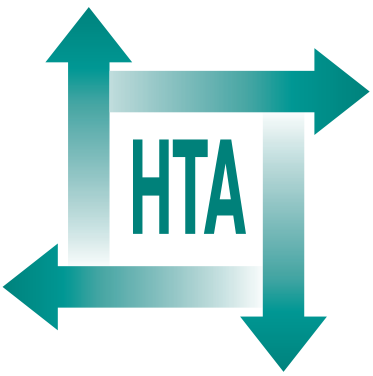
Health Technology Assessment 2004; Vol. 8: No. 10

A systematic review and economic evaluation of magnetic resonance cholangiopancreatography compared with diagnostic endoscopic retrograde cholangiopancreatography

E Kaltenthaler, Y Bravo Vergel, J Chilcott, S Thomas, T Blakeborough, SJ Walters and H Bouchier

March 2004

Health Technology Assessment
NHS R&D HTA Programme



How to obtain copies of this and other HTA Programme reports.
An electronic version of this publication, in Adobe Acrobat format, is available for downloading free of charge for personal use from the HTA website (http://www.hta.ac.uk). A fully searchable CD-ROM is also available (see below).

Printed copies of HTA monographs cost £20 each (post and packing free in the UK) to both public **and** private sector purchasers from our Despatch Agents.

Non-UK purchasers will have to pay a small fee for post and packing. For European countries the cost is £2 per monograph and for the rest of the world £3 per monograph.

You can order HTA monographs from our Despatch Agents:

– fax (with **credit card** or **official purchase order**)
– post (with **credit card** or **official purchase order** or **cheque**)
– phone during office hours (**credit card** only).

Additionally the HTA website allows you **either** to pay securely by credit card **or** to print out your order and then post or fax it.

Contact details are as follows:

HTA Despatch
c/o Direct Mail Works Ltd
4 Oakwood Business Centre
Downley, HAVANT PO9 2NP, UK

Email: orders@hta.ac.uk
Tel: 02392 492 000
Fax: 02392 478 555
Fax from outside the UK: +44 2392 478 555

NHS libraries can subscribe free of charge. Public libraries can subscribe at a very reduced cost of £100 for each volume (normally comprising 30–40 titles). The commercial subscription rate is £300 per volume. Please see our website for details. Subscriptions can only be purchased for the current or forthcoming volume.

Payment methods

Paying by cheque
If you pay by cheque, the cheque must be in **pounds sterling**, made payable to *Direct Mail Works Ltd* and drawn on a bank with a UK address.

Paying by credit card
The following cards are accepted by phone, fax, post or via the website ordering pages: Delta, Eurocard, Mastercard, Solo, Switch and Visa. We advise against sending credit card details in a plain email.

Paying by official purchase order
You can post or fax these, but they must be from public bodies (i.e. NHS or universities) within the UK. We cannot at present accept purchase orders from commercial companies or from outside the UK.

How do I get a copy of *HTA on CD*?

Please use the form on the HTA website (www.hta.ac.uk/htacd.htm). Or contact Direct Mail Works (see contact details above) by email, post, fax or phone. *HTA on CD* is currently free of charge worldwide.

The website also provides information about the HTA Programme and lists the membership of the various committees.

A systematic review and economic evaluation of magnetic resonance cholangiopancreatography compared with diagnostic endoscopic retrograde cholangiopancreatography

E Kaltenthaler,[1*] Y Bravo Vergel,[2] J Chilcott,[1] S Thomas,[3] T Blakeborough,[4] SJ Walters[1] and H Bouchier[1]

[1] ScHARR Rapid Reviews Group, School of Health and Related Research, University of Sheffield, UK
[2] Nuffield Institute for Health, University of Leeds, UK
[3] Northern General Hospital, Sheffield, UK
[4] Royal Hallamshire Hospital, Sheffield, UK

* Corresponding author

Declared competing interests of authors: none of the authors has any financial interest in the companies producing the equipment used to undertake magnetic resonance cholangiopancreatography.

Published March 2004

This report should be referenced as follows:

Kaltenthaler E, Bravo Vergel Y, Chilcott J, Thomas S, Blakeborough T, Walters SJ, *et al*. A systematic review and economic evaluation of magnetic resonance cholangiopancreatography compared with diagnostic endoscopic retrograde cholangiopancreatography. *Health Technol Assess* 2004;**8**(10).

Health Technology Assessment is indexed in *Index Medicus*/MEDLINE and *Excerpta Medica*/EMBASE.

NHS R&D HTA Programme

The NHS R&D Health Technology Assessment (HTA) Programme was set up in 1993 to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS.

The research reported in this monograph was commissioned by the HTA Programme and was funded as project number 02/43/01. Technology assessment reports are completed in a limited time to inform decisions in key areas by bringing together evidence on the use of the technology concerned.

The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health. The editors wish to emphasise that funding and publication of this research by the NHS should not be taken as implicit support for any recommendations made by the authors.

Criteria for inclusion in the HTA monograph series
Reports are published in the HTA monograph series if (1) they have resulted from work commissioned for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The editors and publisher have tried to ensure the accuracy of this report but do not accept liability for damages or losses arising from material published in this report.

ISSN 1366-5278

Published by Gray Publishing, Tunbridge Wells, Kent, on behalf of NCCHTA.
Printed on acid-free paper in the UK by St Edmundsbury Press Ltd, Bury St Edmunds, Suffolk.

Abstract

A systematic review and economic evaluation of magnetic resonance cholangiopancreatography compared with diagnostic endoscopic retrograde cholangiopancreatography

E Kaltenthaler,[1*] Y Bravo Vergel,[2] J Chilcott,[1] S Thomas,[3] T Blakeborough,[4] SJ Walters[1] and H Bouchier[1]

[1] ScHARR Rapid Reviews Group, School of Health and Related Research, University of Sheffield, UK
[2] Nuffield Institute for Health, University of Leeds, UK
[3] Northern General Hospital, Sheffield, UK
[4] Royal Hallamshire Hospital, Sheffield, UK
* Corresponding author

Objectives: To compare the clinical and cost-effectiveness of magnetic resonance cholangiopancreatography (MRCP) with diagnostic endoscopic retrograde cholangiopancreatography (ERCP) for the investigation of biliary obstruction.
Data sources: Electronic bibliographic databases, the reference lists of relevant articles and various health services research-related resources.
Review methods: The data sources were searched and selected studies were assessed using quality criteria. In total, 28 prospective diagnostic studies were identified reporting several suspected conditions plus one of patient satisfaction. Analyses were then performed to establish sensitivities, specificities, likelihood ratios and confidence intervals. The relative cost-effectiveness of adopting MRCP scanning in the investigation of the biliary tree was undertaken using a probabilistic economic model.
Results: The median sensitivity for choledocholithiasis (13 studies) was 93% and the median specificity 94%. The median likelihood ratio for a positive value was 15.75 and for a negative value 0.08. Reported sensitivities for malignancy were somewhat lower, ranging from 81 to 86%, and specificities ranged from 92 to 100%. There was some evidence that MRCP is an accurate diagnostic test in comparison to ERCP, although the quality of studies was moderate. Claustrophobia prevented at least some patients from having MRCP in ten of the 28 studies. The other 18 studies did not mention claustrophobia. The probability of avoiding unnecessary diagnostic ERCP is estimated at 30%. These patients could avoid the unnecessary risk of complications and death associated with diagnostic ERCP, and substantial cost saving would be gained. The overall expected cost saving associated with MRCP is £149; the overall expected gain in quality-adjusted life-year is estimated at 0.011.
Conclusions: There is some evidence that MRCP is an accurate investigation compared with diagnostic ERCP, although the values for malignancy compared with choledocholithiasis were somewhat lower. The quality of studies was moderate. The limited evidence on patient satisfaction showed that patients preferred MRCP to diagnostic ERCP. The estimated clinical and economic impacts of diagnostic MRCP versus diagnostic ERCP are very favourable. The baseline estimate is that MRCP may both reduce cost and result in improved quality of life outcomes compared with diagnostic ERCP. Further research is suggested to compare MRCP and diagnostic ERCP with final diagnosis and also with the full range of target conditions; to examine patient satisfaction and ways of reducing problems with claustrophobia; to look at protocols to help identify who could most benefit from MRCP or ERCP; to assess the relative need and urgency of patient access to magnetic resonance imaging services, and also to determine how demand would affect availability and potential cost savings.

Contents

Glossary and list of abbreviations

Technical terms and abbreviations are used throughout this report. The meaning is usually clear from the context, but a glossary is provided for the non-specialist reader. In some cases, usage differs in the literature, but the term has a constant meaning throughout this review.

Glossary

Accuracy True positives and true negatives as a proportion of all results; true positives + true negatives/total.

Choledocholithiasis Gallstones in the extrahepatic bile ducts.

Cholelithiasis The presence of microscopic crystals or large stones in the gallbladder.

Likelihood ratio of a positive test The likelihood of a positive test being found in a person with the condition compared with in a person without it; sensitivity/(1 – specificity).

Likelihood ratio of a negative test The likelihood of a negative test being found in a person without the condition compared with in a person with it; (1 – sensitivity)/specificity.

Sensitivity The proportion of patients with disease who test positive; true positives/(true positives + false negatives).

Specificity The proportion of patients without disease who test negative; true negatives/(false positives + true negatives).

List of abbreviations

2D	two-dimensional
3D	three-dimensional
CBD	common bile duct
CCTR	Cochrane Controlled Trials Register
CDSR	Cochrane Database of Systematic Reviews
CEAC	cost-effectiveness acceptability curve
CI	confidence interval
CT	computed tomography
EORTC QLQ-30	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-30
ERCP	endoscopic retrograde cholangiopancreatography
EUS	endoscopic ultrasonography
FCE	finished clinical episode
FSE	fast spin-echo
HASTE	half-Fourier single-shot turbo spin echo
HEED	Health Economics Evaluations Database
HES	Hospital Episode Statistics
HRGs	Healthcare Resource Groups
ICD-10	International Classification of Diseases-10
IOC	intraoperative cholangiography
κ	kappa value, used to determine interobserver agreement

continued

List of abbreviations *continued*

LFT	liver function test
LRN	likelihood ratio negative
LRP	likelihood ratio positive
MAICER	maximum acceptable incremental cost-effectiveness ratio
MIP	maximum intensity projection
MR	magnetic resonance
MRCP	magnetic resonance cholangiopancreatography
MRI	magnetic resonance imaging
NHS DARE	Database of Assessment of Reviews of Effectiveness
NHS EED	Economic Evaluations Database
NSRC	National Schedule of Reference Costs
PBJ	pancreatobiliary junction
PSC	primary sclerosing cholangitis
PTC	percutaneous transhepatic cholangiography
QALY	quality-adjusted life-year
RARE	rapid acquisition and relaxation enhancement
RCR	Royal College of Radiologists
ROC	receiver operating characteristic
SD	standard deviation
SE	standard error
TSE	turbo spin echo
TTO	time trade-off

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices in which case the abbreviation is defined in the figure legend or at the end of the table.

Executive summary

Background

Magnetic resonance cholangiopancreatography (MRCP) is an alternative to diagnostic endoscopic retrograde cholangiopancreatography (ERCP) for imaging the biliary tree and investigating biliary obstruction. MRCP is a purely diagnostic test with no therapeutic value. It does not have the small but definite morbidity and mortality associated with ERCP.

Biliary obstruction may be due to choledocholithiasis, tumours or trauma including injury after gallbladder surgery, among other causes. Choledocholithiasis is the most common cause. Between 5 and 22% of the Western population has gallstones. The overall prevalence rate for symptomatic gallstones for England and Wales in 1991–2 was 182 per 10,000 person-years at risk. The incidence rate was 8 for cholelithiasis, 9 for other disorders of the gallbladder and 2 for other disorders of the biliary tract per 10,000 person-years at risk. At the time of cholecystectomy for symptomatic cholelithiasis, 8–25% of patients under 60 years and 15–60% of patients over 60 years also have choledocholithiasis.

MRCP refers to selective or partially selective magnetic resonance imaging (MRI) of the pancreatic and biliary ducts. It was developed in 1991 and techniques have progressively improved since then. Patients should be fasting and the procedure takes a few minutes, usually without sedation. Claustrophobia is a problem with some patients. A major feature of MRCP is that it is not a therapeutic procedure, whereas ERCP is used for diagnosis and treatment. The impact of this is that if ERCP is necessary after MRCP as a therapeutic intervention, MRCP could have been avoided and patients would be able to proceed immediately to treatment. However, if no therapeutic intervention is found to be necessary, MRCP avoids the potential morbidity and mortality associated with ERCP. MRCP is particularly useful where ERCP is difficult, hazardous or impossible. It is also an important option for patients with failed ERCPs. ERCP and MRCP have different contraindications, allowing them to be used as complementary techniques.

There are opportunity costs associated with MRCP, in that if an MRI scanner is used for MRCP it cannot be used for other types of imaging.

Objective

The aim of this review is to compare the clinical and cost-effectiveness of MRCP with diagnostic ERCP for the investigation of biliary obstruction.

Number and quality of studies and direction of evidence

Initially 67 potentially relevant papers were considered for inclusion, of which 38 were excluded owing to poor quality or comparators other than ERCP. In total, 28 prospective diagnostic studies were identified comparing MRCP with diagnostic ERCP. One study of patient satisfaction was also identified. The 28 studies reported several suspected conditions. Choledocholithiasis was included in 18 studies, malignancy in four, obstruction in three, stricture in two, dilatation in five and primary sclerosing cholangitis (PSC) in two studies.

The quality of the studies was moderate. In all but one study, patients selected to have both MRCP and diagnostic ERCP did not have both and often the reasons why were unclear. Only 13 of the 28 studies reported blinding to both clinical information for patients and ERCP results, and only six of the 28 studies reported information on agreement of MRCP results for more than one investigator. Nine studies gave no information on other diagnostic tests and most studies did not adequately report inclusion and exclusion criteria and relevant patient characteristics. Of the 28 studies, seven reported results comparing MRCP with final diagnosis, which included ERCP and other test results. The remaining 21 studies reported results comparing MRCP with ERCP.

Effectiveness was assessed by condition. For choledocholithiasis 15 of the 18 studies reported adequate data for analysis; two of these were removed as they differed in some aspects from the other studies. Owing to statistically significant

heterogeneity between the studies, the median values were considered the most appropriate to report. The median sensitivity for the 13 studies of choledocholithiasis was 0.93 (range 0.81–1.00) and the median specificity 0.94 (0.83–0.99). A likelihood ratio describes how many times a person with disease is more likely to receive a particular test result than a person without disease. The median positive likelihood ratio was 15.75 (range 5.44–64.78) and the median negative likelihood ratio 0.08 (0.00–0.19).

For malignancy, sensitivity ranged from 81 to 94.4% and specificity from 92 to 100%. Positive likelihood ratios ranged from 10.12 to 43 and negative likelihood ratios from 0.15 to 0.21. The sensitivity for dilatation ranged from 87 to 100% and the specificity from 91 to 100%. For obstruction, both sensitivity and specificity ranged from 91 to 100%. Sensitivity for stricture was 100% and specificity ranged from 98 to 99%.

Claustrophobia associated with MRCP in at least some patients was reported in ten of the 28 studies, with no information on claustrophobia reported in the remaining 18 studies. There were no adverse effects associated with MRCP in any of the studies, although six studies reported adverse effects associated with ERCP, including pancreatitis, bleeding and pain. Twenty studies reported no information regarding adverse effects.

One study was identified that dealt with patient satisfaction: most patients preferred MRCP, but there were still some who preferred ERCP. Nearly half of the patients in this small study complained of claustrophobia associated with MRCP, although only 5.9% refused MRCP for this reason.

Summary of benefits

The median sensitivity for choledocholithiasis (13 studies) was 93% (range 81–100%) and the median specificity 94% (83–99%). The median likelihood ratio for a positive value was 15.75 (range 5.44–64.78) and for a negative value 0.08 (0.00–0.19). Reported sensitivities for malignancy were somewhat lower, ranging from 81 to 86%, and specificities ranged from 92 to 100%.

In the 28 studies, which included 38 subgroups, one positive likelihood ratio was less than 5 and four negative likelihood ratios were greater than 0.2. There is therefore some evidence that MRCP is an accurate diagnostic test in comparison to ERCP, although the quality of studies was moderate.

Claustrophobia prevented at least some patients from having MRCP in ten of the 28 studies. The other 18 studies did not mention claustrophobia.

Cost-effectiveness

The probability of avoiding unnecessary diagnostic ERCP, that is, the probability of a true-negative MRCP, is estimated at 30% [95% confidence interval (CI) 20 to 40%]. These patients could avoid the unnecessary risk of complications and death associated with diagnostic ERCP, and substantial cost saving would be gained. The overall expected cost saving associated with MRCP is £149 (£325 to –£15); the overall expected gain in quality-adjusted life-year is estimated at 0.011 (0.000, 0.030).

Conclusions

There is some evidence that MRCP is an accurate investigation compared with diagnostic ERCP, although the values for malignancy compared with choledocholithiasis were somewhat lower. The quality of studies was moderate. The limited evidence on patient satisfaction showed that patients preferred MRCP to diagnostic ERCP.

The estimated clinical and economic impacts of diagnostic MRCP versus diagnostic ERCP are very favourable. The baseline estimate is that MRCP may both reduce cost and result in improved quality of life outcomes compared with diagnostic ERCP. The uncertainty analysis, investigating the impact of parametric uncertainty within the model, indicates that this result is robust. However, there are marked uncertainties in the structure and assumptions within the decision analytical model that are not captured within this parametric uncertainty analysis. The results presented in this assessment will thus overstate the robustness of the economic outcomes for MRCP.

