceptable forms of data: (2 x 2 table OR sensitivity + specificity + number with and without disease OR positive + negative predictive values + number of positive and negative tests) OR total test positive + total test negative + total disease positive + total disease present + total disease absent + accuracy percentage.
Zhang 2012	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Zhang 2015	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient).

Study	Reason for exclusion
	Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Zhong 2012	There was no comparison of whether cancer was present or not.
Zhu 2008	There was no comparison of whether cancer was present or not.
Zhu 2013	This study was not included as no pancreatic mass was present in the patient(s) tested.
Ziak 2011	There was no comparison of whether cancer was present or not.
Zimny 1997	This study was not included as no pancreatic mass was present in the patient(s) tested.
Zimny 1998	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Zimny 1999	The study was not classed as primary research (i.e. not a review or editorial or comment).
Zubarik 2004	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.
Zyrek-Betts 2008	This study included an inadequate reference standard. Our criteria for a reference standard included the following: all surgery, or with negative follow-up of at least 6 months; if EUS-FNA or other imaging modalities used for reference standard (either positive or negative), not accepted unless all patients (positive and negative) were followed up for at least 6 months. Clear evidence of metastases during follow-up in patients with positive diagnosis (an increase in size is not sufficient). Biopsy (but not EUS-FNA cytology) is acceptable for positive results (< 6 months) but not for negative results – if negative, patients must have been followed for at least 6 months.

CT: computed tomography
 EUS: endoscopic ultrasound
 FNA: fine-needle aspiration
 MRI: magnetic resonance imaging
 PET: positron emission tomography

DATA

Presented below are all the data for all of the tests entered into the review.

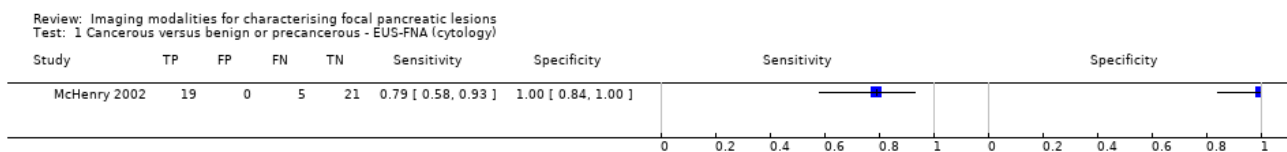
Table Tests. Data tables by test

Test	No. of studies	No. of participants
1 Cancerous versus benign or precancerous - EUS-FNA (cytology)	1	45

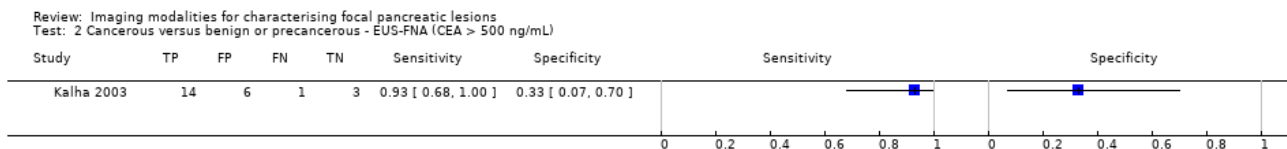
Test	No. of studies	No. of participants
2 Cancerous versus benign or precancerous - EUS-FNA (CEA > 500 ng/mL)	1	24
3 Cancerous versus benign or precancerous - PET	1	76
4 Cancerous versus benign - EUS	2	133
5 Cancerous versus benign - EUS-FNA	3	147
6 Cancerous versus benign - PET	3	99
7 Cancerous versus benign - PET (SUVmax > 3.5)	1	80
8 Cancerous versus benign - CT	2	123
9 Cancerous versus benign - MRI	1	29
10 Precancerous or cancerous versus benign - EUS	1	34
11 Precancerous or cancerous versus benign - EUS-FNA	3	52
12 Precancerous or cancerous versus benign - EUS-FNA (CEA > 50 ng/mL)	1	11
13 Precancerous or cancerous versus benign - PET (SUVmax > 2.4)	1	32
14 Precancerous or cancerous versus benign - CT	1	48
15 Precancerous or cancerous versus benign - MRI	1	27
16 Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS	5	156
17 Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS-FNA	3	158
18 Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS-FNA (CEA > 200 ng/mL)	1	41
19 Cancerous (invasive carcinoma) versus precancerous (dysplasia) - CT	6	326
20 Cancerous (invasive carcinoma) versus precancerous (dysplasia) - MRI	1	32
21 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS	4	196
22 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS-FNA	3	310
23 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS-FNA (CEA > 200 ng/mL)	3	160
24 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS-FNA (CA 19-9 > 1000 U/mL)	1	41
25 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS-FNA (CEA > 692.8 ng/mL)	1	20

Test	No. of studies	No. of participants
26 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - PET (SUVmax 2 to 2.5)	4	124
27 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - CT	3	139
28 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - MRI	3	189
29 Cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia) - EUS	1	51
30 Cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia) - CT	1	46
31 Precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia) - CT	3	106
32 Precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia) - MRI	2	71
33 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) or benign - EUS	1	70
34 Cystic lesion subgroup analysis - Cancerous versus benign - EUS-FNA	1	26
35 Cystic lesion subgroup analysis - Cancerous versus benign - PET	1	80
36 Cystic lesion subgroup analysis - Precancerous or cancerous versus benign - EUS-FNA	2	34

Test 1. Cancerous versus benign or precancerous - EUS-FNA (cytology).

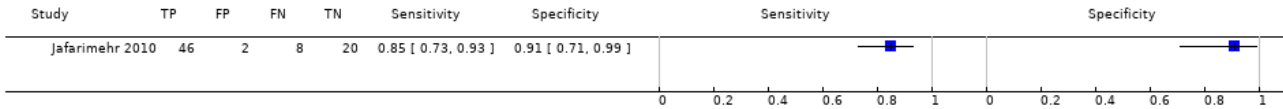


Test 2. Cancerous versus benign or precancerous - EUS-FNA (CEA > 500 ng/mL).