Recommendations for research

The following were identified as areas where further research is needed.

- Good quality studies are needed comparing MRCP and diagnostic ERCP with final diagnosis, stating inclusion/exclusion criteria and relevant patient characteristics. This would help to overcome some of the shortcomings of comparisons with diagnostic ERCP.

- Studies are needed comparing MRCP with diagnostic ERCP for the full range of target conditions, in particular differentiation of benign and malignant strictures and the impact on management and outcome.
- More research is needed in the area of patient satisfaction and ways to reduce problems with claustrophobia and make MRCP more acceptable to patients.
- Protocols, assessing prior risk, are needed to help to identify which patients with which suspected conditions would most benefit from MRCP and which would benefit from ERCP.
- To understand the real opportunity costs associated with MRCP, studies are needed to assess the relative need and urgency of patient access to MRI services.
- As the development of MRCP (a non-invasive test) may result in an increase in requests over what would be expected for ERCP (an invasive test), research is needed to determine how this will affect availability and potential cost savings.

Chapter 1

Aim of the review

Diagnosis of biliary obstruction is usually made or confirmed on the basis of an initial ultrasound examination showing dilated bile ducts. If the ultrasound shows information such as a stone in the bile duct or an inoperable tumour then the patient proceeds directly to endoscopic retrograde cholangiopancreatography (ERCP). ERCP is a diagnostic and therapeutic modality that has a small but definite morbidity and mortality.[1] Magnetic resonance cholangiopancreatography (MRCP) is an alternative to diagnostic ERCP for imaging the bile ducts. MRCP is a purely diagnostic test with no therapeutic capability, but does not have the risks associated with ERCP. ERCP may be used therapeutically for stone extraction, sphincterotomy and stent insertion. MRCP may be appropriate where ERCP is indicated for diagnostic purposes only.

The overall aim of the review is to assess the clinical effectiveness and cost-effectiveness of the use of MRCP compared with diagnostic ERCP. More specifically, the review aims:

- to evaluate the clinical effectiveness of MRCP in terms of test reliability, diagnostic accuracy, diagnostic impact, therapeutic impact and patient outcomes in comparison with diagnostic ERCP
- to evaluate cost-effectiveness in comparison with diagnostic ERCP
- to estimate the possible overall cost in England and Wales.

Chapter 2
Background

Description of underlying health problem

Biliary obstruction

Biliary obstruction can be due to a variety of causes, including gallstones, tumours of the bile ducts or pancreas, other tumours that have spread to the biliary system, trauma including injury from gallbladder surgery, choledochal cysts, enlarged nodes in the porta hepatis and inflammation of the bile ducts.[2] Risk factors for biliary obstruction include a history of cholelithiasis (gallstones), chronic pancreatitis or pancreatic cancer, recent biliary surgery, recent biliary cancer and abdominal trauma. Symptoms of biliary obstruction include pale-coloured stools, dark urine, jaundice, itching, abdominal pain in the upper right quadrant, fever, nausea and vomiting. Jaundice is the most common presentation of patients with liver and biliary disease.[3] Diseases affecting the gallbladder and bile ducts occur commonly in the elderly.[4] One of the most common causes of biliary obstruction is choledocholithiasis, also known as common bile duct (CBD) stones.

Primary sclerosing cholangitis (PSC) is an idiopathic chronic fibrosing inflammatory disease of the bile ducts that eventually leads to bile duct obliteration, cholestasis and biliary cirrhosis.[5] The prevalence of this disease of uncertain aetiology is 1–6 per 100,000 people.[6]

Choledocholethiasis

CBD stones can be divided into primary stones, which form in the biliary ducts, and secondary stones, which form in the gallbladder and later migrate into the biliary ducts. Most CBD stones (95%) are secondary.[7] It is difficult to estimate the exact prevalence of choledocholithiasis as small stones can migrate from the CBD into the duodenum without symptoms.[7]

All patients with symptomatic gallbladder stones (cholelithiasis) need to be assessed for CBD stones, and treatment of CBD stones is usually suggested as the occurrence of symptoms or complications is unpredictable.[8] Patients may remain symptom free but later develop symptoms and require further treatment. Between 5 and 22% of the population in the Western world have gallstones.[7] In the Morbidity Statistics from General Practice for England and Wales in 1991–2, gallstones were found to be most prevalent among women aged 45–64 years. The overall prevalence rate was 182 per 10,000 person-years at risk.[9] The incidence rate was 8 for cholelithiasis, 9 for other disorders of the gallbladder and 2 for other disorders of the biliary tract per 10,000 person-years at risk.[9]

Since the advent of laproscopic cholecystectomy there has been renewed interested in the preoperative diagnosis of choledocholithiasis.[10] At the time of cholecystectomy for symptomatic cholelithiasis, 8–15% of patients under 60 years of age and 15–60% of patients over the age of 60 have CBD stones.[8] Mortality associated with cholethiasis and cholecystitis for England and Wales in 1999 was 679 for underlying cause of death and 1431 for mentioned cause.[11]

Malignancy

Patients with malignant biliary strictures usually present with cholestasis and jaundice.[4] Malignant biliary obstruction usually has a poor prognosis and is usually managed with palliation of the jaundice.[12] A small group of patients may be suitable for surgical resection.[13] Palliation usually takes the form of stent insertion.[14] In one study of 182 patients with malignant biliary obstruction, management was endoscopic and palliative. At the end of one year 20.4% were still alive.[12]

The most common malignant cause of biliary obstruction is carcinoma of the head of the pancreas. Another less common malignancy, cholangiocarcinoma, is a form of adenocarcinoma, primary to the biliary tree.[15] Of these, 10% are primary intrahepatic masses, 25% occur at the confluence of the right and left ducts (Klatskin tumours), 30% arise in the proximal common ducts and 35% arise in the distal common duct.[15] Cholangiocarcinoma is an uncommon neoplasm, representing approximately 0.5–1% of all cancers and 30% of hepatic primary malignancies.[5] Survival of patients with Klatskin tumours that are advanced and incurable is usually less than 6 months.[14]

According to the National Cancer Statistics for England, in 1997 there was a total of 1836 newly diagnosed cases of malignant neoplasms of the

liver and intrahepatic bile ducts, 404 cases of malignant neoplasm of the gallbladder, and 590 cases of malignant neoplasm of other and unspecified parts of the biliary tract.[16]

Significance in terms of ill-health

Biliary obstruction can lead to infections and be life-threatening if not corrected. If the obstruction continues for a long period, chronic liver disease can result. Obstructions caused by cancer frequently have a worse outcome. Complications include infections, sepsis and liver disease such as biliary cirrhosis if obstructions are left untreated.[2]

Biliary obstruction presents as an acute or chronic condition. Jaundice without pain suggests a malignant cause, and prompt diagnosis and treatment are important. Choledocholithiasis can present with severe pain and patients may be admitted to hospital. Pain may be intermittent and for this reason the condition is often not immediately diagnosed. PSC is a chronic condition, although there may be acute exacerbations.

Current service provision

Patients presenting with symptoms of biliary obstruction (jaundice and/or abdominal pain) initially have laboratory investigations, which usually include liver function tests. Ultrasonography is the first-line imaging investigation in patients with jaundice or right upper quadrant pain.[3] Although ultrasonography is non-invasive, quick and inexpensive it is very operator and patient dependent. Bowel gas frequently obscures the lower end of the CBD. Computed tomography (CT) may also be used and experience is required to interpret these images, as well as magnetic resonance imaging (MRI) results. Those patients with a high probability of CBD stones on the basis of the ultrasound investigations usually proceed directly to ERCP.

ERCP

ERCP was developed approximately 30 years ago and is both an endoscopic and a radiological procedure.[17] It is one of several invasive direct cholangiography techniques, along with percutaneous transhepatic cholangiography (PTC). ERCP is both a diagnostic and therapeutic intervention.[18] It is usually performed with the use of conscious sedation. An endoscope is passed to the ampulla (the opening of the bile and pancreatic ducts), located in the second portion of the duodenum. In diagnostic procedures, catheters are passed through the channel of the endoscope into the duct of interest and contrast medium is injected to outline the ductal structures. Sphincter pressure measurements can be achieved, although this is not routine and has a significant risk of producing acute pancreatitis. Therapeutic manoeuvres are performed by incising the sphincter muscle at the opening of the bile duct or pancreatic duct. Other accessories may be passed through the endoscope channel into the duct to remove stones, insert stents or ablate tissue.[17] The results are very dependent on the skills of the team involved.[19]

ERCP is currently the 'gold standard' for the diagnosis of pancreatic and biliary ductal pathology.[20] Approximately 10% of ERCPs performed are unsuccessful, approximately 15% will demonstrate normal results and many will demonstrate abnormalities that do not require further endoscopic therapy.[21] Since the introduction of endoscopic ultrasonography (EUS) and MRCP for the diagnosis of CBD stones, it has become clear that ERCP is imperfect and sphincterotomy and balloon or basket trawl of the duct may possibly be a more appropriate gold standard for diagnosis in the future.[22]

ERCP failure

ERCP is a technically demanding procedure, with reported failure rates between 3 and 12%.[23] Success rate is highly variable from one centre to another depending on the disease entities being treated, the availability of dedicated accessories and well-trained staff, and the skill of the endoscopists.[24] Other factors include the proportion of patients with adverse anatomical factors (large diverticula and stones, tortuous ducts).[25] PTC and intraoperative cholangiography (IOC) are either of inferior diagnostic quality or invasive and therefore associated with high complication rates.[26]

ERCP complications

Diagnostic ERCP has a complication rate of 5–6% and a mortality rate ranging from 0.01[1] to 0.089%.[27] Therapeutic ERCP has a complication rate of 4–10%, although some authors put the rate as high as > 20%,[28] and a mortality rate ranging from 0.07[1] to 0.3%.[29] Risk factors for complications after ERCP are patient related, procedure related or operator related. Patient-related risk factors include underlying coagulopathy and suspected dysfunction of the sphincter of Oddi. Procedure-related complications include difficult bile duct cannulation, injection of radiographic contrast material into the pancreatic duct and precut biliary sphincterotomy. Complication rates are

somewhat lower in diagnostic ERCP than in therapeutic ERCP. Higher post-ERCP complications are associated with centres where lower numbers of ERCPs are performed and when endoscopists have low ERCP caseloads.[17,28] ERCP may be impossible in some patients, such as those who have had a Billroth II gastrectomy, Roux-en-Y diversions, pancreatic pseudocysts, sclerosing cholangitis or prior serious ERCP complications.[20]

ERCP is an invasive procedure and is associated with risks such as pancreatitis and perforation.[17] Risk factors for pancreatitis include patient age under 60, use of precut papillotomy and failed clearance of bile duct stones.[24] Pancreatitis is the most frequent complication and occurs in about 5–10% of cases.[4] One large single centre study found that pancreatitis constituted 70% of complications.[27] There is also a 1% risk of bleeding, perforation and cholangitis.[4] The main advantage in using ERCP is that it is also a therapeutic intervention and can follow on immediately after diagnostic ERCP. Major disadvantages are that diagnostic ERCP in a healthy patient may result in the morbidity or mortality described above. In addition, if MRCP follows diagnostic ERCP in patients with malignancies, it is difficult to identify and accurately stage the pancreatic mass, especially after insertion of a stent into the lower CBD.

Costs and variation in services

Costs for a diagnostic ERCP examination of the bile duct are approximately £846 (2002 costs).[30] When complications are present the cost rises to approximately £1113 (2002 costs), although this ranges from £570 to £1409.[30] Costs for therapeutic ERCP, including extraction of CBD stones, are approximately £1108 (2002 costs).[30]

The provision of ERCP within a hospital setting will depend on several factors. These include demand for the procedure as this will influence waiting time. The expertise of endoscopists varies widely, which will have an impact on the number of failures and complication rates. One study reported a mean hospital stay of 2.6 days for post-ERCP pancreatitis, although this was longer in severe cases.[31]

MRCP

MRCP refers to selective or partially selective MRI of the pancreatic and biliary ducts.[32] MRCP is used to investigate suspected choledocholithiasis, neoplastic obstruction (tumours), benign and malignant strictures, chronic pancreatitis, primary sclerosing cholangitis, mucinous ductal ectasia, anatomical variants and postcholecystectomy biliary disorders.[32] Indications for the use of MRCP include unsuccessful or contraindicated ERCP, patient preference for non-invasive imaging, patients with a low index of suspicion for pancreatic or biliary disease, patients where the need for therapeutic ERCP is considered unlikely and those with suspected neoplastic, pancreatic or biliary obstruction.[32]

MRCP was first developed in 1991,[33] since when there have been significant improvements in technique.[34] MRCP broadly involves two methods, the acquisition of a volume of data that can be acquired at different angles, and multislice acquisition in coronal/axial planes and the production of composite images using maximum intensity projection (MIP). MRCP is based on heavily T2-weighted images, resulting in contrast between stationary fluids (bile and pancreatic) and background (hepatic and pancreatic parenchymas, abdominal fat). The bile presents a very high signal intensity compared with the low signal intensity background. Sequences and saturation pulses are selected to produce no signal from flowing blood. Contiguous thin slices obtained in a coronal plane are reconstructed in multiple angles with MIP. This provides an overview of the biliary tree and pancreatic ducts similar to conventional direct cholangiopancreatography. The pancreatic duct and bile duct can be observed from several angles. MRCP techniques involve the following variables: pulse sequences, two- or three-dimensional (2D or 3D) acquisition, single-slice or multislice acquisition, coil, respiration (breath-holding or non-breath-holding) and background suppression.[35]

Initially, T2-weighted 3D gradient echo sequences were used.[35] 2D fast spin-echo (FSE) sequences were then reported, but these required a relatively long breath-holding period (44–60 seconds). Third generation MRCP is a non-breath-holding FSE technique. With this technique, clear images are produced but a long acquisition time is required (11–15 minutes), depending on respiratory rate. Finally, a fourth-generation MRCP technique, single-shot turbo spin echo (TSE) sequence has been developed. The advent of FSE sequences has shortened imaging time significantly.[36] These are rapid acquisition and relaxation enhancement (RARE) techniques. The acquisition of data and the filling of K-space has allowed these sequences to become breath-holding using half-Fourier methods to fill K-space, for example in the half-Fourier single-shot turbo spin echo (HASTE) sequence.

No patient preparation is required for MRCP, although fasting for 2–4 hours is useful in reducing fluid in the gastric antrum and duodenum and filling the biliary tree and gallbladder.[18] In most patients sedation is not required.[34] MRI allows imaging in any plane and any thickness of image section.

Many patients requiring investigations with MRCP are elderly and may find it difficult to hold their breath for long periods; therefore, the use of non-breath-holding techniques has been explored. However, major limitations of using non-breath-holding techniques include limitations in the evaluation of intrahepatic ducts due to both motion artefacts and limited spatial resolution of the 2D technique.[33] Non-breath-holding techniques are often based on FSE sequences.[37] More recently, investigators have explored the possibility of MRCP with quiet breathing. Patients lie supine and a flexible torso coil is strapped to the upper abdomen. Initially some breath-holding images are obtained to identify adjacent anatomy and to allow positioning of subsequent MRCP images. Current imaging techniques usually require breath-holds of 1–15 seconds, but diagnostic quality images can still be obtained without breath-holding.

Indications and contraindications for the use of MRCP

Biliary obstruction represents the main indication for MRCP, owing to the ability of this technique to access the presence, site and cause of obstruction.[37] MRCP is particularly useful where ERCP is difficult, hazardous or impossible, such as in patients who have had Billroth II gastrectomy, Roux-en-Y diversions, pancreatic pseudocysts, sclerosing cholangitis and prior serious ERCP complications.[20] MRCP can be used to determine duct calibre, anomalies, strictures, dilatation, filling defects (calculi) and extraductal collections of fluid (cysts, diverticula and fistulae).[38] It is important to assess which subgroups of patients will benefit from pre- or postoperative MRCP;[39] also, if patients do not have an obstruction, they have not suffered unnecessary invasive procedures. MRCP is an important option for patients with failed ERCPs. Another important advantage of MRCP is that it can be coupled with MRI of adjacent viscera for identification, characterisation and staging of malignant strictures.[40]

The contraindications for ERCP and MRCP are different, allowing them to be employed as complementary techniques capable of imaging the pancreaticobiliary ducts in virtually all types of patient.[41]

Contraindications to MRCP, as in all MRI, include cardiac pacemakers, retinal metal fragments and, in some cases, subarachnoid aneurysm ferromagnetic surgical clips.[41] Other patients unsuitable for MRCP include those with severe claustrophobia, massive ascites or haemodynamic instability.[18] Patient obesity may limit the quality of MRCP images and prevent patients from being able to enter the MRI scanner.[34] There are no known risks associated with MRCP provided patients have been carefully screened.[34] Claustrophobia and emotional distress prevent completion of the MRI procedure in up to 5% of patients.[42]

In one study exploring the value of MRCP results to alter differential diagnosis and to prevent diagnostic and/or therapeutic ERCP, the authors found that the value of MRCP information may be limited if patient selection is inappropriate and may differ depending on the speciality of the physicians involved.[20] Physicians appeared most concerned that MRCP might miss small bile duct stones or subtle ductal strictures. When ERCP was planned, the addition of MRCP to ERCP did not reduce the differential diagnosis significantly and prevented few diagnostic or therapeutic ERCPs. Further research was recommended to evaluate the usefulness of MRCP to a variety of physicians for patients with normal examinations or for whom the pretest need for ERCP was uncertain.