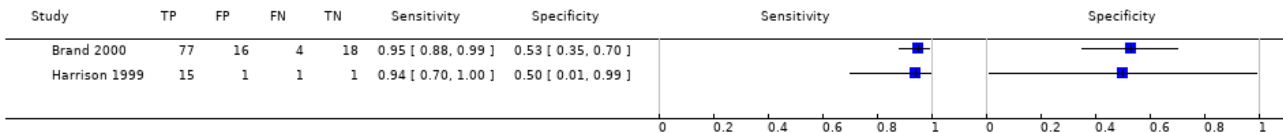
Test 3. Cancerous versus benign or precancerous - PET.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 3 Cancerous versus benign or precancerous - PET



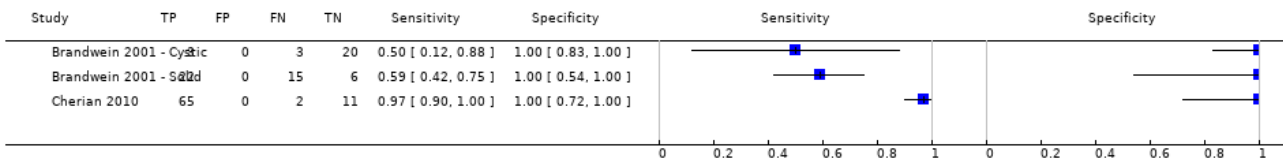
Test 4. Cancerous versus benign - EUS.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 4 Cancerous versus benign - EUS



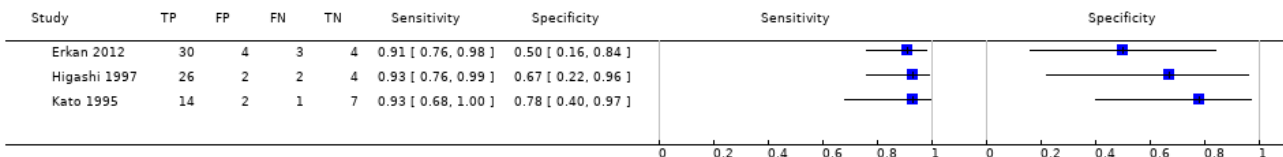
Test 5. Cancerous versus benign - EUS-FNA.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 5 Cancerous versus benign - EUS-FNA



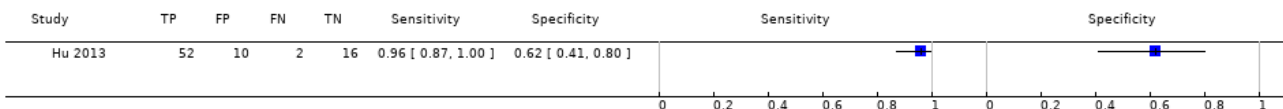
Test 6. Cancerous versus benign - PET.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 6 Cancerous versus benign - PET



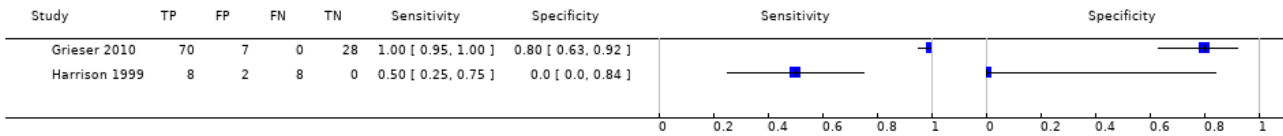
Test 7. Cancerous versus benign - PET (SUVmax > 3.5).

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 7 Cancerous versus benign - PET (SUVmax > 3.5)



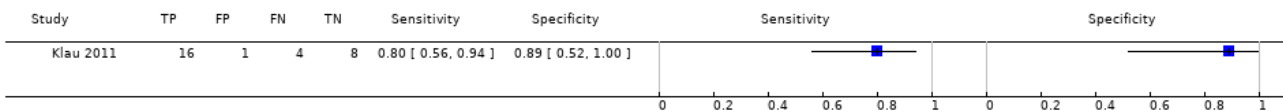
Test 8. Cancerous versus benign - CT.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 8 Cancerous versus benign - CT



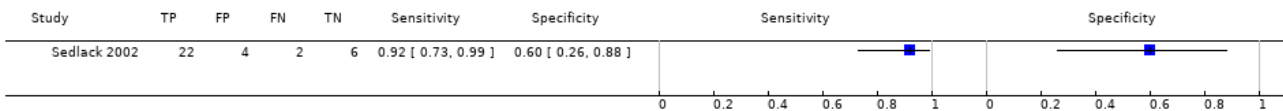
Test 9. Cancerous versus benign - MRI.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 9 Cancerous versus benign - MRI



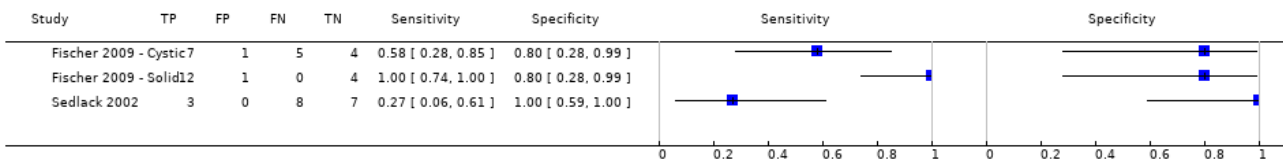
Test 10. Precancerous or cancerous versus benign - EUS.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 10 Precancerous or cancerous versus benign - EUS



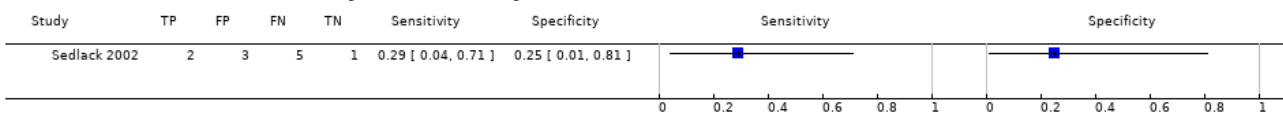
Test 11. Precancerous or cancerous versus benign - EUS-FNA.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 11 Precancerous or cancerous versus benign - EUS-FNA



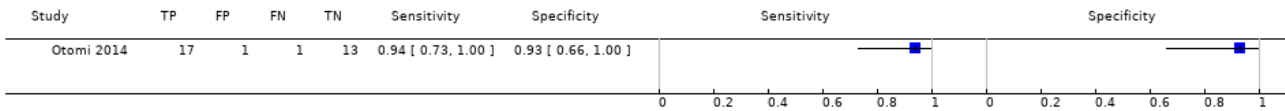
Test 12. Precancerous or cancerous versus benign - EUS-FNA (CEA > 50 ng/mL).

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 12 Precancerous or cancerous versus benign - EUS-FNA (CEA > 50 ng/mL)



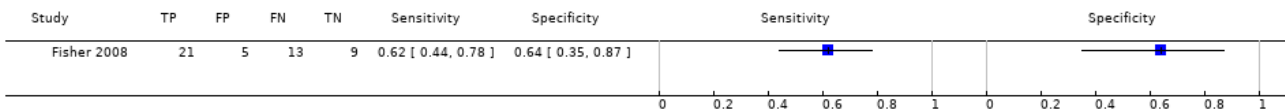
Test 13. Precancerous or cancerous versus benign - PET (SUVmax > 2.4).

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 13 Precancerous or cancerous versus benign - PET (SUVmax > 2.4)



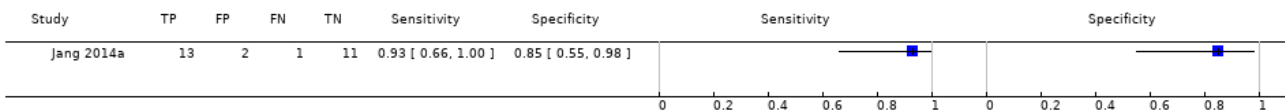
Test 14. Precancerous or cancerous versus benign - CT.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 14 Precancerous or cancerous versus benign - CT



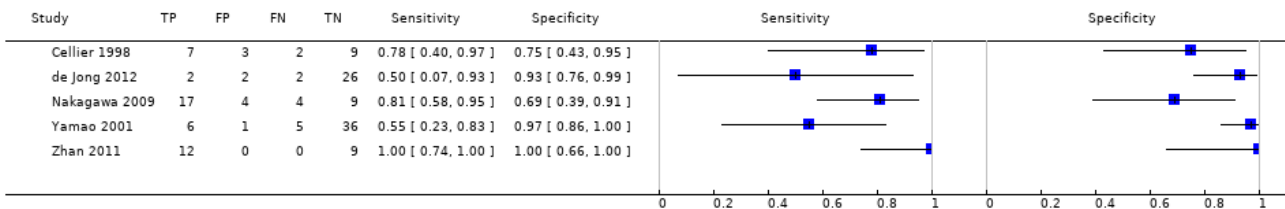
Test 15. Precancerous or cancerous versus benign - MRI.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 15 Precancerous or cancerous versus benign - MRI



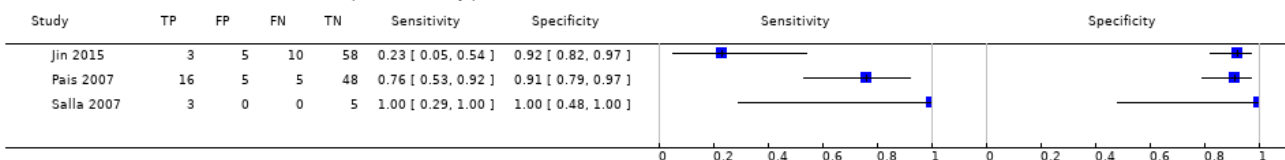
Test 16. Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 16 Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS



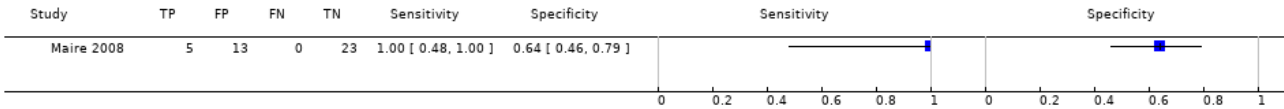
Test 17. Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS-FNA.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 17 Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS-FNA



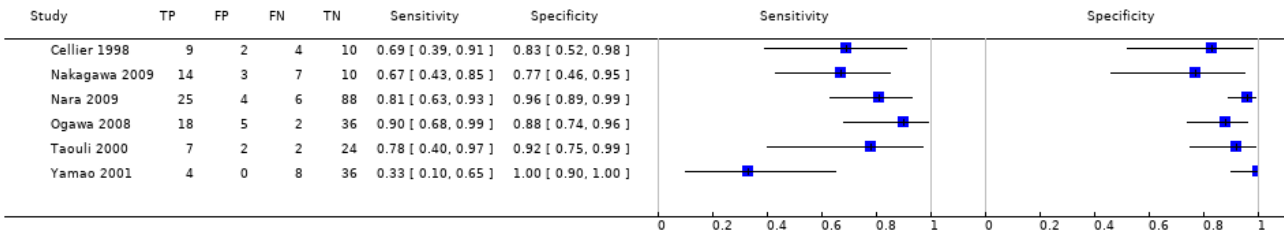
Test 18. Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS-FNA (CEA > 200 ng/mL).

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 18 Cancerous (invasive carcinoma) versus precancerous (dysplasia) - EUS-FNA (CEA > 200 ng/mL)



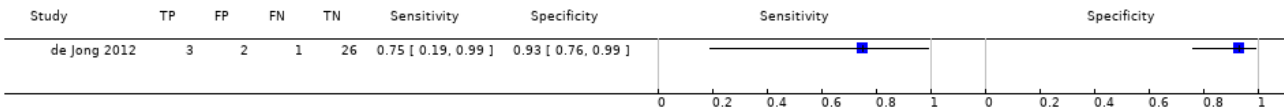
Test 19. Cancerous (invasive carcinoma) versus precancerous (dysplasia) - CT.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 19 Cancerous (invasive carcinoma) versus precancerous (dysplasia) - CT



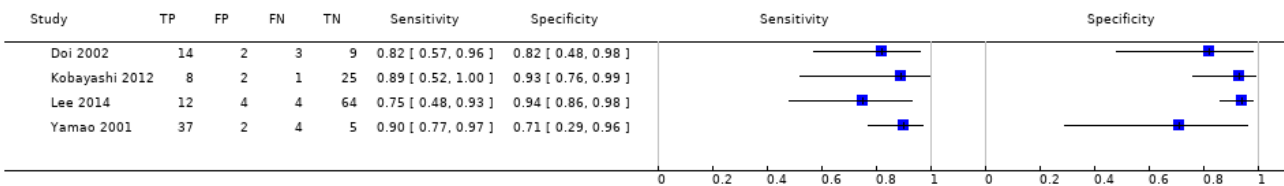
Test 20. Cancerous (invasive carcinoma) versus precancerous (dysplasia) - MRI.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 20 Cancerous (invasive carcinoma) versus precancerous (dysplasia) - MRI



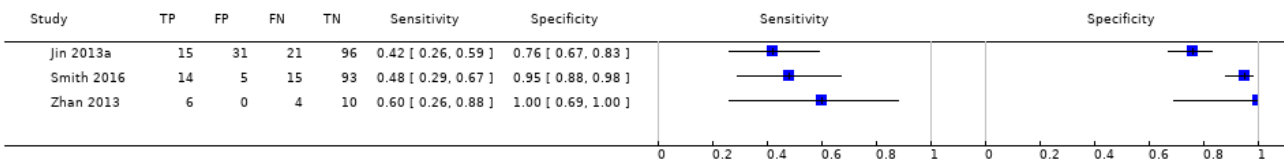
Test 21. Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 21 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS



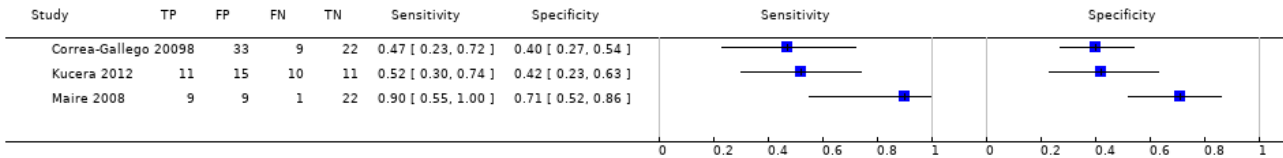
Test 22. Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS-FNA.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 22 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS-FNA



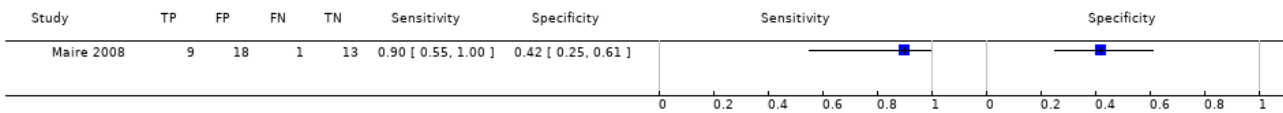
Test 23. Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS-FNA (CEA > 200 ng/mL).

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 23 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS-FNA (CEA > 200 ng/mL)



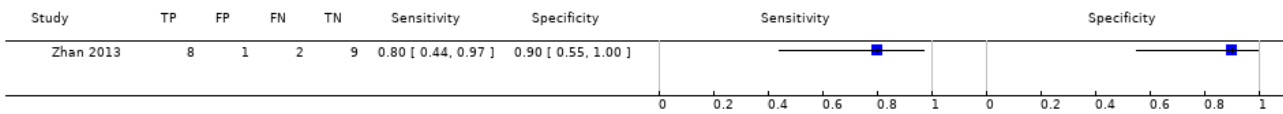
Test 24. Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS-FNA (CA 19-9 > 1000 U/mL).

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 24 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS-FNA (CA 19-9 > 1000 U/mL)



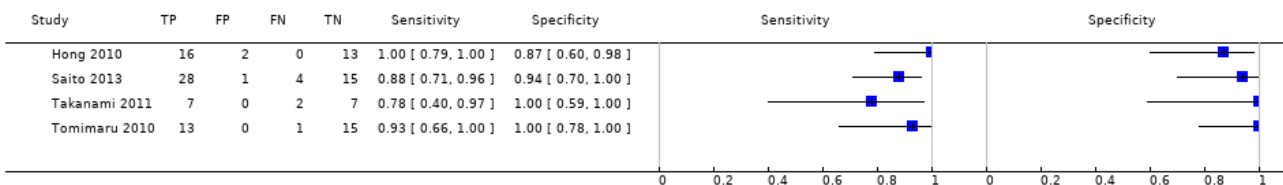
Test 25. Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS-FNA (CEA > 692.8 ng/mL).

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 25 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - EUS-FNA (CEA > 692.8 ng/mL)



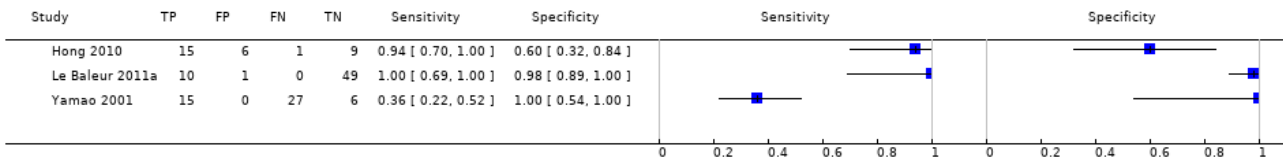
Test 26. Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - PET (SUVmax 2 to 2.5).

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 26 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - PET (SUVmax 2 to 2.5)



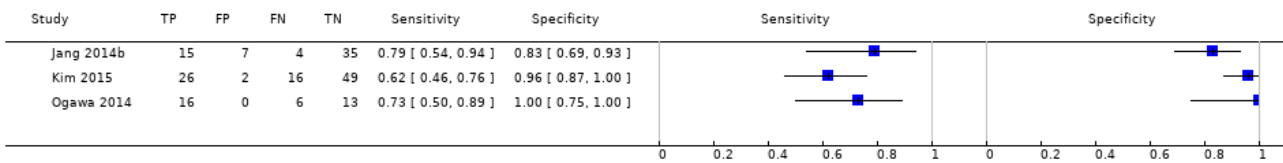
Test 27. Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - CT.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 27 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - CT



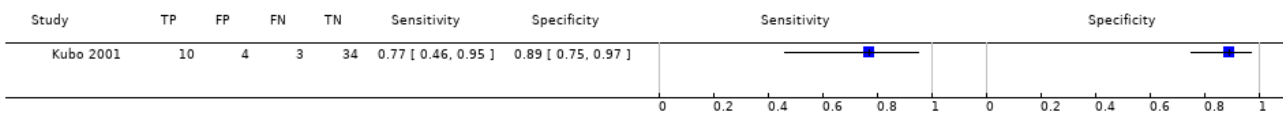
Test 28. Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - MRI.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 28 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) - MRI



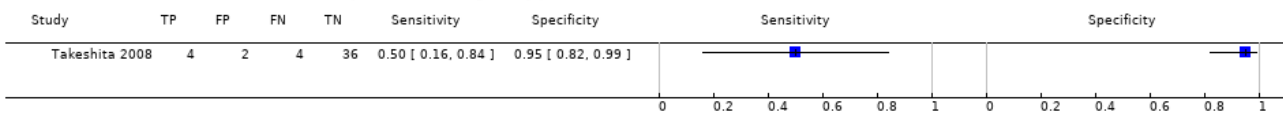
Test 29. Cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia) - EUS.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 29 Cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia) - EUS