Limitations of MRCP

There are several limitations associated with MRCP. Smaller CBD stones can be missed by MRCP.[43] However, usually stones up to 2–3 mm in size are visible. Papilla can only be seen in about 40% of patients who have MRCP.[43] There may also be difficulty in depicting minor narrowing of the cystic and pancreatic ducts.[44] Another problem associated with MRCP is that MIP reconstructed images may completely obscure small filling defects and may demonstrate respiratory motion artefacts. Source images should always be interrogated, so in practice this is not an issue. The major problem with multislice MRCP (for MIP) is respiratory misregistration. Another issue is T2 weighting, which may vary with different MRI sequences and influence findings. MRCP may be associated with diagnostic errors, and several technical and interpretive pitfalls have been associated with its use.[45] Incomplete imaging may create confusion regarding ductal anatomy or disease. MRCP yields only static images and may fail to depict various anomalies.[46] It is therefore important that both source images and projection images are analysed in order to visualise and evaluate the anatomy of the entire

pancreatobiliary tract. MRCPs of diagnostic quality can be obtained in 92–97% of patients.[23]

It should be noted that MRCP is only a diagnostic procedure. The impact of this is that if ERCP is necessary afterwards as a therapeutic intervention, MRCP could have been avoided and patients would be able to proceed immediately to treatment. For this reason, routine use of MRCP for confirmation of the presence of biliary obstruction before ERCP is difficult to justify. However, if no therapeutic intervention is found to be necessary, MRCP avoids the potential morbidity and mortality associated with ERCP.

Personnel, setting and equipment necessary for MRCP

MRCP is usually performed by a radiologist with training in MRCP techniques in a hospital setting. An MRI scanner is needed, with the software necessary to perform MRCP. Such MRI scanners are usually less than 8 years old, although it is possible to upgrade scanners so that MRCP can be performed. Periodic software upgrades are undertaken on MRI scanners. Some mobile scanning units are able to perform MRCP. MRCP, like ERCP, is an elective procedure. An MRCP investigation takes approximately 15 minutes of room time, and the sequences take seconds to minutes. The number of MRCP scans undertaken may be strongly influenced by the amount of time the MRI scanner is allocated to undertake such investigations. Depending on the findings at MRCP, patients may proceed to ERCP, surgery or palliative treatment. Costs have been estimated to be £454 per MRCP.[30] MRCP is estimated to cost about 30–50% of the cost of ERCP.[40] There are opportunity costs associated with MRCP in that if an MRI scanner is used for MRCP it cannot be used for other types of imaging. This will have an impact on the provision of other MRI investigations.

Chapter 3

Effectiveness

Methods for reviewing effectiveness

Search strategy

The search strategy aimed to identify all literature relating to the clinical and cost effectiveness of the use of MRCP. The main searches were conducted in January 2003.

Thirteen electronic bibliographic databases were searched, covering biomedical, science, health economic and grey literature. A list of databases is provided in Appendix 1.

In addition, the reference lists of relevant articles were handsearched and various health services research-related resources were consulted via the Internet. These included health economics and health technology assessment organisations, guideline-producing agencies, generic research and trials registers, and specialist sites. A list of these additional sources is given in Appendix 2.

A combination of free-text and thesaurus terms was used. 'Population' search terms (e.g. biliary, biliary tract, bile, gallbladder, choledocholithiasis) were combined with 'intervention' terms (e.g. magnetic resonance imaging, MRI, non-invasive diagnostic imaging). To inform the cost-effectiveness review and background to the review, additional searches were conducted on the epidemiology of biliary obstruction within the UK (England and Wales), endoscopic retrograde cholangiography, cost–utility analyses for gastrointestinal cancer and quality of life associated with extrahepatic bile duct cancer. Copies of the main search strategies used in the major databases are included in Appendix 3.

No language or study/publication-type restrictions were applied to the main searches. An economic evaluations methodological search filter was used to identify articles for the cost-effectiveness part of the review (refer to Appendix 4)

Inclusion and exclusion criteria

The titles and abstracts of the papers identified through the search process outlined above were assessed for relevance to the study question using the following criteria.

Inclusion criteria

- Subjects: adult patients with suspected biliary obstruction or dilatation
- intervention: MRCP
- comparators: diagnostic ERCP
- outcome measures to include:
  - sensitivity in different patient groups
  - specificity in different patient groups
  - likelihood ratios in different patient groups
  - acceptability to patients
  - adverse effects
- methodology to include, where available:
  - systematic reviews
  - randomised controlled trials
  - non-randomised studies: prospective diagnostic trials
  - economic evaluations.

Full copies were obtained of all those papers that appeared to be relevant, or that could not be assessed on the basis of the abstract alone.

Exclusion criteria

Studies involving pancreatic ductal system abnormalities were excluded as the main focus of this review was biliary ductal system abnormalities. Studies were also excluded that compared two or more forms of MRCP but did not include a comparison with diagnostic ERCP. Review papers that were not systematic were also excluded.

Initially, 67 papers were considered for inclusion as they included a comparison of MRCP with diagnostic ERCP. Of these, 38 papers were excluded.

Reasons for exclusion were:

- published before 1995
- comparison with failed or unsuccessful ERCP
- multiple comparators (apart from PTC, IOC and surgery)
- repetition of trial data from another included study
- MRCP results informed the decision to proceed to ERCP
- case–control design
- retrospective study design.

The reason for the exclusion of studies before 1995 is that the technology for MRCP has changed so

rapidly since then that it was felt to be inappropriate to include studies before that date as they would not be comparable. Studies involving a comparison with failed or unsuccessful ERCP were excluded as the aim of the study was to compare outcomes of MRCP with diagnostic ERCP as the gold standard. If ERCP failed or was unsuccessful then this comparison was not possible. Studies involving multiple comparators were excluded only if the outcomes for comparison with diagnostic ERCP were not reported separately. The last three reasons for exclusion are based on Lijmer and colleagues[47] as these factors have been found to alter the observed diagnostic performance. The 38 excluded studies are listed in Appendix 5.

Figure 1 shows a summary of study selection and exclusion.

Data extraction strategy

Data were extracted from papers by one researcher using a standardised data extraction form. Non-English language papers were excluded from the review.

Where available, the following data were reviewed in relation to MRCP and ERCP:

- study characteristics
- suspected condition
- patient characteristics
- diagnosis
- sensitivity
- specificity
- likelihood ratios
- positive and negative predictive values
- accuracy
- prevalence.

Quality assessment strategy

The studies were assessed using quality criteria for diagnostic or screening tests.[48] The ten questions outlined in Greenhalgh[48] for assessing reports of diagnostic or screening tests are as follow.

- Is the test potentially relevant?
- Has the test been compared with a true gold standard?
- Did the validation study include an appropriate spectrum of patients?
- Has work-up bias been avoided?
- Has expectation bias been avoided?
- Was the test shown to be reproducible?
- What are the features of the test as derived from this validation study?
- Were confidence intervals given?
- Has a sensible 'normal range' been derived?
- Has this test been placed in the context of other potential tests in the diagnostic sequence?

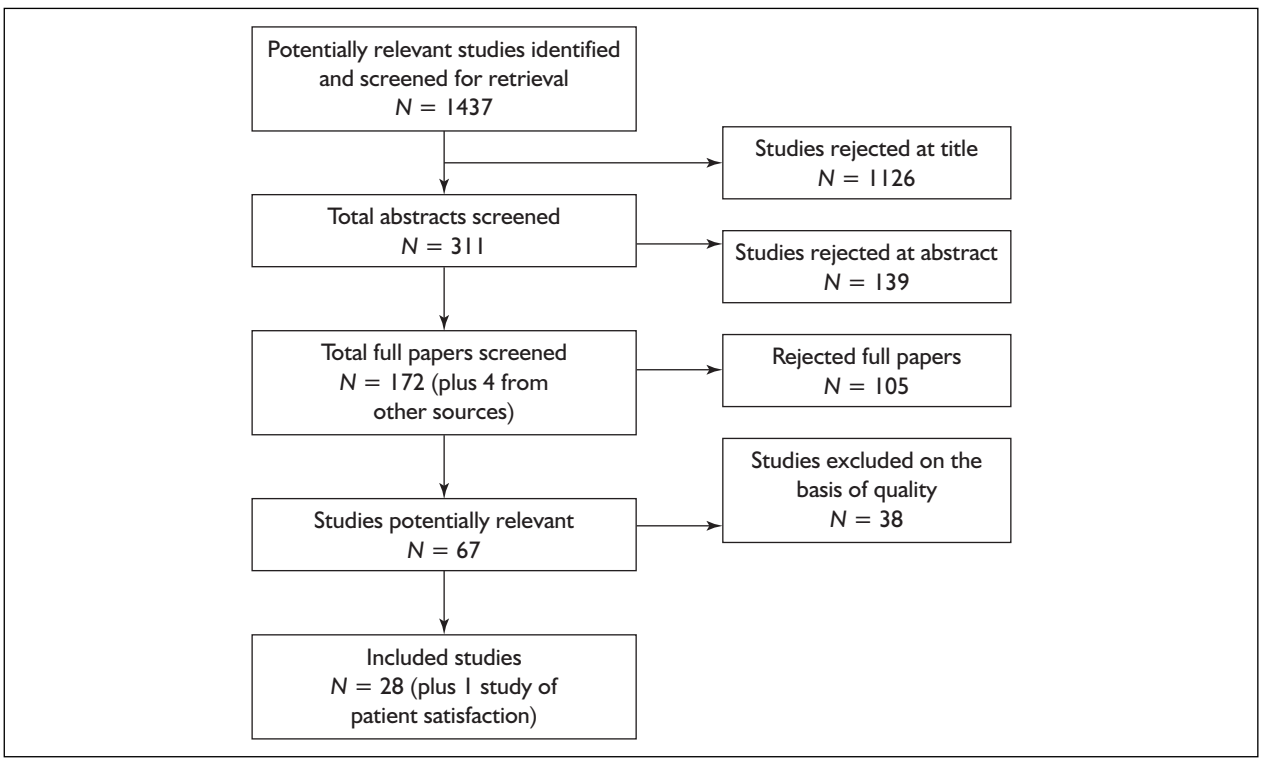


FIGURE 1 *Summary of flow of study selection and exclusion: clinical effectiveness*

Synthesis and presentation of results

Likelihood ratios were not reported in any of the 28 studies. These were therefore calculated using standard formulae.[49] A likelihood ratio describes how many times a person with disease is more likely to have a particular test result than a person without disease. Positive likelihood ratios are usually a number greater than 1, while negative likelihood ratios are usually a number between 0 and 1.[49] As a guide, positive likelihood ratios greater than 10 or negative likelihood ratios less than 0.1 provide convincing diagnostic evidence. Those above 5 and below 0.2 give strong diagnostic evidence, but this will depend on pretest probability and context.[49] Likelihood ratios combine sensitivity and specificity [sensitivity/(1 – specificity)].

Positive predictive value refers to the proportion of those with positive test results who have the disease (number of true positives/total positive), while negative predictive value is the proportion of those with negative test results who do not have the disease (number of true negatives/total negative). They describe the probabilities that positive or negative test results are correct. They depend on the prevalence of the disease in the sample, unlike sensitivity, specificity and likelihood ratios. Because disease prevalence is rarely constant across studies, positive and negative predictive values are often associated with an unacceptably high level of heterogeneity, making them unsuitable choices for effect measures.[49]

Ninety-five per cent confidence intervals (95% CI) for the sensitivity, specificity, likelihood ratio for a positive test result and likelihood ratio for a negative test result were calculated for each individual study using the Wilson[50] method, as recommended by Altman and colleagues.[51]

The point estimates and 95% confidence intervals for the above summary statistics for selected studies were presented graphically as forest plots. The combining of the sensitivities, specificities and likelihood ratios from studies of diagnostic accuracy should only be applied in the absence of variability in the diagnostic threshold. This can be examined graphically by plotting receiver operating characteristic (ROC) curves and scatterplots of sensitivity versus specificity for the studies. Calculation of the correlation coefficient between sensitivities and specificities will test whether they are related, as would be the case if there were variation in the diagnostic threshold. Sensitivities and specificities for selected studies were pooled using an approximation to the inverse variance approach as described in Deeks.[49]

Ninety-five per cent confidence intervals for the pooled sensitivity and specificity estimates were also calculated. The homogeneity of the sensitivities and specificities for the selected studies was tested using a standard chi-squared test, as both measures are simple proportions.

To avoid computational problems with sensitivities, specificities and likelihood ratios, 0.5 was added to all four cells in the 2×2 table if any one of them was zero.

Likelihood ratios are ratios of probabilities, and in a meta-analysis can be treated as risk ratios. A weighted average of the likelihood ratios can be computed using the standard Mantel–Haenszel method of meta-analysis for risk ratios. The heterogeneity of the likelihood ratios was also tested by standard heterogeneity tests after combining the statistics in a meta-analysis.

If there is any evidence of heterogeneity or that the diagnostic threshold varies between the studies, then the best summary of the results will be an ROC curve rather than a single point. Littenberg and Moses[52,53] proposed a method of fitting a whole family of summary ROC curves that allow for variation in diagnostic odds ratio with diagnostic threshold. The Littenberg and Moses method involves regression of the log diagnostic ratio (D) on the measure of diagnostic threshold (S). Ordinary least squares linear regression was used to produce estimates of the parameters a and b from the regression equation, $D = a + bS$. These estimates of a and b were used to calculate a summary ROC curve, which was plotted on a graph alongside the original data.

Results

Quantity and quality of research available

In total, 28 studies were identified that directly compared MRCP with diagnostic ERCP (*Table 1*). In addition to these 28 studies, one study was identified that covered patient satisfaction;[54] this is covered later in this chapter ('Patient satisfaction', p. 14).

Study characteristics

Appendix 6, Table 15, outlines the study characteristics of the 28 included studies.

Sample selection

The ideal sample in a study to compare diagnostic techniques is a consecutive or randomly selected series of patients recruited from a relevant clinical

TABLE I *Included studies*

Study, year; country	Suspected condition	Total no. of patients
Adamek *et al.*, 1998[55]; Germany	CBD obstruction	86
Alcaraz *et al.*, 2000[56]; Spain	Obstruction of the biliary tree	81
Angulo *et al.*, 2000[57]; USA	Symptoms consistent with biliary disease, emphasis on PSC	73
Barish *et al.*, 1995[58]; USA	Biliary or pancreatic disease	29
Calvo *et al.*, 2002[59]; Spain	Choledocholithiasis	61
Chan *et al.*, 1996[60]; Hong Kong	Choledocholithiasis	47
Demartines *et al.*, 2000[21]; Switzerland	Cholelithiasis	40
Dwerryhouse *et al.*, 1998[61]; UK	Choledocholithiasis	40
Feldman *et al.*, 1997[62]; USA	Pancreaticobiliary neoplasm	20
Guibaud *et al.*, 1995[63]; Canada	Bile duct obstruction	79
Hintze *et al.*, 1997[64]; Germany	Disorder affecting biliary or pancreatic duct system	78
Holzknecht *et al.*, 1998[65]; Germany	Not reported (planned ERCP)	61
Laokpessi *et al.*, 2001[66]; France	Choledocholithiasis	101
Lee *et al.*, 1997[67]; South Korea	Biliary disease	46
Lomanto *et al.*, 1997[68]; Italy	Choledocholithiasis, stenosis of bile ducts and biliary–enteric anastomosis	136
Lomas *et al.*, 1999[69]; UK	Biliary strictures or choledocholithiasis	76
Macaulay *et al.*, 1995[70]; USA	Biliary obstruction	29
Regan *et al.*, 1996[71]; USA	Choledocholithiasis	23
Reinhold *et al.*, 1998[72]; Canada	Bile duct obstruction	110
Soto *et al.*, 1996[73]; USA	Not reported (planned ERCP)	46
Soto *et al.*, 2000[74]; Columbia	Choledocholithiasis	57
Soto *et al.*, 2000[75]; Columbia	Choledocholithiasis	51
Stiris *et al.*, 2000[76]; Norway	Choledocholithiasis	50
Sugiyama *et al.*, 1998[77]; Japan	Pancreatobiliary disease	159
Taylor *et al.*, 2002[78]; Australia	Biliary tract disease in 96% (the other 4% had pancreatic duct disease)	146
Textor *et al.*, 2002[6]; Germany	PSC	150
Varghese *et al.*, 2000[79]; Ireland	Not reported (planned ERCP)	191
Zidi *et al.*, 1999[80]; France	Choledocholithiasis	70

population. Selection bias may be introduced by selecting patients for inclusion in a non-random method.[49] Of the 28 studies, one reported a non-consecutive sample[77] and in 13 studies the method of sample selection was not reported.[21,55–57,59,61,62,64,68,69,71,74,75] Barish and colleagues[58] and Soto and colleagues[73] report random selection of referrals, and Macaulay and colleagues[70] a sequential sample selection, although it is not clear whether or not the sequence was consecutive. Therefore, only 13 studies used appropriate methods of sample selection. The data for seven patients were duplicated in two of the studies.[58,73]

Sample sizes of the studies also varied. The smallest reported sample size was 20 patients who had MRCP[62] and the largest reported sample size was 159 who had completed ERCP.[77]

Procedures

Some studies reported considerably more detail regarding the type of MRCP. Four studies reported the use of a non-breath-holding procedure.[60,61,70,80] Only one study[76] reported that all patients had both MRCP and ERCP. Six other studies reported some failed MRCP or MRCP not of diagnostic quality.[6,58,72,74,78,79] Claustrophobia in patients associated with MRCP was reported in ten studies.[55,57,61,63,64,69,71,72,75,78] One study reported that one patient was unable to undergo MRCP owing to obesity.[69]

Failed ERCP procedures were reported in 12 studies, with no indication as to whether or not subsequent investigations were attempted.[6,55,59,60,63,64,65,69,71,74,75,6,77] In the remaining studies, other forms of direct cholangiography (PTC, IOC, preoperative cholangiography) or surgery were reported.[21,56–58,61,66,68,70,72,73,78–80] In two studies it was not clear why some patients did not have ERCP.[62,67]

Time between procedures

The time between MRCP and ERCP is important, particularly in the diagnosis of choledocholithiasis, as spontaneous stone fragmentation or movement

may result in some stones being diagnosed in the one procedure but not in the other. Ideally, the time between procedures should be no more than a few hours. In five studies the time between procedures was not reported.[21,55,56,62,68] In only ten studies did patients receive both procedures within 24 hours of each other.[57,58,60,64,69,71,73,76,78,80] In one study[70] ERCP was performed 109 days before MRCP in one patient.