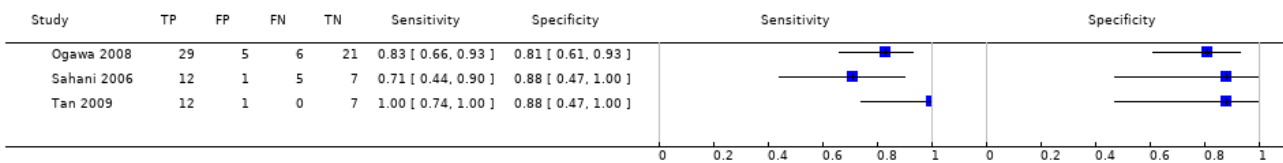
Test 30. Cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia) - CT.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 30 Cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia) - CT



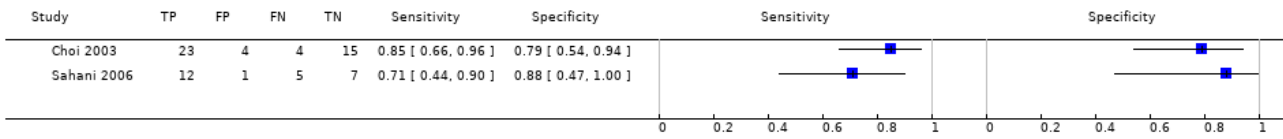
Test 31. Precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia) - CT.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 31 Precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia) - CT



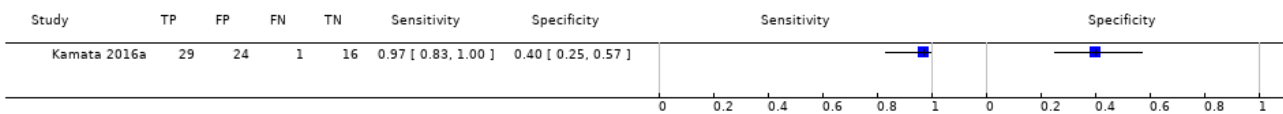
Test 32. Precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia) - MRI.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 32 Precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia) - MRI



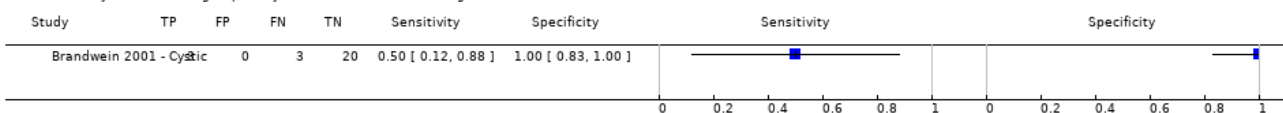
Test 33. Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) or benign - EUS.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 33 Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia) or benign - EUS



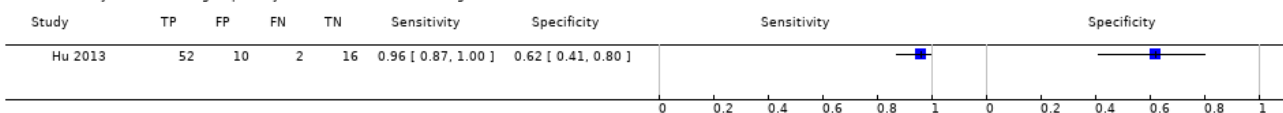
Test 34. Cystic lesion subgroup analysis - Cancerous versus benign - EUS-FNA.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 34 Cystic lesion subgroup analysis - Cancerous versus benign - EUS-FNA



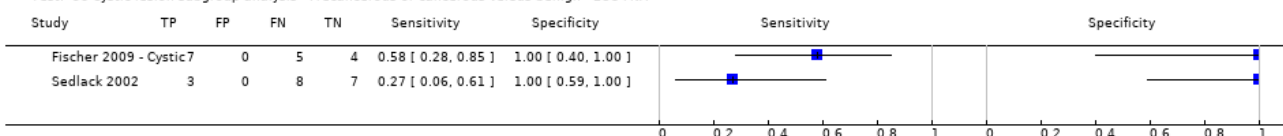
Test 35. Cystic lesion subgroup analysis - Cancerous versus benign - PET.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 35 Cystic lesion subgroup analysis - Cancerous versus benign - PET



Test 36. Cystic lesion subgroup analysis - Precancerous or cancerous versus benign - EUS-FNA.

Review: Imaging modalities for characterising focal pancreatic lesions
Test: 36 Cystic lesion subgroup analysis - Precancerous or cancerous versus benign - EUS-FNA



ADDITIONAL TABLES

Table 1. QUADAS-2 classification

Domain	Signalling question	Signalling question	Signalling question	Risk of bias	Concerns for applicability
1: Patient sampling	Was a consecutive or random sample of patients enrolled?	Was a case-control design avoided?	Did the study avoid inappropriate exclusions?	Could the selection of participants have introduced bias?	Are there concerns that the included participants and setting do not match the review question?
	<p>Yes: all consecutive patients or random sample of patients with focal pancreatic lesions were enrolled</p> <p>No: selected patients were enrolled</p> <p>Unclear: this was not clear from the report</p>	<p>Yes: case-control design was avoided</p> <p>No: case-control design was not avoided</p> <p>Unclear: this was not clear from the report</p>	<p>Yes: the study avoided inappropriate exclusions (i.e. difficult-to-diagnose patients)</p> <p>No: the study excluded patients inappropriately</p> <p>Unclear: this was not clear from the report</p>	<p>Low risk: 'yes' for all signalling questions</p> <p>High risk: 'no' or 'unclear' for at least 1 signalling question</p>	<p>Low concern: the selected participants represent the patients in whom the tests will be used in clinical practice (please see diagnostic pathway (Figure 1))</p> <p>High concern: there is high concern that participant selection was performed in such a way that the included participants did not represent the patients in whom the tests will be used in clinical practice</p>
2: Index test(s)	Were the index test results interpreted without knowledge of the results of the reference standard?	If a threshold was used, was it prespecified?	—	Could the conduct or interpretation of the index test have introduced bias?	Are there concerns that the index test, its conduct, or its interpretation differ from the review question?
	<p>Yes: index test results were interpreted without knowledge of the results of the reference standard</p> <p>No: index test results were interpreted with knowledge of the results of the reference standard</p> <p>Unclear: this was not clear from the report</p>	<p>Yes: if the criteria for a positive test were prespecified</p> <p>No: if the criteria for a positive test were not prespecified</p> <p>Unclear: this was not clear from the report</p>	—	<p>Low risk: 'yes' for all signalling questions</p> <p>High risk: 'no' or 'unclear' for at least 1 of the 2 signalling questions</p>	<p>High concern: there is high concern that the conduct or interpretation of the index test differs from the way it is likely to be used in clinical practice</p> <p>Low concern: there is low concern that the conduct or interpretation of the</p>

Table 1. QUADAS-2 classification (Continued)

					index test differs from the way it is likely to be used in clinical practice
3: Target condition and reference standard(s)	Is the reference standard likely to classify the target condition correctly?	Were the reference standard results interpreted without knowledge of the results of the index tests?	—	Could the reference standard, its conduct, or its interpretation have introduced bias?	Are there concerns that the target condition as defined by the reference standard does not match the review question?
	<p>Yes: histopathological examination of the entire lesion by surgical resection</p> <p>No: histopathological examination (irrespective of how the tissues were obtained for histopathological examination) in patients with positive test (for cancerous or precancerous lesions) and clinical follow-up by a doctor (with or without sequential follow-up with imaging) of all patients with negative test for a period of at least 6 months and for a maximum period of 24 months</p> <p>Unclear: this was not clear from the report. Such studies will be excluded</p> <p>Yes: reference standard results were interpreted without knowledge of the results of the index test</p> <p>No: reference standard results were interpreted with knowledge of the results of the index test</p> <p>Unclear: this was not clear from the report</p>	—	<p>Low risk: 'yes' for all signalling questions</p> <p>High risk: 'no' or 'unclear' for at least 1 of the 2 signalling questions</p>	<p>Low concern: histopathological examination of the entire lesion by surgical resection</p> <p>High concern: histopathological examination (irrespective of how the tissues were obtained for histopathological examination) in patients with positive test (for cancerous or precancerous lesions) and clinical follow-up by a doctor (with or without sequential follow-up with imaging) of all patients with negative test for a period of at least 6 months and for a maximum period of 24 months</p>	—
4: Flow and timing	Was there an appropriate interval between index test and reference standard?	Did all patients receive the same reference standard?	Were all patients included in the analysis?	Could the patient flow have introduced bias?	—
	<p>Yes:</p> <p>histopathological examination of the entire lesion (gold standard) - performed within 2 months (chosen arbitrarily).</p>	<p>Yes: histopathological examination of the entire lesion by surgical resection</p> <p>No: histopathological examina-</p>	<p>Yes: all patients meeting the selection criteria (selected participants) were included</p>	<p>Low risk: 'yes' for all signalling questions</p> <p>High risk: 'no' or 'unclear' for at least 1 signalling question</p>	—

Table 1. QUADAS-2 classification (Continued)

<p>Histopathological examination (irrespective of how the tissues were obtained for histopathological examination) in patients with positive test (for cancerous or precancerous lesions) performed within 2 months and clinical follow-up (including sequential follow-up with imaging) of all patients with negative test for a period of at least 6 months</p>	<p>tion (irrespective of how the tissues were obtained for histopathological examination) in patients with positive test (for cancerous or precancerous lesions) and clinical follow-up by a doctor (with or without sequential follow-up with imaging) of all patients with negative test for a period of at least 6 months and for a maximum period of 24 months</p>	<p>in the analysis, or data on all of the selected participants were available so that a 2 x 2 table including all selected participants could be constructed</p>
<p>No:</p> <p>the histopathological examination was performed beyond 2 months of the index tests.</p> <p>The clinical follow-up (including sequential follow-up imaging) was performed less than 6 months after the index test, because some tumours may be slow-growing</p> <p>Unclear: this was not clear from the report</p>	<p>Unclear: this was not clear from the report. Such studies will be excluded</p>	<p>No: not all patients meeting the selection criteria were included in the analysis, or the 2 x 2 table could not be constructed using data on all selected participants</p> <p>Unclear: this was not clear from the report</p>

Table 2. Summary sensitivity and specificity of different tests for different target conditions

Comparison	Name of test	Sensitivity	Specificity
Cancerous versus benign or precancerous	EUS-FNA (cytology)	0.79 (95% CI 0.60 to 0.91)	1.00 (95% CI 0.85 to 1.00)
Cancerous versus benign or precancerous	EUS-FNA (CEA > 500 ng/mL)	0.93 (95% CI 0.70 to 0.99)	0.33 (95% CI 0.12 to 0.65)
Cancerous versus benign or precancerous	PET (criteria unspecified)	0.85 (95% CI 0.73 to 0.92)	0.91 (95% CI 0.72 to 0.97)
Cancerous versus benign	EUS	0.95 (95% CI 0.84 to 0.99)	0.53 (95% CI 0.31 to 0.74)
Cancerous versus benign	EUS-FNA (cytology)	0.79 (95% CI 0.07 to 1.00)	1.00 (95% CI 0.91 to 1.00)
Cancerous versus benign	PET (criteria unspecified)	0.92 (95% CI 0.80 to 0.97)	0.65 (95% CI 0.39 to 0.85)
Cancerous versus benign	PET (SUVmax > 3.5)	0.96 (95% CI 0.87 to 0.99)	0.62 (95% CI 0.43 to 0.78)

Table 2. Summary sensitivity and specificity of different tests for different target conditions (Continued)

Cancerous versus benign	CT	0.98 (95% CI 0.00 to 1.00)	0.76 (95% CI 0.02 to 1.00)
Cancerous versus benign	MRI	0.80 (95% CI 0.58 to 0.92)	0.89 (95% CI 0.57 to 0.98)
Precancerous or cancerous versus benign	EUS	0.92 (95% CI 0.74 to 0.98)	0.60 (95% CI 0.31 to 0.83)
Precancerous or cancerous versus benign	EUS-FNA (cytology)	0.73 (95% CI 0.01 to 1.00)	0.94 (95% CI 0.15 to 1.00)
Precancerous or cancerous versus benign	EUS-FNA (CEA > 50 ng/mL)	0.29 (95% CI 0.08 to 0.64)	0.25 (95% CI 0.05 to 0.70)
Precancerous or cancerous versus benign	PET (SUVmax 2.4)	0.94 (95% CI 0.74 to 0.99)	0.93 (95% CI 0.69 to 0.99)
Precancerous or cancerous versus benign	CT	0.62 (95% CI 0.45 to 0.76)	0.64 (95% CI 0.39 to 0.84)
Precancerous or cancerous versus benign	MRI	0.93 (95% CI 0.69 to 0.99)	0.85 (95% CI 0.58 to 0.96)
Cancerous (invasive carcinoma) versus precancerous (dysplasia)	EUS	0.78 (95% CI 0.45 to 0.94)	0.91 (95% CI 0.61 to 0.98)
Cancerous (invasive carcinoma) versus precancerous (dysplasia)	EUS-FNA (cytology)	0.66 (95% CI 0.03 to 0.99)	0.92 (95% CI 0.73 to 0.98)
Cancerous (invasive carcinoma) versus precancerous (dysplasia)	EUS-FNA (CEA > 200 ng/mL)	1.00 (95% CI 0.57 to 1.00)	0.64 (95% CI 0.48 to 0.78)
Cancerous (invasive carcinoma) versus precancerous (dysplasia)	CT	0.72 (95% CI 0.50 to 0.87)	0.92 (95% CI 0.81 to 0.97)
Cancerous (invasive carcinoma) versus precancerous (dysplasia)	MRI	0.75 (95% CI 0.30 to 0.95)	0.93 (95% CI 0.77 to 0.98)
Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia)	EUS	0.86 (95% CI 0.74 to 0.92)	0.91 (95% CI 0.83 to 0.96)
Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia)	EUS-FNA (cytology)	0.47 (95% CI 0.24 to 0.70)	0.91 (95% CI 0.32 to 1.00)
Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia)	EUS-FNA (CEA > 200 ng/mL)	0.58 (95% CI 0.28 to 0.83)	0.51 (95% CI 0.19 to 0.81)
Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia)	EUS-FNA (CA 19-9 > 1000 U/mL)	0.90 (95% CI 0.60 to 0.98)	0.42 (95% CI 0.26 to 0.59)