Patient characteristics

Patient characteristics are shown in Appendix 6, Table 16. No information regarding the age of patients was reported in two studies.[61,62] Three studies did not report age ranges[6,21,59] and six studies reported ranges that included children (age less than 17 years),[55,63–65,72,77] with one,[64] including at least one child aged 5 years. The lowest reported mean was 48.6 years[6] and the highest was 71 years.[80]

Most studies reported more females than males, apart from five studies with more males than females[21,55,59,60,70] and one study with an equal number of males and females.[69] Three studies did not report the gender of patients.[61,62,73]

All studies apart from three[65,73,79] reported the condition under investigation. Suspected conditions included obstruction in five studies,[55,56,63,70,72] biliary disease or disorder in six studies,[57,58,64,67,77,78] neoplasm in one,[62] PSC in one[6] and CBD stones or choledocholithiasis in 12 studies.[21,59–61,66,68,69,71,74,75,76,80]

Inclusion and exclusion criteria of the studies were assessed and there was considerable variation in the amount of detail provided in the studies. Three studies reported no inclusion criteria.[77,79,80] Four studies stated only that patients referred for ERCP were included[58,65,73,78] and one study mentioned only that patients included were 18 years of age or older.[75] Twelve of the included studies did not report exclusion criteria.[6,56,60,62,64,68,70,71,73,76,77,80]

Quality assessment

All 28 studies included in the review had most patients receiving the gold standard diagnostic test, ERCP. Appendix 6, Table 17, shows the quality assessment criteria applied to each study. It was difficult to determine whether or not the studies included an appropriate spectrum of patients. All studies included patients with biliary tree abnormalities of some description. Studies reporting both pancreatic and biliary tree abnormalities were included if the biliary abnormality results were reported separately. As stated above, some studies did not provide detailed inclusion and exclusion criteria or state the suspected condition, making it difficult to ascertain exactly what type of patient was included in the study.

Work-up bias refers to whether or not all patients had both ERCP and MRCP. Ideally, all patients who were selected should have had both tests. No studies where the MRCP results informed the decision to proceed to ERCP were included in this review. ERCP is associated with a high failure rate, so it would be expected that some patients who were included in a study would not have a successful ERCP. Failure rates of between 3 and 10% have been reported in the literature. With regard to MRCP, claustrophobia is a problem in some patients; therefore, it would be expected that not all patients in every study would be able to have MRCP. In only one study[76] did all patients have both MRCP and ERCP. There is no mention of ERCP failures or claustrophobia in patients having MRCP in this study. Therefore, work-up bias was not apparent in any of the included studies and information regarding number of patients from the original sample not receiving both tests is present if it was reported in the studies.

Expectation bias refers to whether or not blinded assessment was undertaken. Of the 28 studies, 25 reported at least partial blinded assessment. One study[68] did not report any information on blinding, one study[77] reported that blinding did not take place and another study reported that results were assessed independently.[69] Thirteen studies reported that clinicians were blinded to findings of other investigations as well as clinical information,[6,21,56–58,60,62,63,70,73,74,75,80] while the other studies either reported partial blinding (only of the other diagnostic test under investigation)[55,59,72,79] or made no mention of other tests.[61,64,65–67,71,76,78]

Most studies made no mention of the issue of reproducibility, meaning that if the same person performs the same test on two occasions on a patient whose characteristics remain the same the results would not vary. It is also important to confirm that the findings of two different people performing the same test on the same patient would be similar. This second question was addressed by six studies that reported kappa values relating to agreement between reviewers.[6,56,63,67,72,74] One study reported the imaging interpretation results for both an off-site radiologist and an on-site radiologist.[65]

Features of the tests refer to sensitivity, specificity, likelihood ratios, and positive and negative predictive values. These were calculated for all studies where sufficient raw data were reported in the studies. The results are reported in the Outcomes section (see below). Nine studies reported confidence intervals.[60,63,66,69,71,72,74,75,78]

To place MRCP and ERCP results in context it is important to know what other tests were conducted and what the results of the tests were. Potentially important investigations include ultrasound, CT, clinical presentation and laboratory tests. Some studies do not report the use of any other tests,[56,58,62,65,67,70,73,74,77] whereas some studies report that other tests took place but do not give their results[6,55,57,59–61,63,64,66,68,69,71,72,76,80] and others report some of these test results.[21,75,78,79]

Inclusion and exclusion criteria were reported earlier in this chapter. When little or no information regarding inclusion and exclusion criteria is reported in studies, it is difficult to ascertain whether or not an appropriate spectrum of patients has been included in the study. It is also difficult to determine whether or not studies are comparable, as different patient groups may have been included.

Diagnoses and reported sensitivities and specificities

In Appendix 6, Table 18, the final diagnoses reported in the studies, as well as sensitivity, specificity and adverse events reported in the studies, are shown. Although most studies provide details of the diagnosis of most patients taking part in the study, five report only the number of patients with the diagnosis under investigation, giving no indication of the other diagnoses obtained.[21,61,68,75,76]

If sensitivities and specificities were not reported in the studies, they were calculated provided the raw data were published in the study. Calculated values are reported in parentheses in Appendix 6, Table 18. No studies reported likelihood ratios. These have been calculated and are reported below (Outcomes).

Comparators

Some studies calculated sensitivities and specificities in comparison to ERCP or equivalent (PTC, IOC and surgery) and some to final diagnosis. Information on final diagnosis definition for the studies is given in Appendix 6, Table 18. Seven studies compared MRCP with final diagnosis[6,55,62,66,67,70,71] and of these three also reported sensitivities and specificities for ERCP compared with final diagnosis.[66,67,71] In all cases ERCP formed the major component of final diagnosis, apart from one.[6] The remaining 21 studies compared MRCP with ERCP or equivalent.[21,56–61,63–65,68,69,72–80] Zidi and colleagues[80] included sonography as a comparator as well as direct cholangiography and surgery.

For the three studies comparing ERCP with final diagnosis as well as MRCP, the results are as follows. Lee and colleagues[67] reported ERCP to have a sensitivity of 71% and a specificity of 92% for malignancy. Laokpessi and colleagues[66] reported ERCP to have a sensitivity of 95% and a specificity of 100% for CBD stones. Finally, Regan and colleagues[71] reported ERCP to have both a sensitivity and a specificity of 100% for CBD stones.

Adverse effects

Adverse effects are reported in Appendix 6, Table 18. None of the 28 studies reported any adverse effects associated with MRCP. Six studies reported adverse effects associated with ERCP.[6,55,57,59,72,76] Two studies reported that no adverse events occurred[21,56] and the remaining 20 studies did not report any information regarding adverse effects. None of the 28 studies reported mortality associated with ERCP.

Outcomes

Tables 2–5 show the sensitivity, specificity with confidence intervals, likelihood ratios with confidence intervals, and positive and negative predictive values, prevalence and accuracy. Three studies were not included in these calculations as they did not provide sufficient data for the necessary calculations[56,62,64] The remaining 25 studies are listed in the tables. If sufficient data were provided to calculate sensitivities and specificities, these are presented for every condition for which the data were provided.

Holzknecht,[65] Macaulay,[70] Reinhold[72] and Soto and colleagues[74] provided results for different reviewers (but the same patients). Soto[75] also provided data on the same patients using different MRCP techniques. These data were combined and a mean calculated for each study to generate an overall value for sensitivity and specificity by condition for each individual study where the raw data were provided.

Patient satisfaction

The 28 studies included in this review did not report information on patient satisfaction. However, one study was identified that dealt with

TABLE 2 *Sensitivity*

Study	Condition	Sensitivity	Lower CI	Upper CI
Adamek[55]	Abnormality	0.89	0.77	0.95
Adamek[55]	Malignancy	0.81	0.63	0.92
Angulo[57]	Normal	0.86	0.67	0.95
Angulo[57]	Dilatation CBD	0.93	0.81	0.97
Angulo[57]	Obstruction	1.00	0.91	1.00
Angulo[57]	CBD stones	0.50	0.24	0.76
Angulo[57]	PSC	0.83	0.63	0.93
Barish[58]	Dilatation	0.87	0.62	0.96
Calvo[59]	Choledocholithiasis	0.91	0.76	0.97
Chan[60]	Choledocholithiasis	0.95	0.75	0.99
Demartines[21]	CBD stones	1.00	0.83	1.00
Dwerryhouse[61]	CBD stones	0.88	0.53	0.98
Guibaud[63]	Obstruction	0.91	0.83	0.96
Guibaud[63]	Choledocholithiasis	0.81	0.65	0.91
Guibaud[63]	Malignancy	0.86	0.60	0.96
Holzknecht[65]	Choledocholithiasis	0.86	0.60	0.96
Holzknecht[65]	Dilatation	0.94	0.81	0.98
Holzknecht[65]	Stenosis	0.86	0.71	0.94
Holzknecht[65]	Overall	0.91	0.80	0.97
Laokpessi[66]	CBD stones	0.93	0.87	0.96
Lee[67]	Malignancy	0.81	0.60	0.92
Lomanto[68]	Choledocholithiasis	0.92	0.74	0.98
Lomas[69]	Choledocholithiasis	1.00	0.70	1.00
Lomas[69]	Stricture	1.00	0.83	1.00
Macaulay[70]	Dilatation	1.00	0.82	1.00
Regan[71]	Choledocholithiasis	0.93	0.70	0.99
Reinhold[72]	Obstruction	0.91	0.82	0.95
Reinhold[72]	Choledocholithiasis	0.90	0.74	0.97
Soto[73]	Dilatation	0.96	0.82	0.99
Soto[74]	Choledocholithiasis	0.96	0.80	0.99
Soto[75]	Choledocholithiasis	0.96	0.81	0.99
Stiris[76]	CBD stones	0.88	0.72	0.95
Sugiyama[77]	Anomalous PBJ	0.82	0.52	0.95
Taylor[78]	Choledocholithiasis	0.98	0.89	1.00
Taylor[78]	Stricture	1.00	0.76	1.00
Textor[6]	PSC	0.88	0.73	0.95
Varghese[79]	Choledocholithiasis	0.91	0.77	0.97
Zidi[80]	Choledocholithiasis	0.57	0.43	0.70

PBJ, pancreatobiliary junction.

patient satisfaction only.[54] The study did not attempt to define clinical outcome of performance of MRCP versus ERCP. This study recruited 34 patients who were to undergo ERCP. MRCP was to be performed before ERCP. However, two patients were unable to undergo MRCP owing to claustrophobia, leaving 32 patients who underwent both procedures.

Patients were asked to complete validated questionnaires using a series of seven-point Likert scales to measure the degree of anxiety, pain, discomfort, expectations and willingness to repeat each test. The first set of postprocedure Likert scales assessed each test separately without reference to the other test. No significant differences in degree of anxiety were reported between MRCP and ERCP. Patients reported a significantly lower degree of discomfort with MRCP than with ERCP (2.47 ± 1.6 vs 3.09 ± 1.7, respectively; $p = 0.047$) and a lower degree of pain (1.3 ± 0.8 vs 2.7 ± 1.8; $p < 0.001$). MRCP was found to be 'more difficult than expected' to a greater degree than was ERCP (-0.7 ± 1.5 vs -1.3 ± 1.5; $p = 0.012$). Patients were equally willing to repeat either procedure, although the trend favoured MRCP ($p = 0.09$).

In the second set of Likert scales the questions made a direct comparison between MRCP and ERCP. With regard to anxiety, pain and discomfort, patients had a greater satisfaction after

TABLE 3 *Specificity*

Study	Condition	Specificity	Lower CI	Upper CI
Adamek[55]	Abnormality	0.92	0.67	0.99
Adamek[55]	Malignancy	1.00	0.90	1.00
Angulo[57]	Normal	0.96	0.86	0.99
Angulo[57]	Dilatation CBD	0.93	0.78	0.98
Angulo[57]	Obstruction	0.91	0.76	0.97
Angulo[57]	CBD stones	0.98	0.91	1.00
Angulo[57]	PSC	0.98	0.89	1.00
Barish[58]	Dilatation	1.00	0.61	1.00
Calvo[59]	Choledocholithiasis	0.83	0.55	0.95
Chan[60]	Choledocholithiasis	0.85	0.66	0.94
Demartines[21]	CBD stones	0.90	0.71	0.97
Dwerryhouse[61]	CBD stones	0.93	0.79	0.98
Guibaud[63]	Obstruction	1.00	0.92	1.00
Guibaud[63]	Choledocholithiasis	0.98	0.93	0.99
Guibaud[63]	Malignancy	0.98	0.94	1.00
Holzknecht[65]	Choledocholithiasis	0.94	0.83	0.98
Holzknecht[65]	Dilatation	0.93	0.77	0.98
Holzknecht[65]	Stenosis	0.88	0.70	0.96
Holzknecht[65]	Overall	0.80	0.55	0.93
Laokpessi[66]	CBD stones	1.00	0.90	1.00
Lee[67]	Malignancy	0.92	0.75	0.98
Lomanto[68]	Choledocholithiasis	1.00	0.91	1.00
Lomas[69]	Choledocholithiasis	0.97	0.89	0.99
Lomas[69]	Stricture	0.98	0.90	1.00
Macaulay[70]	Dilatation	0.91	0.62	0.98
Regan[71]	Choledocholithiasis	0.88	0.53	0.98
Reinhold[72]	Obstruction	1.00	0.90	1.00
Reinhold[72]	Choledocholithiasis	0.96	0.90	0.99
Soto, 1996[73]	Dilatation	0.94	0.73	0.99
Soto[74]	Choledocholithiasis	0.96	0.80	0.99
Soto[75]	Choledocholithiasis	1.00	0.87	1.00
Stiris[76]	CBD stones	0.94	0.74	0.99
Sugiyama[77]	Anomalous PBJ	1.00	0.97	1.00
Taylor[78]	Choledocholithiasis	0.89	0.81	0.94
Taylor[78]	Stricture	0.99	0.95	1.00
Textor[6]	PSC	0.99	0.95	1.00
Varghese[79]	Choledocholithiasis	0.98	0.95	0.99
Zidi[80]	Choledocholithiasis	1.00	0.85	1.00

MRCP, although discomfort associated with ERCP compared with MRCP did not reach statistical significance. Scores were 0.6 (95% CI 0.02 to 1.2), 0.9 (0.5 to 1.3) and 0.4 (–1.2 to 1.0), respectively. Two patients expressed no preference between MRCP and ERCP, whereas 19 (59%, 95% CI 41–76%) preferred MRCP to ERCP. Using the Likert scales patients showed a significantly higher preference for MRCP than for ERCP (mean score = 0.8, 95% CI 0.2 to 1.4; $p = 0.01$).

Several subgroup analyses were performed. The first was in patients who did not complain of claustrophobia or noise ($n = 15$; 46.8%). The results were more striking in this subgroup without claustrophobia. In the subgroup undergoing purely diagnostic ERCP there were clear preferences for MRCP. In this study, MRCP was always performed first and this may have influenced the results. On the whole patients preferred MRCP over ERCP, although there was still some patients who preferred ERCP to MRCP. They suggest ways to overcome problems associated with MRCP, including better patient selection, fenestrated scanners, earplugs and selective sedation.

In addition to the above study, one of the 28 studies described above[66] reported that 4% of patients in that study found the noise of the MRCP investigation to be disturbing.

Assessment of effectiveness

A total of 28 studies was included in this systematic review. Of these, 25 provided enough

TABLE 4 *Likelihood ratios*

Study	Condition	LRP	LRP lower CI	LRP upper CI	LRN	LRN lower CI[a]	LRN upper CI[a]
Adamek[55]	Abnormality	11.62	1.76	76.57	0.12	0.02	0.76
Adamek[55]	Malignancy	54.64	3.47	861.18	0.20	0.01	3.14
Angulo[57]	Normal	20.73	5.28	81.31	0.14	0.04	0.56
Angulo[57]	Dilatation CBD	13.44	3.52	51.33	0.08	0.02	0.30
Angulo[57]	Obstruction	11.00	3.74	32.36	0.00	–	–
Angulo[57]	CBD stones	30.00	3.90	230.73	0.51	0.07	3.91
Angulo[57]	PSC	38.83	5.53	272.37	0.18	0.03	1.25
Barish[58]	Dilatation	11.81	0.81	172.17	0.17	0.01	2.45
Calvo[59]	Choledocholithiasis	5.44	1.53	19.36	0.11	0.03	0.40
Chan[60]	Choledocholithiasis	6.16	2.48	15.26	0.06	0.03	0.15
Demartines[21]	CBD stones	10.50	2.81	39.24	0.00	–	–
Dwerryhouse[61]	CBD stones	13.13	3.35	51.36	0.1	0.03	0.52
Guibaud[63]	Obstruction	87.00	5.52	1372.23	0.09	0.01	1.49
Guibaud[63]	Choledocholithiasis	38.19	9.60	151.97	0.19	0.05	0.76
Guibaud[63]	Malignancy	48.00	11.96	192.72	0.15	0.04	0.58
Holzknecht[65]	Choledocholithiasis	14.00	4.58	42.78	0.15	0.05	0.47
Holzknecht[65]	Dilatation	13.18	3.46	50.23	0.06	0.02	0.24
Holzknecht[65]	Stenosis	7.18	2.46	20.91	0.16	0.05	0.46
Holzknecht[65]	Overall	4.57	1.66	12.63	0.11	0.04	0.29
Laokpessi[66]	CBD stones	64.78	4.13	1015.86	0.08	0.00	1.19
Lee[67]	Malignancy	10.12	2.64	38.86	0.21	0.05	0.79
Lomanto[68]	Choledocholithiasis	70.20	4.46	1105.97	0.10	0.01	1.60
Lomas[69]	Choledocholithiasis	30.00	7.68	117.19	0.00	–	–
Lomas[69]	Stricture	50.00	7.18	348.04	0.00	–	–
Macaulay[70]	Dilatation	11.00	1.70	71.28	0.00	–	–
Regan[71]	Choledocholithiasis	7.47	1.19	46.94	0.08	0.01	0.48
Reinhold[72]	Obstruction	63.18	4.03	991.27	0.10	0.01	1.55
Reinhold[72]	Choledocholithiasis	24.00	7.86	73.31	0.10	0.03	0.32
Soto[73]	Dilatation	16.37	2.44	109.77	0.04	0.01	0.26
Soto[74]	Choledocholithiasis	23.96	3.50	163.78	0.04	0.01	0.30
Soto[75]	Choledocholithiasis	49.11	3.15	765.62	0.06	0.00	0.88
Stiris[76]	CBD stones	15.75	2.33	106.28	0.13	0.02	0.89
Sugiyama[77]	Anomalous PBJ	235.92	14.60	3811.82	0.21	0.01	3.38
Taylor[78]	Choledocholithiasis	9.02	4.86	16.74	0.02	0.01	0.05
Taylor[78]	Stricture	118.00	16.76	830.78	0.00	–	–
Textor[6]	PSC	95.79	13.56	676.70	0.12	0.02	0.86
Varghese[79]	Choledocholithiasis	47.72	15.48	147.06	0.09	0.03	0.28
Zidi[80]	Choledocholithiasis	25.08	1.60	392.61	0.44	0.03	6.89

[a] With likelihood ratios of zero, the data are unsuitable for the calculation of 95% CI.
LRP, likelihood ratio positive; LRN, likelihood ratio negative.

data to calculate sensitivities, specificities, likelihood ratios and confidence intervals. The sensitivities and specificities are presented here by condition.

Assessment of effectiveness by condition

Choledocholithiasis

There were 18 studies investigating choledocholithiasis or CBD stones. The data from 15 of these studies are presented graphically in *Figures 2–12*. Three of the original 18 studies with results for choledocholithiasis were not included in this analysis, two owing to lack of blinded assessment[68,69] and one because no information was provided regarding the age and gender of patients.[61]

Figure 2 shows the ROC curve for the 15 studies. Two studies (Zidi[80] and Angulo[57]) stand out as having sensitivities somewhat lower than the other 13 studies.

Figure 3 shows a scatterplot of sensitivity versus specificity for the 15 studies. There does not appear to be any correlation between these estimates. One can crudely test for a diagnostic threshold effect by computing the correlation between sensitivities and specificities across the

TABLE 5 *Predictive values, accuracy and prevalence*

Study	Condition	Positive predictive value	Negative predictive value	Accuracy	Prevalence
Adamek[55]	Abnormality	0.98	0.71	0.90	0.78
Adamek[55]	Malignancy	1.00	0.87	0.92	0.45
Angulo[57]	Normal	0.90	0.94	0.93	0.31
Angulo[57]	Dilatation CBD	0.95	0.90	0.93	0.59
Angulo[57]	Obstruction	0.93	1.00	0.96	0.53
Angulo[57]	CBD stones	0.83	0.92	0.91	0.14
Angulo[57]	PSC	0.95	0.92	0.93	0.33
Barish[58]	Dilatation	1.00	0.75	0.90	0.71
Calvo[59]	Choledocholithiasis	0.94	0.77	0.89	0.73
Chan[60]	Choledocholithiasis	0.82	0.96	0.89	0.42
Demartines[21]	CBD stones	0.90	1.00	0.95	0.48
Dwerryhouse[61]	CBD stones	0.78	0.97	0.92	0.21
Guibaud[63]	Obstruction	1.00	0.87	0.94	0.63
Guibaud[63]	Choledocholithiasis	0.93	0.94	0.94	0.25
Guibaud[63]	Malignancy	0.86	0.98	0.97	0.11
Holzknecht[65]	Choledocholithiasis	0.80	0.96	0.92	0.22
Holzknecht[65]	Dilatation	0.94	0.93	0.94	0.55
Holzknecht[65]	Stenosis	0.91	0.81	0.87	0.59
Holzknecht[65]	Overall	0.93	0.75	0.89	0.76
Laokpessi[66]	CBD stones	1.00	0.81	0.95	0.77
Lee[67]	Malignancy	0.89	0.85	0.87	0.46
Lomanto[68]	Choledocholithiasis	1.00	0.95	0.97	0.39
Lomas[69]	Choledocholithiasis	0.82	1.00	0.97	0.13
Lomas[69]	Stricture	0.95	1.00	0.99	0.28
Macaulay[70]	Dilitation	0.95	1.00	0.97	0.62
Regan[71]	Choledocholithiasis	0.93	0.88	0.91	0.65
Reinhold[72]	Obstruction	1.00	0.83	0.94	0.69
Reinhold[72]	Choledocholithiasis	0.90	0.96	0.95	0.27
Soto[73]	Dilatation	0.96	0.94	0.95	0.61
Soto[74]	Choledocholithiasis	0.96	0.96	0.96	0.49
Soto[75]	Choledocholithiasis	1.00	0.96	0.98	0.51
Stiris[76]	CBD stones	0.97	0.81	0.90	0.64
Sugiyama[77]	Anomalous PBJ	1.00	0.99	0.99	0.07
Taylor[78]	Choledocholithiasis	0.83	0.99	0.92	0.36
Taylor[78]	Stricture	0.92	1.00	1.00	0.09
Textor[6]	PSC	0.97	0.96	0.96	0.23
Varghese[79]	Choledocholithiasis	0.91	0.98	0.97	0.18
Zidi[80]	Choledocholithiasis	1.00	0.50	0.70	0.70

15 studies. The estimated correlation was –0.43, which was not statistically significant ($p = 0.11$).

Sensitivities and specificities along with 95% CI for these estimates for the 15 studies are presented in *Figures 4* and *5*. From the graphs all of the confidence intervals overlap, although the confidence intervals for some studies are wide, reflecting the small sample sizes and variability in the sensitivity estimates. Two studies, Angulo[57] and Zidi,[80] have point estimates (*Figure 4*) of sensitivity that are clearly different from the other 13 studies, suggesting, as with the ROC plot (*Figure 2*), that these studies may be outliers.

Sensitivity

The overall estimate of mean sensitivity is 0.87 (95% CI: 0.85 to 0.91) from the 15 studies. However, a chi-squared test confirms the statistical significance of the heterogeneity observed in *Figure 4* ($\chi^2 = 70.8.8$, df = 14, $p < 0.0001$). The large between-study heterogeneity is clearly evident in *Figure 6*, with the results of two studies (Angulo[57] and Zidi[80]) lying some distance from the summary sensitivity estimate of 0.87. In such a situation it is probably inappropriate to consider pooling sensitivities at all, and it may be better to note the heterogeneity by describing the median sensitivity (0.91) and the range (0.50 to 1.00) between which the sensitivities are seen to vary.

If the Angelo and Zidi studies are excluded then the overall pooled estimate across the 13 studies now becomes 0.92 (95% CI 0.89 to 0.95). The

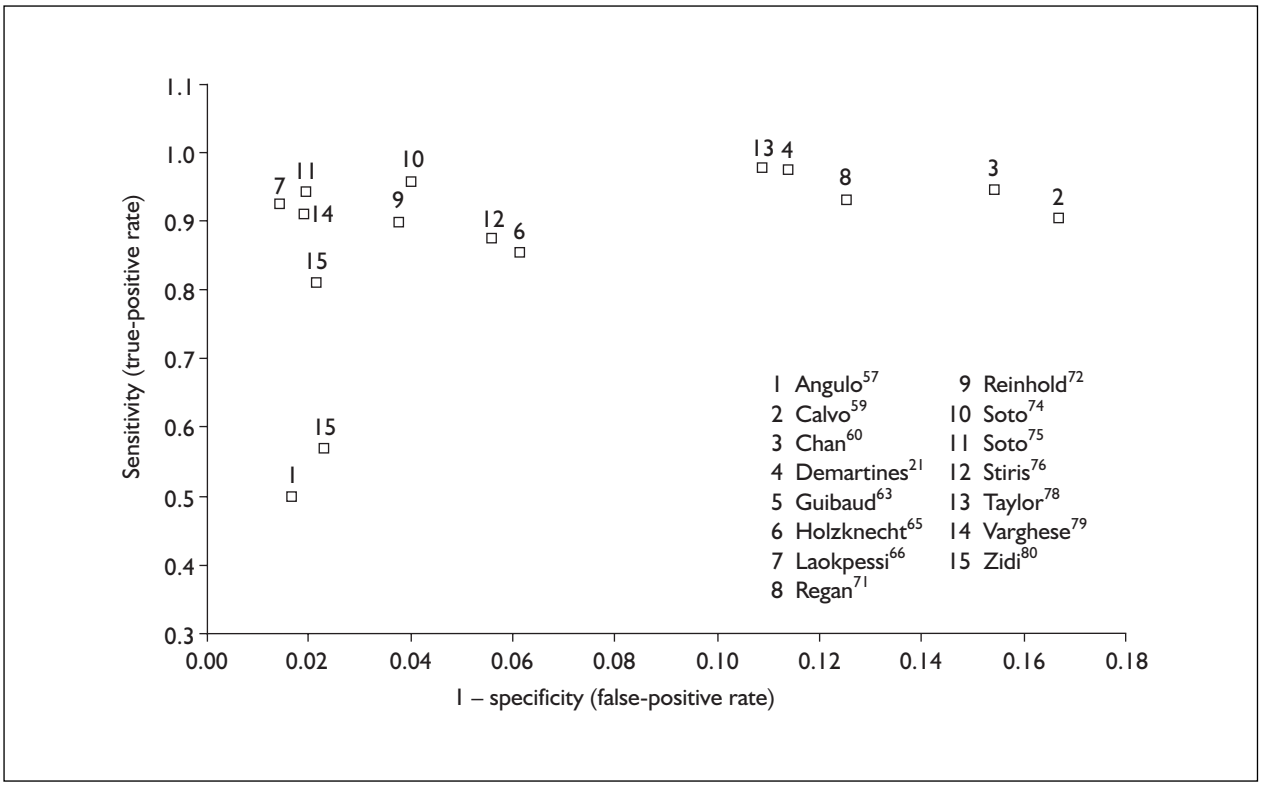


FIGURE 2 *ROC curve for 15 studies*

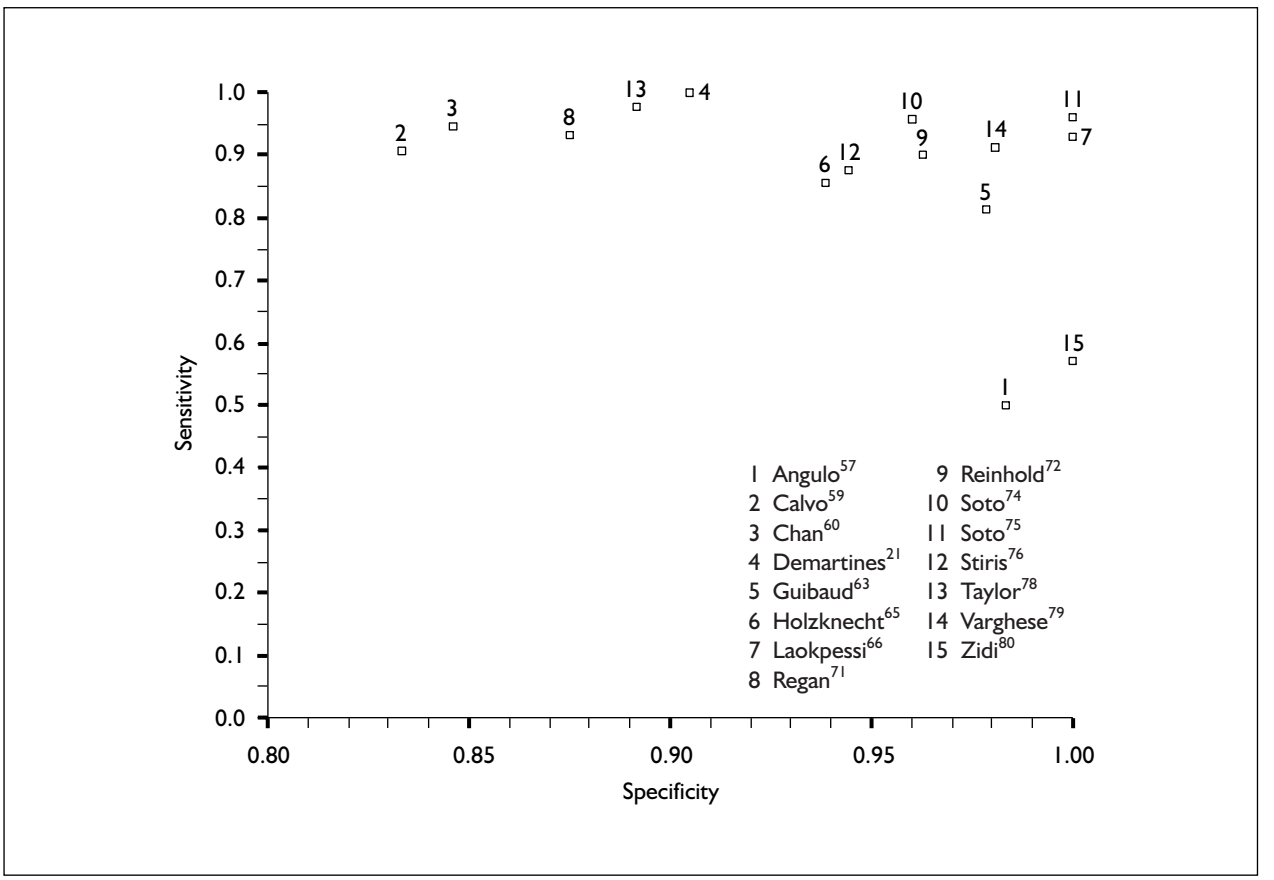


FIGURE 3 *Scatterplot of sensitivities versus specificities* (n = *15*, r = *–0.43*, p = *0.11*)