Table 2. Summary sensitivity and specificity of different tests for different target conditions (Continued)

Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia)	EUS-FNA (CEA > 692.8 ng/mL)	0.80 (95% CI 0.49 to 0.94)	0.90 (95% CI 0.60 to 0.98)
Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia)	PET (SUVmax > 2 to 2.5)	0.90 (95% CI 0.79 to 0.96)	0.94 (95% CI 0.81 to 0.99)
Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia)	CT	0.87 (95% CI 0.00 to 1.00)	0.96 (95% CI 0.00 to 1.00)
Cancerous (high-grade dysplasia or invasive carcinoma) versus precancerous (low- or intermediate-grade dysplasia)	MRI	0.69 (95% CI 0.44 to 0.86)	0.93 (95% CI 0.43 to 1.00)
Cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia)	EUS	0.77 (95% CI 0.50 to 0.92)	0.89 (95% CI 0.76 to 0.96)
Cancerous (invasive carcinoma) versus precancerous (low-grade dysplasia)	CT	0.50 (95% CI 0.22 to 0.78)	0.95 (95% CI 0.83 to 0.99)
Precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia)	CT	0.83 (95% CI 0.68 to 0.92)	0.83 (95% CI 0.64 to 0.93)
Precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia)	MRI	0.80 (95% CI 0.58 to 0.92)	0.81 (95% CI 0.53 to 0.95)
Precancerous or cancerous (intermediate- or high-grade dysplasia or invasive carcinoma) versus precancerous (low-grade dysplasia) or benign	EUS	0.97 (95% CI 0.83 to 0.99)	0.40 (95% CI 0.26 to 0.55)
Cystic lesion subgroup analysis	Cancerous versus benign - EUS-FNA (cytology)	0.50 (95% CI 0.19 to 0.81)	1.00 (95% CI 0.84 to 1.00)
Cystic lesion subgroup analysis	Cancerous versus benign - PET (SUVmax > 3.5)	0.96 (95% CI 0.87 to 0.99)	0.62 (95% CI 0.43 to 0.78)
Cystic lesion subgroup analysis	Precancerous or cancerous versus benign - EUS-FNA (cytology)	0.43 (95% CI 0.19 to 0.71)	1.00 (95% CI 0.74 to 1.00)

CA 19-9: carbohydrate antigen 19-9

CEA: carcinoembryonic antigen

CI: confidence interval

CT: computed tomography

EUS: endoscopic ultrasound

FNA: fine-needle aspiration

MRI: magnetic resonance imaging

PET: positron emission tomography

SUVmax: maximum standardised uptake values

APPENDICES

Appendix 1. Glossary of terms

Ablation: destruction of tissue.

Adenocarcinoma: cancer arising from cells that secrete digestive enzymes (proteins that help with the breakdown of food into simple substances that the gut can absorb).

Algorithm: order in which diagnostic tests are performed and actions taken depending upon the results of the tests (in this context).

Asymptomatic: not showing any signs of disease or illness.

Benign: non-cancerous (in this context).

Biomarkers: substances in an organism that indicate disease or illness.

Chemotherapy: medication used to treat or control cancer (in this context).

Contraindication: something that causes a specific treatment or procedure to be withheld because it would cause harm.

Cystic: related to an abnormal enclosed sac found within the body that is filled with a fluid or semifluid substance.

Cytology: the study of cells obtained from a tissue to determine whether the cell is cancerous (in this context).

Density: the measure of how compact something is (in this context).

Diffuse: spread out.

Disseminated: spread of cancer (in this context).

Dysplasia: abnormal growth or development of cell; precancerous (in this context).

Focal: characterised as being a specific or limited area of disease (in this context).

Gastrointestinal: related to the stomach and intestines.

Histological: examination of tissues under a microscope.

Histopathological: examination of tissues under a microscope to determine the changes related to a disease or illness.

Hormone: a chemical substance secreted by the body's cells that acts on other cells of the body, stimulating them to perform their role or suppressing the functions of the cells. Hormones are generally transported in the blood or other body fluids (e.g. stomach juice) from the cell that secretes the hormones to the cell on which they act.

Immunocytochemistry: examination of tissues under a microscope using special stains that bind to specific types of cells or tissues.

Ionising radiation: radiation consisting of particles, X-rays, or gamma rays with sufficient energy to cause ionisation in the medium through which it passes, thereby damaging cells (in this context).

Laparoscopy: a surgical procedure in which an instrument is inserted through a small incision in the abdomen to view the organs or permit a surgical procedure using small instruments.

Lesions: abnormal changes in the structure of all or part of an organ due to disease (in this context).

Malignancies: cancers.

Metastases: the spread of cancer beyond its original source.

Modality: method.

Morphological: related to structure.

Mortality: death.

Peptic: related to stomach or the upper part of the intestine.

Percutaneous: performed through the skin.

Perioperative: around the time of surgery.

Prognosis: outcomes resulting from disease or illness or related to the treatment of disease or illness.

Proteomic: related to the study of proteins.

Radiological: related to X-rays or ultrasound.

Resection: removal of all or part of an organ.

Steatorrhea: excessive fat in stools.

Surveillance: close observation.

Vascularity: the degree of vessels (tubes that carry blood in humans).

Appendix 2. Cochrane search strategy

#1 (pancreas OR pancreatic)

#2 (CT OR tomodesitometry OR PET OR MRI OR NMRI OR zeugmatogra* OR ((computed OR computerised OR computerized OR emission OR positron OR magneti* OR MR OR NMR OR proton OR acoustic OR ARFI) AND (tomogra* OR scan OR scans OR imaging)) OR endosonogra* OR EUS OR ((echogra* OR ultrason* OR ultrasound) AND endoscop*) OR elastogr* OR sonoelastogr* OR acoustogra*)

#3 #1 AND #2

Appendix 3. MEDLINE search strategy

1. exp Pancreas/

2. exp Pancreatic Neoplasms/di [Diagnosis]

3. exp Pancreatitis, Chronic/di [Diagnosis]

4. exp Pancreatic Cyst/di [Diagnosis]

5. (pancreas or pancreatic).ti,ab.

6. 1 or 2 or 3 or 4 or 5

7. (sensitiv: or diagnos:).mp. or di.fs.

8. 6 and 7

9. (CT or tomodesitometry or PET or MRI or NMRI or zeugmatogra* or ((computed or computerised or computerized or emission or positron or magneti* or MR or NMR or proton or acoustic or ARFI) and (tomogra* or scan or scans or imaging)).ti,ab.

10. exp Tomography, X-Ray Computed/ or Positron-Emission Tomography/ or exp Magnetic Resonance Imaging/

11. 9 or 10

12. exp Endosonography/

13. (endosonogra* or EUS).ti,ab.

14. 12 or 13

15. exp Ultrasonography/

16. (echogra* or ultrason* or ultrasound).ti,ab.

17. 15 or 16

18. exp Endoscopy, Gastrointestinal/

19. endoscop*.ti,ab.

20. 18 or 19

21. 17 and 20

22. 14 or 21

23. exp Elasticity Imaging Techniques/

24. (elastogr* or sonoelastogr* or acoustogra*).ti,ab.

25. 23 or 24

26. 11 or 22 or 25

27. 8 and 26

Appendix 4. Embase search strategy

1. exp pancreas/

2. exp pancreas tumor/di [Diagnosis]

3. exp chronic pancreatitis/di [Diagnosis]

4. exp pancreas cyst/di [Diagnosis]

5. (pancreas or pancreatic).ti,ab.

6. 1 or 2 or 3 or 4 or 5

7. sensitiv.:tw. or diagnostic accuracy.sh. or diagnostic.tw.

8. 6 and 7

9. (CT or tomodensitometry or PET or MRI or NMRI or zeugmatogra* or ((computed or computerised or computerized or emission or positron or magneti* or MR or NMR or proton or acoustic or ARFI) and (tomogra* or scan or scans or imaging))).ti,ab.

10. exp computer assisted tomography/ or positron emission tomography/ or exp nuclear magnetic resonance imaging/

11. 9 or 10

12. endoscopic echography/

13. (endosonogra* or EUS).ti,ab.

14. 12 or 13

15. exp ultrasound/

16. (echogra* or ultrason* or ultrasound).ti,ab.

17. 15 or 16

18. exp gastrointestinal endoscopy/

19. endoscop*.ti,ab.

20. 18 or 19

21. 17 and 20

22. 14 or 21

23. exp elastography/

24. (elastogr* or sonoelastogr* or acoustogra*).ti,ab.

25. 23 or 24

26. 11 or 22 or 25

27. 8 and 26

Appendix 5. Science Citation Index Expanded search strategy

#1 TS=(pancreas OR pancreatic)

#2 TS=(CT OR tomiodensitometry OR PET OR MRI OR NMRI OR zeugmatogra* OR ((computed OR computerised OR computerized OR emission OR positron OR magneti* OR MR OR NMR OR proton OR acoustic OR ARFI) AND (tomogra* OR scan OR scans OR imaging)) OR endosonogra* OR EUS OR ((echogra* OR ultrason* OR ultrasound) AND endoscop*) OR elastogr* OR sonoelastogr* OR acoustogra*)

#3 TS=(sensitiv* OR "predictive value" OR diagnostic OR accuracy)

#4 #1 AND #2 AND #3

CONTRIBUTIONS OF AUTHORS

L Best, K Gurusamy, and V Rawji wrote sections of the review. SP Pereira and BR Davidson critically commented on the review.

DECLARATIONS OF INTEREST

This project was supported by the National Institute for Health Research (NIHR), via Cochrane Infrastructure, Cochrane Programme Grant, or Cochrane Incentive funding to the Upper Gastrointestinal and Pancreatic Diseases Group and Cochrane Hepato-Biliary Group. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, National Health Service (NHS), or the Department of Health.

LMJB: none known.

VR: none known.

SPP: none known.

BRD: none known.

KSG: none known.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

1. We have included sensitivity-maximising diagnostic filters for searching MEDLINE and Embase databases because the original searches without the filters retrieved more than 50,000 references (Haynes 2004; Wilczynski 2005). We also made some modifications to the search strategy because we needed to balance the possibility of missing some studies against the risk of not being able to complete the review. We decided that it is useful to have evidence from major studies rather than having no information at all.
2. We did not search the Cochrane Register of Diagnostic Test Accuracy Studies, as we believe it is no longer maintained.
3. We have performed the related search function through MEDLINE (OvidSP) rather than MEDLINE (PubMed) and also performed a cited reference search in MEDLINE (via OvidSP).
4. We have reworded the [Statistical analysis and data synthesis](#) section to bring this in line with our recent reviews. There were no material differences to the plan of statistical analysis except that we also planned to perform a bivariate analysis, which takes into account the correlation between sensitivity and specificity for tests with explicit thresholds as well. We did this because the summary sensitivity and specificity (and hence the positive likelihood ratio and negative likelihood ratio from which the post-test probabilities can be calculated) are available from the bivariate model.
5. We have simplified the analysis in the presence of sparse data based on the article by Takwoingi and colleagues (Takwoingi 2015).
6. We have presented the post-test probabilities only for the median prevalence in the comparison to avoid presenting readers with an overwhelming amount of data.

INDEX TERMS**Medical Subject Headings (MeSH)**

Diagnostic Imaging [*methods]; Elasticity Imaging Techniques; Endoscopic Ultrasound-Guided Fine Needle Aspiration; Endosonography; Magnetic Resonance Imaging; Pancreatic Diseases [diagnostic imaging]; Pancreatic Neoplasms [*diagnostic imaging]; Positron-Emission Tomography; Precancerous Conditions [*diagnostic imaging]; Sensitivity and Specificity; Tomography, X-Ray Computed

MeSH check words

Humans