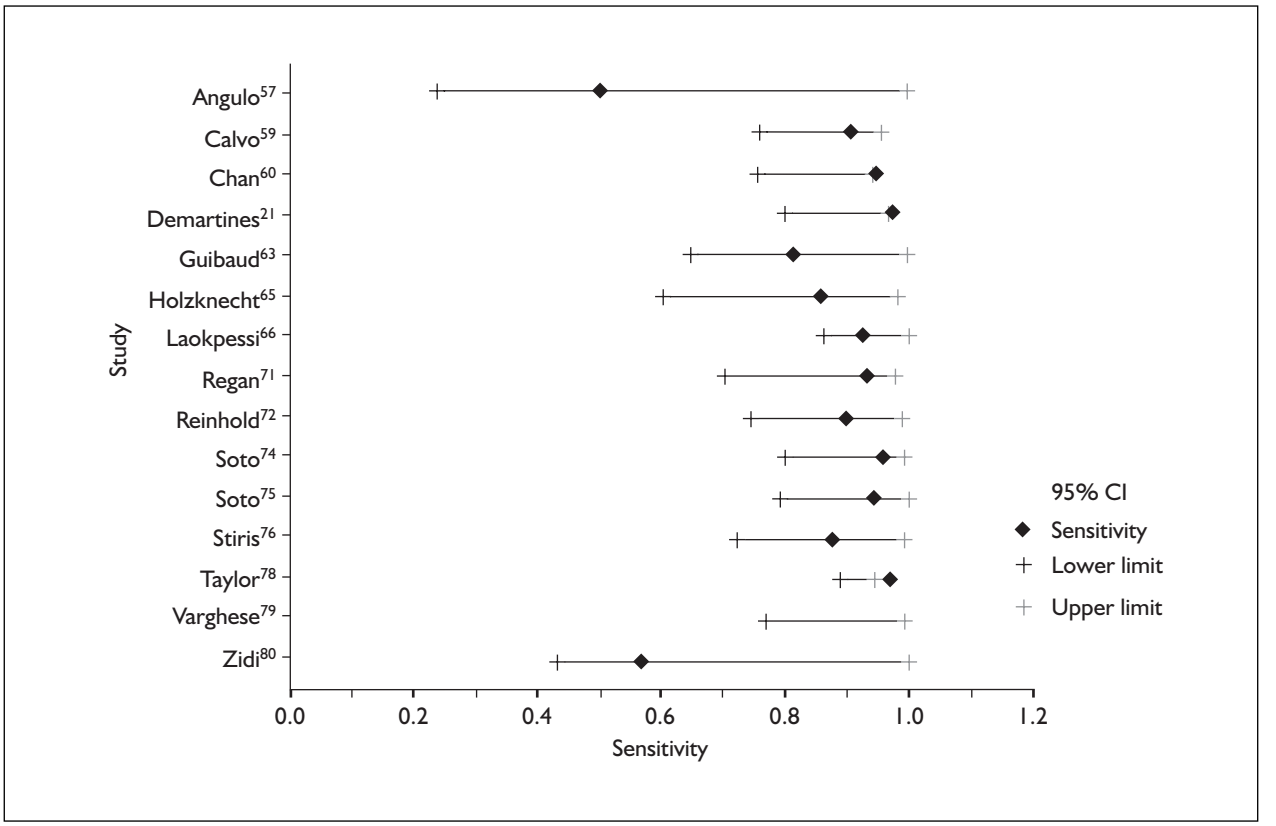


FIGURE 4 *Forest plot of estimated sensitivities* (n = *15)*

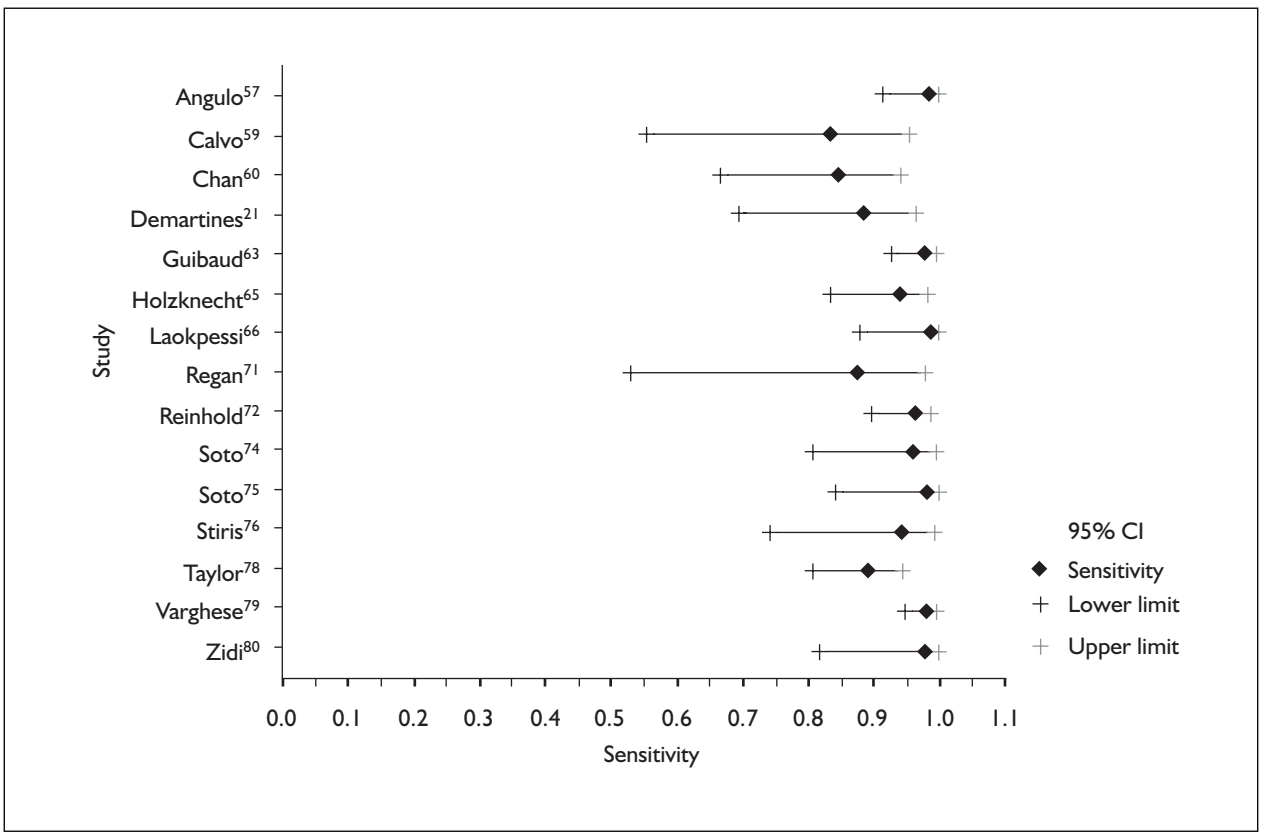


FIGURE 5 *Forest plot of estimated specificities* (n = *15)*

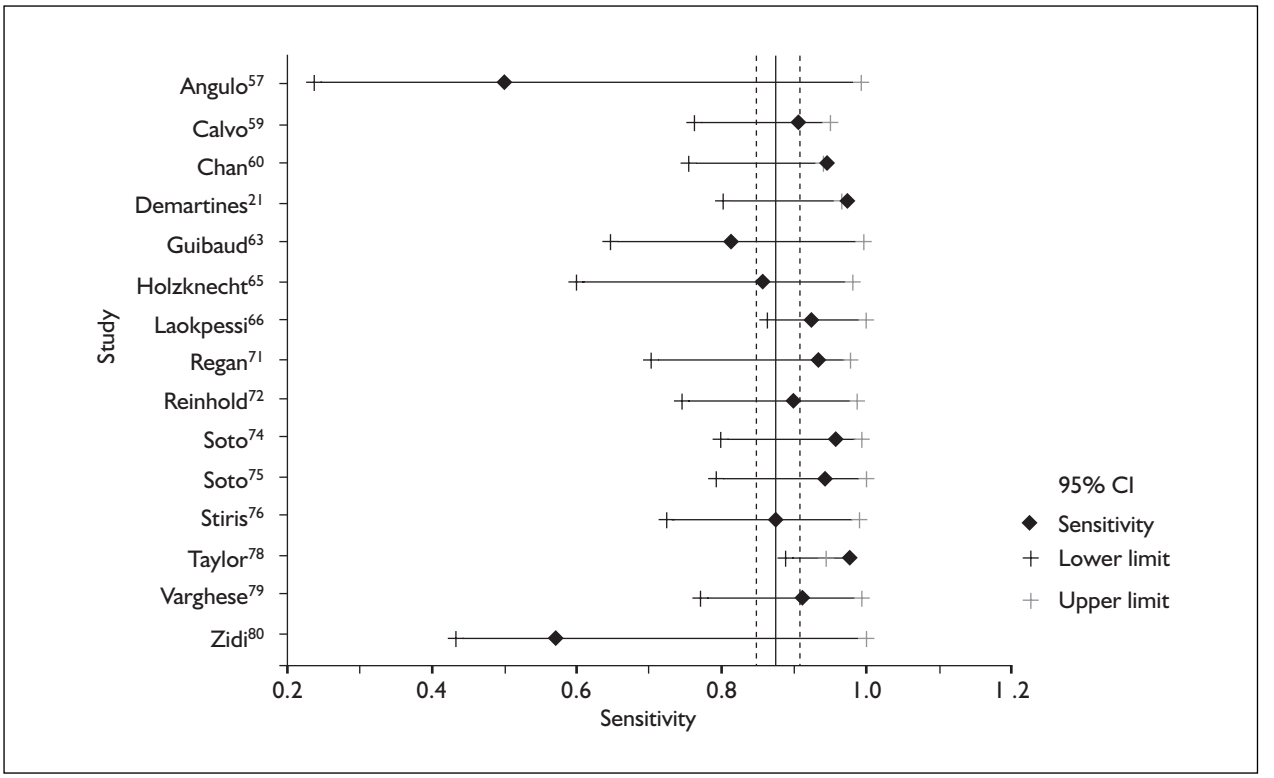


FIGURE 6 *Forest plot of estimated sensitivities with summary estimate (n = 15)*

sensitivities for these 13 studies now show no evidence of significant heterogeneity (χ^2 = 10.7, df = 12, p =0.55). The median sensitivity for the 13 studies is 0.93, with a range 0.81 to 1.00.

Specificity

Following the same calculations as for the sensitivities, the overall estimate of mean specificity is 0.95 (95% CI 0.94 to 0.97) from the 15 studies. However, a chi-squared test confirms the statistical significance of the heterogeneity observed in *Figure 7* (χ^2 = 27.8, df = 14, p < 0.015). The large between-study heterogeneity is clearly evident in *Figure 7*, with the results of many studies lying some distance from the summary specificity estimate of 0.95. In such a situation it is probably inappropriate to consider pooling specificities at all, and it may be better to note the heterogeneity by describing the median specificity (0.96) and the range (0.83 to 0.99) between which the specificities are seen to vary.

As before, if the Angulo and Zidi studies are excluded then the overall estimate of mean specificity is 0.95 (95% CI 0.93 to 0.97) from the 13 studies. However, a chi-squared test confirms the statistical significance of the heterogeneity (χ^2 = 24.3, df = 12, p < 0.018). The median specificity for the 13 studies is 0.94 and the range, as before, is 0.83 to 0.99.

Likelihood ratios

The positive likelihood ratios show no evidence of significant heterogeneity (χ^2 = 19.6, df = 14, p = 0.14), the Mantel–Haenszel pooled estimate for 15 studies being 16.3 (95% CI 11.5 to 23.2) (*Figure 8*). However, owing to the hetereogeneity reported for both sensitivities and specificities above it is probably more appropriate to report the median values for positive likelihood ratios. The median positive likelihood ratio is 23.96 with the range between 5.44 and 64.78.

Combining negative likelihood ratios for the 15 studies using the Mantel–Haenszel method yields an overall estimate of 0.13 (95% CI 0.10 to 0.16) (*Figure 9*). However, as with the sensitivities and specificities, there is significant heterogeneity in negative likelihood ratios between studies (χ^2 = 86.4, df = 14, p < 0.001). The estimate of 0.13 is outside the 95% confidence intervals for two of the 15 studies (Angulo and Zidi). The median negative likelihood ratio for the 15 studies is 0.09, with a range of 0.00 to 0.51.

As before, if the Angelo and Zidi studies are excluded from the analysis, then the positive likelihood ratios show no evidence of significant heterogeneity (χ^2 = 18.8, df = 12, p =0.093), the Mantel–Haenszel pooled estimate for 13 studies being 15.9 (95% CI 11.2 to 22.7) (*Figure 10*). The

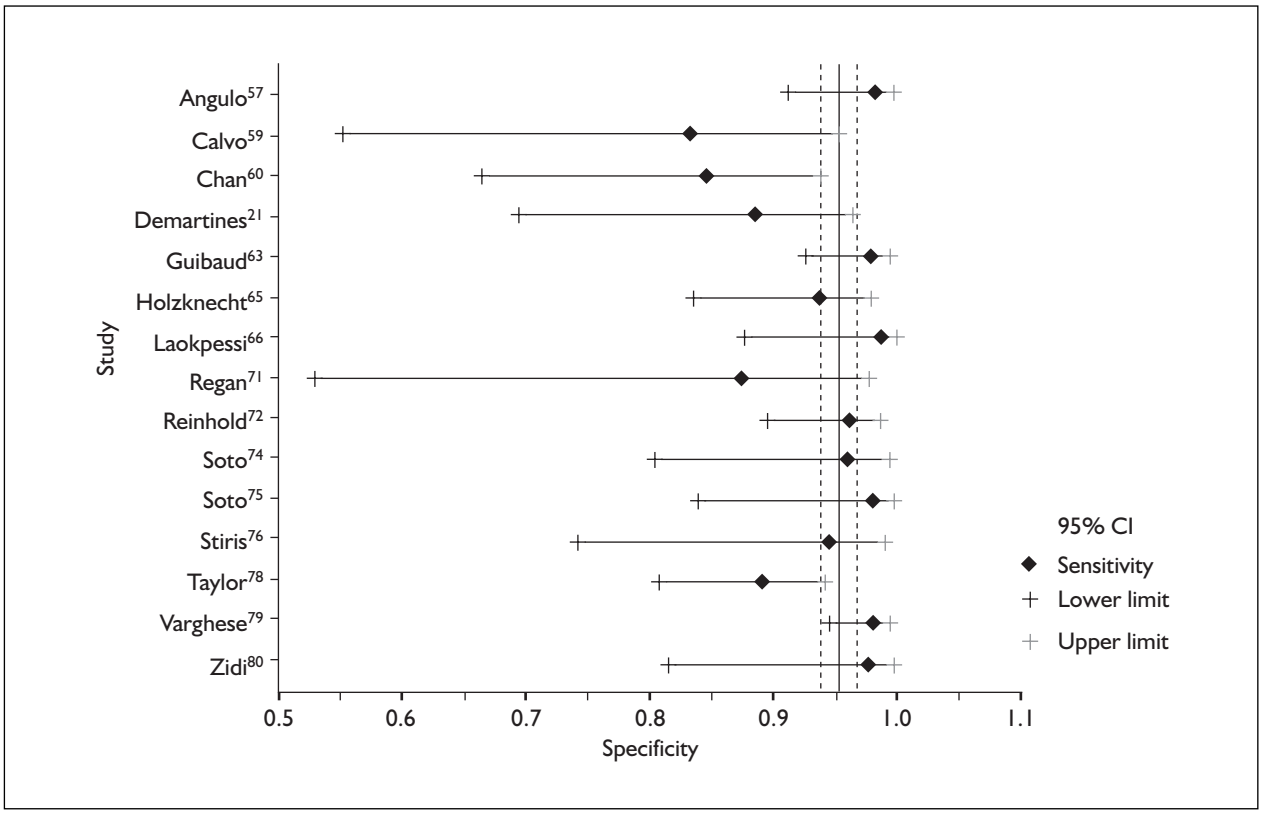


FIGURE 7 *Forest plot of estimated specificities with summary estimate* (n = *15)*

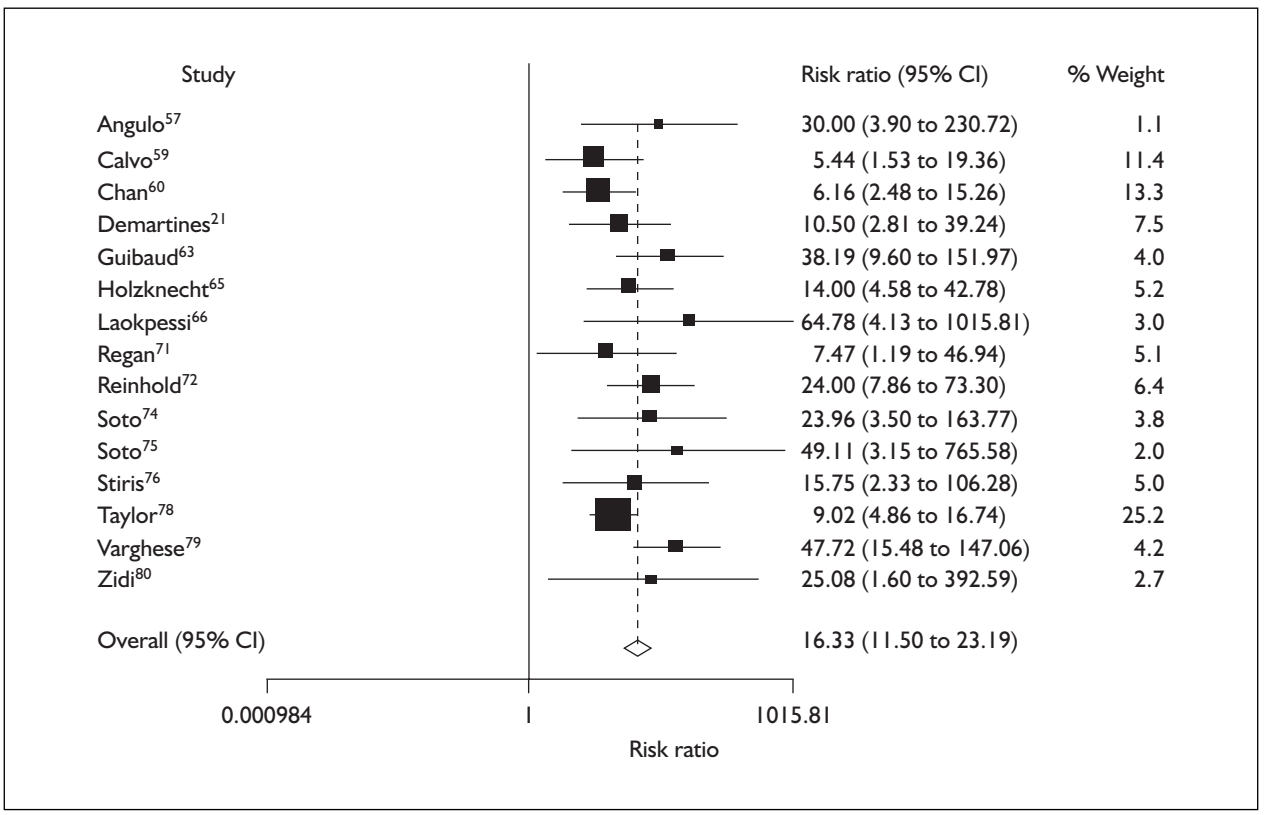


FIGURE 8 *Forest plot of estimated likelihood ratios for a positive test result* (n = *15)*

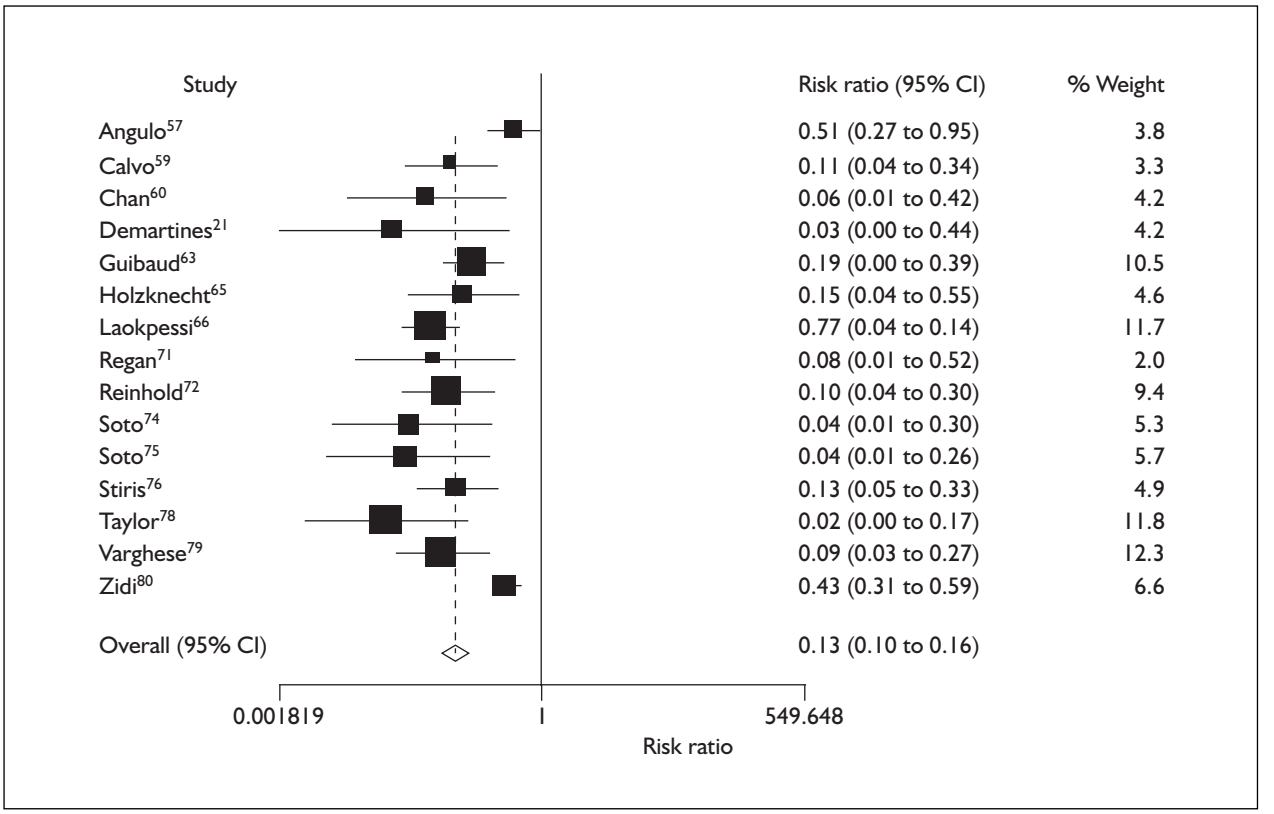


FIGURE 9 *Forest plot of estimated likelihood ratios for a negative test result* (n = *15)*

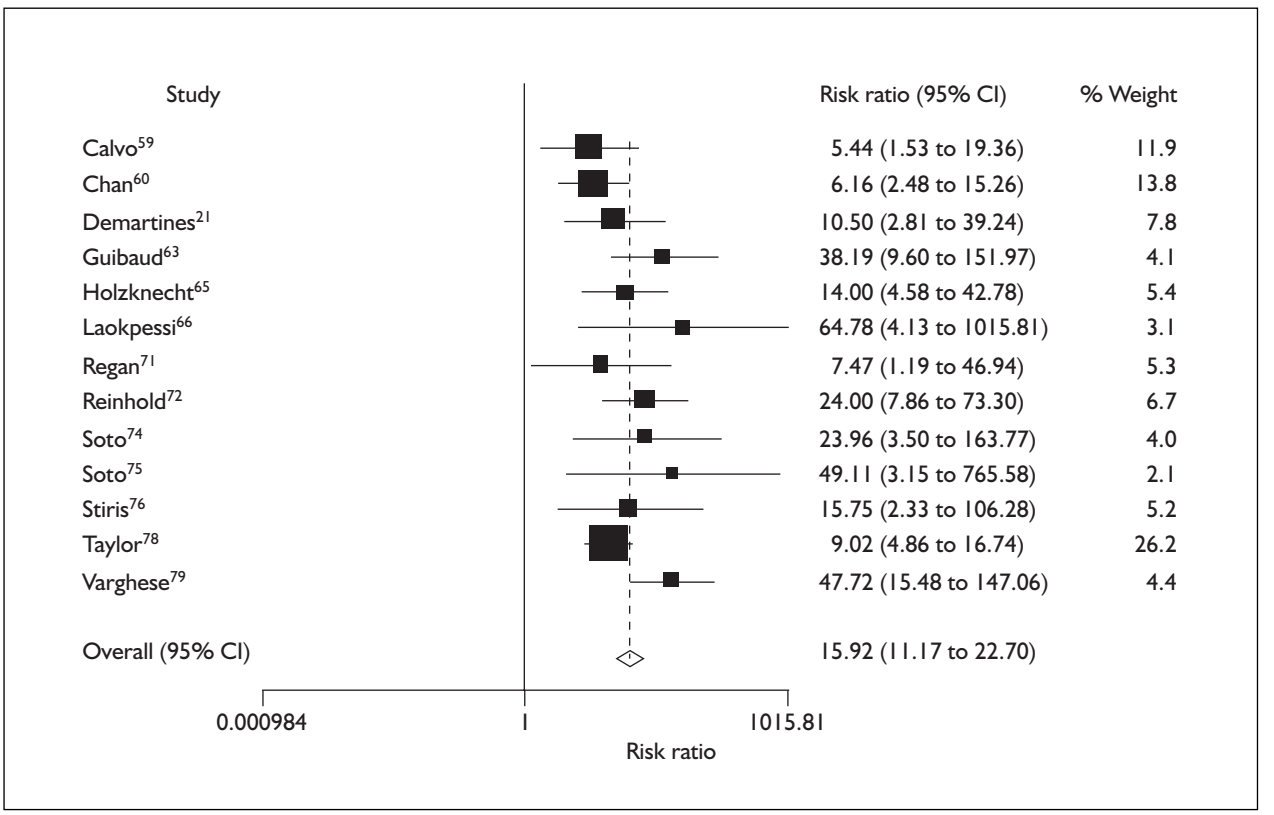


FIGURE 10 *Forest plot of likelihood ratios for a positive test result* (n =*13)*

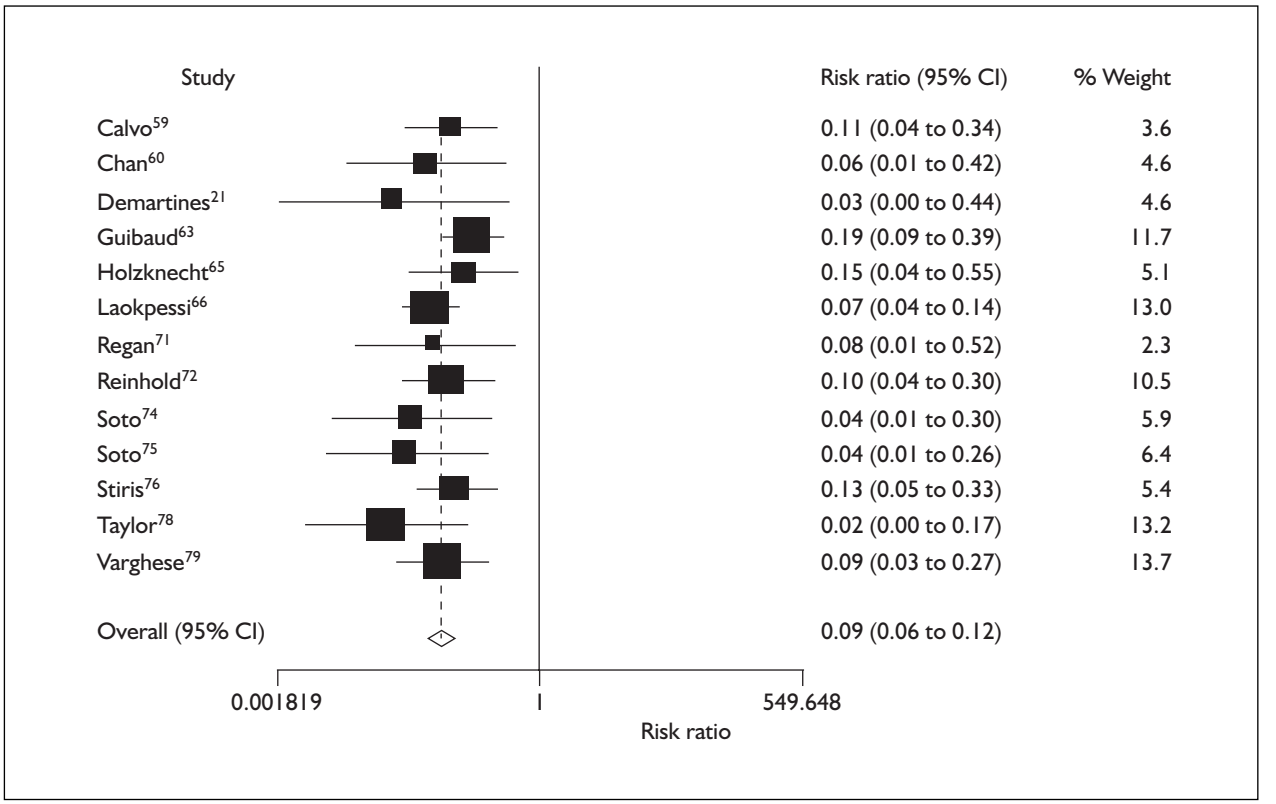


FIGURE 11 *Forest plot of likelihood ratios for a negative test result* (n = *13)*

TABLE 6 *Parameter estimates for Littenberg–Moses summary ROC curve* (n = *13 studies)*

		Coefficient[a]					
		Unstandardised coefficients				95% CI for B	
Model		B	SE		Sig.	Lower bound	Upper bound
1	(Constant)	5.386	0.264	20.437	0.000	4.806	5.966
	S	–0.213	0.199	–1.073	0.306	–0.650	0.224

[a] Dependent variable: log (diagnostic odds ratio).

median positive likelihood ratio for the 13 studies is 15.75, with a range of 5.44 to 64.78. Similarly, the negative likelihood ratios show no evidence of significant heterogeneity (χ^2 = 10.3, df = 12, p = 0.587), the Mantel–Haenszel pooled estimate for 13 studies being 0.09 (95% CI 0.06 to 0.12) (*Figure 11*). The median negative likelihood ratio for the 13 studies was 0.08, with a range between 0.00 and 0.19.

Differences between studies in patient groups, test execution and study design can introduce variability in diagnostic thresholds. Finally, because of the suspected heterogeneity in the studies (even after excluding the Angulo and Zidi studies) and the suspected variation in diagnostic threshold, it was felt appropriate to calculate a summary ROC curve for the studies.

Summary ROC curves

Regression of the log diagnostic odds ratio (D) on the measure of diagnostic threshold (S) for the 13 studies produces estimates of the parameters a and b from the regression equation, $D = a + bS$. The parameter estimates are reported in *Table 6*.

The r^2 for the regression model is 0.095 and the overall F-statistic (df 1,11) is 1.15 (p = 0.31). The non-significant result for the S coefficient (p = 0.306) suggests that there is no reliable

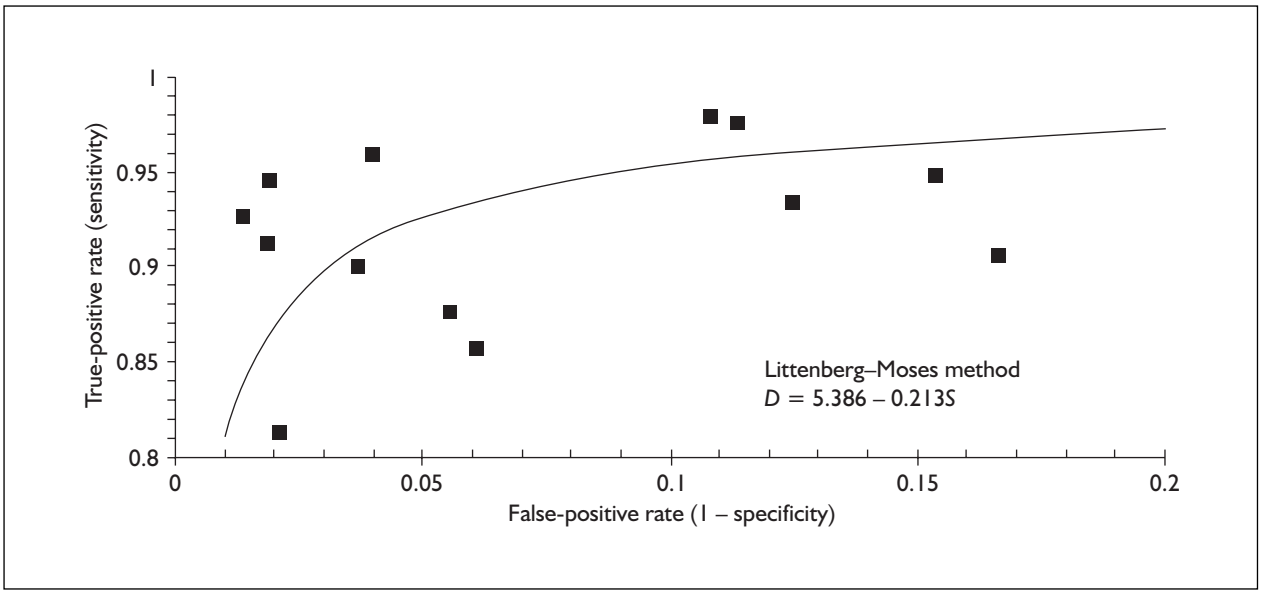


FIGURE 12 *Littenberg–Moses summary ROC curve and actual data for 13 studies*

statistical evidence that the diagnostic odds ratio changes with threshold ($p = 0.306$). A similar analysis including the two previously excluded studies with high specificities and low sensitivities gave very similar results.

Figure 12 shows the results of the Littenberg–Moses method for the estimation of a summary ROC curve. However, there is no unique joint summary estimate of sensitivity and specificity from this plot. It is only possible to obtain a summary estimate of one value conditional on the value of the other. To interpret both diagnostic odds ratios and summary ROC curves it is necessary to have some knowledge of either the sensitivity or the specificity of the test in the population to which it is to be applied. The Littenberg–Moses curve shows the relationship between sensitivities and specificities across the 13 studies. The ROC curve presentation is unlikely to be useful for individual clinicians in practice as, without knowledge of the diagnostic threshold being applied, it is impossible to know where on the ROC curve an individual is operating. For the purposes of an economic analysis of the technology across a broad population of clinicians, however, the ROC curve, if it can be generated, would be the most appropriate method of analysis.

However, the results from the linear regression suggest that there is no statistically significant evidence that the diagnostic odds ratio changes with threshold. Furthermore the fact that the overall fit of the model is very poor, with only 10% of the variability being explained by the measure of threshold, implies that there is insufficient evidence within this data set to quantify the expected relationship between sensitivity and specificity.

Malignancy

Three studies presented sensitivities and sensitivities for malignancy.[55,63,67] Adamek and colleagues[55] reported malignant strictures in 27 patients due to pancreatic carcinoma, ampullary carcinoma or cholangiocarcinoma. Guibaud and colleagues[63] reported biliary malignant biliary obstruction in 14 patients, with six due to ampullary tumours, four to pancreatic cancers, three to cholangiocarcinomas and one to external compression from metastasis. Lee and colleagues[67] did not report the type of malignancy, but presented sensitivity and specificity for distinguishing malignant from benign lesions. Sensitivities ranged from 81% for Adamek[55] and Lee[67] to 86% for Guibaud.[63] Specificities ranged from 92% for Lee[67] to 100% for Adamek.[55] Although raw data were not provided in the study by Feldman and co-workers,[62] the reported sensitivity for malignancy in this study was 94.4%.

Dilatation

Five studies present figures for dilatation,[57,58,65,70,73] with sensitivities ranging from 87%[58] to 100%[70] and specificities ranging from 91%[70] to 100%.[58]

Obstruction

Three studies present data on obstruction,[57,63,72] with sensitivities ranging from 91%[63,72] to 100%[57] and specificities ranging from 91%[57] to 100%.[63,72]

Stricture
Two studies present data on strictures, with both reporting a sensitivity of 100%[69,78] and specificities of 98%[69] and 99%.[78]

PSC
Two studies present data on PSC.[6,57] Sensitivity ranges from 83%[57] to 88%[6] and specificity ranges from 98%[57] to 99%.[6]

The remaining studies present data for any abnormality[55] (sensitivity 89%, specificity 92%), stenosis[65] (sensitivity 86%, specificity 88%), anomalous PBJ[77] (sensitivity 82%, specificity 100%) and overall figures[65] (sensitivity 91%, specificity 80%).

Likelihood ratios
Likelihood ratios [sensitivity/(1 – specificity) for a positive test and (1 – sensitivity)/specificity for a negative test] describe how many times a person with disease is more likely to have a particular test result compared with a person without the disease. Positive likelihood ratios greater than 5 and negative likelihood ratios less than 0.2 give strong diagnostic evidence that a test is accurate. In the 28 studies in this review, which included 38 subgroups, only one positive likelihood ratio was less than 5.[65] This value was based on the mean data from two reviewers. In total, four negative likelihood ratios in the 38 subgroups were greater than 0.2.[57,67,77,80] These included one study looking at a subgroup of CBD stones, although the main objective of the study was to investigate PSC,[57] one study investigating patients with suspected malignancy,[67] one study that involved sonography as a comparator as well as diagnostic ERCP,[80] and one study investigating diagnosis of an anomalous PBJ.[77]

Factors affecting results
Several factors may have influenced the results in these studies. First, comparisons were made with ERCP in 21 studies and with final diagnosis in seven studies, making comparisons between all studies difficult. ERCP is not a perfect gold standard, so differences in diagnosis between MRCP and ERCP may be due not to MRCP giving an incorrect result but rather to ERCP giving an incorrect result. Reporting in the studies was poor as varying definitions for final diagnosis were given and it was not entirely clear that those studies stating ERCP as the comparator did not incorporate other test results as well.

Another factor affecting the results is the date of the investigations. MRCP techniques are continually improving. Studies taking place in 1995–8 may have used less accurate techniques than those undertaken more recently.

The quality of the studies was moderate and this would have a potential impact on the results. In all but one study, selected patients did not have both MRCP and diagnostic ERCP, and often the reasons why not were unclear. Only 13 of the 28 studies reported adequate blinding and only six of the 28 studies reported information on agreement of MRCP results by more than one investigator. Nine studies gave no information on other diagnostic tests and most studies did not adequately report inclusion and exclusion criteria.

Summary and conclusions
The median sensitivity for choledocholithiasis (n = 13 studies) was 93% (range 81–100%) and specificity 94% (range 83–99%). The median likelihood ratio for a positive value was 15.75 and for a negative value 0.08. For malignancy reported sensitivities were somewhat lower, ranging from 81 to 86%, and specificities ranged from 92 to 100%. All positive likelihood ratios, apart from one, were greater than 5, and all negative likelihood ratios, apart from four, were less than 0.2.

No studies reported any adverse effects associated with MRCP, although six studies reported adverse effects associated with ERCP. Twenty studies reported no information regarding adverse effects. Claustrophobia prevented at least some patients from having MRCP in ten of the 28 studies. The other 18 studies make no mention of claustrophobia. In the one study identified dealing with patient satisfaction, on the whole patients preferred MRCP to ERCP. There is, therefore, some evidence that MRCP is an accurate diagnostic test in comparison to ERCP, although study quality was moderate.

Chapter 4

Economic analysis

Role of diagnostic ERCP and MRCP in the diagnosis of biliary tree obstruction

ERCP has established itself as the conventional modality for imaging the pancreaticobiliary tree and affording the opportunity for therapeutic intervention.

However, the procedure remains operator dependent and carries significant morbidity and mortality rates. Whereas the complication rate for therapeutic ERCP is acceptable, considering that the complications of surgical management are significantly higher, diagnostic ERCP can be associated with very serious and even fatal complications.[23] Furthermore, with reported initial failure rate for cannulation of the duct between 3 and 12%,[23,41] repeated ERCP significantly contributes to overall workload and morbidity.

MRCP is becoming increasingly available to clinicians for non-invasive evaluation of the biliary and pancreatic ducts. The technique can provide diagnostic information comparable to diagnostic ERCP, both with regard to the presence of obstruction and in a range of common clinical situations, such as suspected choledocholithiasis or stricture.[21,56] The evidence provided by the systematic review suggests that MRCP is an accurate diagnostic test in comparison to ERCP (see Chapter 3).

Although the spatial resolution of MRCP does not yet match that of ERCP and potential pitfalls in MRCP interpretation should be taken into account,[46] its projectional display and ability to demonstrate obstructed as well as normal duct segments make it an appropriate test for evaluating patients with suspected biliary disease and may limit ERCP to those who require therapy.[21] MRCP does not require contrast media injection, unlike ERCP, providing particular advantages where this is not technically possible or may introduce infection.

However, the main criticism of MRCP, when compared with ERCP or PTC, has been the fact that no therapeutic option can be offered at the same time and that it may only add further to the cost of the diagnostic work-up in these patients. This is the main reason why, in an era of cost awareness, routine use of MRCP for the confirmation of presence of biliary obstruction before ERCP is difficult to justify.

Potential clinical applications of MRCP have been identified in the literature.

- MRCP can be especially useful in cases where ERCP fails, such as biliary–enteric anastomosis, or is inconclusive, for example in cases of complete ductal obstruction.[21]
- In the case of patients with low risk of choledocholithiasis, on the basis of clinical history, liver blood tests and abdominal ultrasound examination.[21]
- In the case of strictures in general, conventional MR images obtained with MRCP may add specificity by allowing visualisation of the extraductal anatomy, particularly for cholangiocarcinoma. However, continued investigation is needed to determine the ability of MRCP with conventional MRI to differentiate between benign and malignant disease. Many of these patients will also require endoscopic biliary stenting.[81]
- In the evaluation of malignant strictures, MRCP can provide a detailed map of the biliary tree above the stricture, also showing isolated segmental ducts not evaluated directly at ERCP, playing an important role in planning surgery.[81] However, MRCP in malignant strictures should be considered as part of a complete upper abdominal evaluation, together with conventional MR images.[33]

It can be concluded that MRCP may substantially decrease the need for purely diagnostic ERCP. If MRCP can replace a fraction of the ERCPs currently being obtained for diagnostic purposes, it is reasonable to assume that the number of complications and the cost of diagnostic evaluation per patient would decrease. In other words, the potential exists not only for improvement in patient management but also for a reduction in the cost of diagnostic work-up. The decision analytical model seeks to provide quantified estimates of these clinical and economic trade-offs.

Ideally, if the aetiology of the obstruction could be predicted with accuracy, based on the clinical arguments reported above, the decision regarding which diagnostic test to choose would be less of a dilemma. However, decisions on whether to pursue diagnostic ERCP, MRCP or PTC (especially for proximal biliary obstruction) as defined at the initial ultrasound examination in the patient are not recommendable. Because of its ability to delineate the level of biliary obstruction and the added benefit of being non-invasive, free of complication and relatively inexpensive, ultrasound is widely advocated as the initial non-invasive imaging study in evaluating suspected biliary obstruction, to guide further radiographic evaluation. However, ultrasound fails to define the aetiology of biliary obstruction, especially choledocholithiasis and cholangiocarcinoma, in approximately two out of three cases.[82]

In short, clinical judgement based on liver function tests (LFT) or previous ultrasound examination cannot provide certainty as no perfect test exists to evaluate the presence and underlying causes of biliary obstruction. That is the main reason why the pool of patients considered for the modelling comprises adult patients with suspected biliary obstruction, with or without preliminary diagnosis after initial ultrasound examination. (In younger patients the duct systems are frequently of smaller calibre and contain less bile, making them more difficult to visualise.) The economic impact of MRCP and diagnostic alternative strategies with different probabilities of CBD stones or strictures associated with ultrasound and LFT results, is estimated later in this chapter ('Synthesis of results', p. 38), based on work by SM Everett and colleagues (unpublished conference abstract, UGW, 2002) (see *Table 14*).

Decision analytical modelling

The primary objective of modelling was to evaluate the relative cost-effectiveness of MRCP compared with the conventional practice of diagnostic ERCP for the investigation of biliary tree obstruction, for those patients for whom a choice is available; for example, excluding patients suffering from severe claustrophobia and those with previous gastric surgery that prevent endoscopic access to the ampulla.

Evaluation of the relative cost-effectiveness of adopting MRCP scanning in the investigation of the biliary tree will be undertaken using a probabilistic economic model. Uncertainty analysis will include presentation of a cost-effectiveness acceptability curve (CEAC) and analysis of the impact of different risks of CBD stones.

Perspective

Ideally, cost-effectiveness analyses should take a broad societal perspective, that is, include the health outcomes and costs for everyone affected by the intervention. This analysis uses the perspective of the healthcare provider, excluding informal carers because of their relatively minor importance given the characteristics of both diagnostic technologies.

Decision tree

The pool of patients considered for the modelling comprises adult patients with suspected biliary obstruction, with or without preliminary diagnosis after initial ultrasound examination. The reason for this decision was justified above.

Two possible conditions are considered:

- Choledocholithiasis (i.e. gallstones in the extrahepatic bile duct), also known as CBD stones.
- Biliary strictures: these can be due to a number of underlying conditions, the most common being benign and malignant strictures (cancer).

These are the most frequent conditions affecting the biliary tree, where MRCP can provide diagnostic information comparable to diagnostic ERCP.[21,23,41,56]

From the results presented later in the chapter, it can be concluded that there is moderate evidence that MRCP is an accurate investigation in comparison to diagnostic ERCP.

The structure of the decision analytical model includes both CBD stones and benign and malignant strictures, to approximate the level of uncertainty to clinical practice. For further details on causes of biliary obstruction see Chapter 2.

Treatment options for patients with the most common cause of obstruction, symptomatic CBD stones, include therapeutic ERCP (for clearance of the bile duct), endoscopic decompression by internal stent, and dissolution. The first two options have been simplified as therapeutic ERCP with sphincterotomy, for the sake of simplicity of the model. Dissolution is not included in this analysis as its efficacy is still debatable. Very small stones that only require regular checks have not been modelled.

Pancreatic head lesions, and in particular cancer of the head of the pancreas, are the most common malignant neoplasm in the hepatobiliary area, causing in many cases an indirect dilatation in the biliary ducts. Periampullary carcinoma, in the region of the ampulla of Vater, is less common than head of the pancreas cancer and is associated with lower mortality. Although more uncommon than malignant neoplasm of the head of pancreas, cholangiocarcinoma occurs most frequently in the extrahepatic biliary tree but can also arise from intrahepatic bile ducts. Extrahepatic lesions may present as biliary stricture, involving the CBD (30–36%), the common hepatic duct (15–30%) and the biliary bifurcation with the typical features of Klatskin's tumour (10–26%).[33,81]

For the purposes of modelling, cholangiocarcinoma in the intrahepatic bile duct and PSC are excluded, because they are uncommon conditions and usually more associated with liver problems and liver treatments.

Treatment options for patients with malignant strictures are either curative or palliative. In general, the probability that curative resection is appropriate is quite low, and aggressive surgical therapy has to be carefully considered taking into account age and mortality risk. With the exception of cholangiocarcinoma in the CBD, where resection is possible in around 30% of cases, palliative treatment through endoscopic stent placement is considered the standard treatment for extrahepatic malignant biliary stricture.[83]

Benign extrahepatic strictures are normally the result of a major complication of laparoscopic cholecystectomy or chronic pancreatitis. Surgical reconstruction is required in most cases (about 85%) and can be safely accomplished with minimal morbidity and excellent long-term outcomes.[84]

Regarding the potential economic benefits of MRCP versus diagnostic ERCP, MRCP may avert the need for invasive diagnostic testing in patients who ultimately do not require therapeutic ERCP intervention, so minimising the costs of failed examinations and morbidity and mortality associated with diagnostic ERCP. Thus, MRCP is potentially most beneficial in patients with a high probability of having a non-obstructive dilatation (true negatives) and in patients with suspected malignant strictures (i.e. cancer), who can benefit from its important role in planning surgery.

In contrast, diagnostic information provided by ERCP allows immediate therapeutic intervention required for the removal of CBD stones and introduction of stents to relieve biliary obstruction, and also further diagnostic tests such as biopsies. So, especially in the case of patients with a high probability of choledocholithiasis, the risks of morbidity and mortality associated with ERCP could be compensated in terms of health outcomes, by an immediate and accurate therapeutic intervention, and also in terms of cost savings. The waiting time between MRCP and therapeutic ERCP is crucial, particularly in the case of stone extraction, as spontaneous stone fragmentation and natural expulsion may result in unnecessary therapeutic ERCP, with an impact on both costs and avoidable risks for the patient. These potential benefits from both diagnostic technologies are summarised in *Table 7*.

The clinician is faced with the problem of deciding between these possible diagnostic strategies to maximise health outcomes. The decision problem is illustrated in the structure of the decision tree (*Figure 13*) that follows the actual chronology of the acts, states and outcomes.

The MRCP or ERCP test option is illustrated at the main decision node. The product of the health state utilities and probabilities are combined at chance nodes. The treatment decisions (i.e. therapeutic ERCP, open surgery or palliative stent treatment) are illustrated at chance nodes because they are not part of the main decision, and are dependent on the clinician's perception of the clinical state of the individual patient.

Patients who are incorrectly diagnosed will be treated at some point in the future, but during this time they will experience reduced quality of life. This is especially true for patients suffering from malignant lesions of the biliary tree, for whom a considerable improvement in quality of life related to pain relief is not provided. The reduced quality of life for patients suffering from chest and back pain relating to CBD stones, mainly intermittent, is modelled as the negation of pain relief. These patients will be diagnosed and treated at some point in the future. However, given that the options of treatment after diagnosis do not have an important impact on survival, future costs for the system as well as follow-up treatments are not modelled (*Figure 14*).

The prognosis for most patients suffering from pancreatic head lesions, the most common of all malignant lesions of the biliary tree, is very poor and more than three-quarters die within a year of diagnosis.[85] This is the main reason why the

TABLE 7 *Potential economic benefits of MRCP versus diagnostic ERCP*

Advantages of MRCP	**Disadvantages of ERCP**
Cancer patients treated with MRCP can benefit from its important role in planning surgery	In cancer patients treated a priori with diagnostic ERCP, the invasive nature of the diagnostic therapy can affect imaging MRCP ERCP may also affect the ability to stage the tumour accurately and thus affect management decisions, especially in the context of pancreatic cancers
MRCP demonstrates ducts proximal to stricture or obstruction, so the cause of the obstruction can be determined with higher level of accuracy	ERCP often does not demonstrate these ducts; if it does, they need to be drained because of the high risk of ensuing infection and cholangitis
In the case of true negatives (i.e. non-obstructive dilatation) MRCP represents the advantage that it is risk free for the patient, so there is no health outcome loss	A healthy patient tested using the ERCP diagnostic option has a lower health outcome than a healthy patient tested with MRCP, because of the 4–5% associated morbidity (haemorrhage, sepsis, pancreatitis, bile leakage) as well as recognised mortality
Disadvantages of MRCP	**Advantages of ERCP**
No therapeutic option offered at the same time. If MRCP results in disease (true-positive), when ERCP is a recommendable therapeutic intervention MRCP costs could have been avoidable. In the case that the waiting time between MRCP diagnostic and intervention is considerable, spontaneous stone fragmentation can change the accuracy of the diagnostic into false-positive, with associated impact in costs and disutilities	ERCP diagnostic information allows immediate and accurate therapeutic intervention when required (e.g. removal of CBD stones, introduction of stents)

survival horizon of the modelling has been limited to 12 months. In the case of patients with CBD stones, the relief of pain is experienced in the short term after the removal of the stones.

Assumptions

To facilitate the modelling, the following assumptions have been introduced.

- Repeated MRCP, therapeutic ERCP and surgery are not modelled. Although a realistic option of clinical practice, repeated diagnostic ERCP after failed cannulation is not modelled either.
- In most cases therapeutic ERCP is performed with sphincterotomy. For the sake of simplification the option ERCP without sphincterotomy is not modelled.
- The patient either is sick (i.e. biliary obstruction) or healthy (i.e. normal ducts). There is some risk associated with both the treatments and the ERCP diagnostic test, so a healthy patient who is tested or treated with ERCP has a lower outcome than a healthy patient who is not.
- MRCP is generally considered risk free, so the utility of a healthy patient who is tested with MRCP equals 1. However, one should take into account in the discussion of results that in terms of patient satisfaction, MRCP scores lower than expected by clinicians because of reasons relating to noise and claustrophobia.[54]
- Patients who present contraindications for an MRCP test (i.e. usual general exclusions for MRI, such as claustrophobia and cardiac pacemakers) or ERCP (i.e. previous gastric surgery which may prevent endoscopic access to the ampulla) are excluded from this analysis because they do not have a real choice between technologies.

Base case values and parameters

The parameters used in the model and the sources from which these are derived are given in *Table 8*.

Annual incidence

Hospital Episode Statistics (HES) were used to estimate the annual incidence of patients with suspected biliary obstruction and incidence of different biliary tree disorders. Finished clinical episode (FCE) records for primary diagnosis (i.e. the main condition investigated during the relevant episode of healthcare) were used to estimate the pool of patients with suspected biliary obstruction/disorder. Appropriate FCE records for 2001/2 for England and Wales, grouped by four character International Classification of Diseases (ICD-10) codes were identified and are presented in *Table 9*.

It is recognised that there are important limitations in using this database to estimate

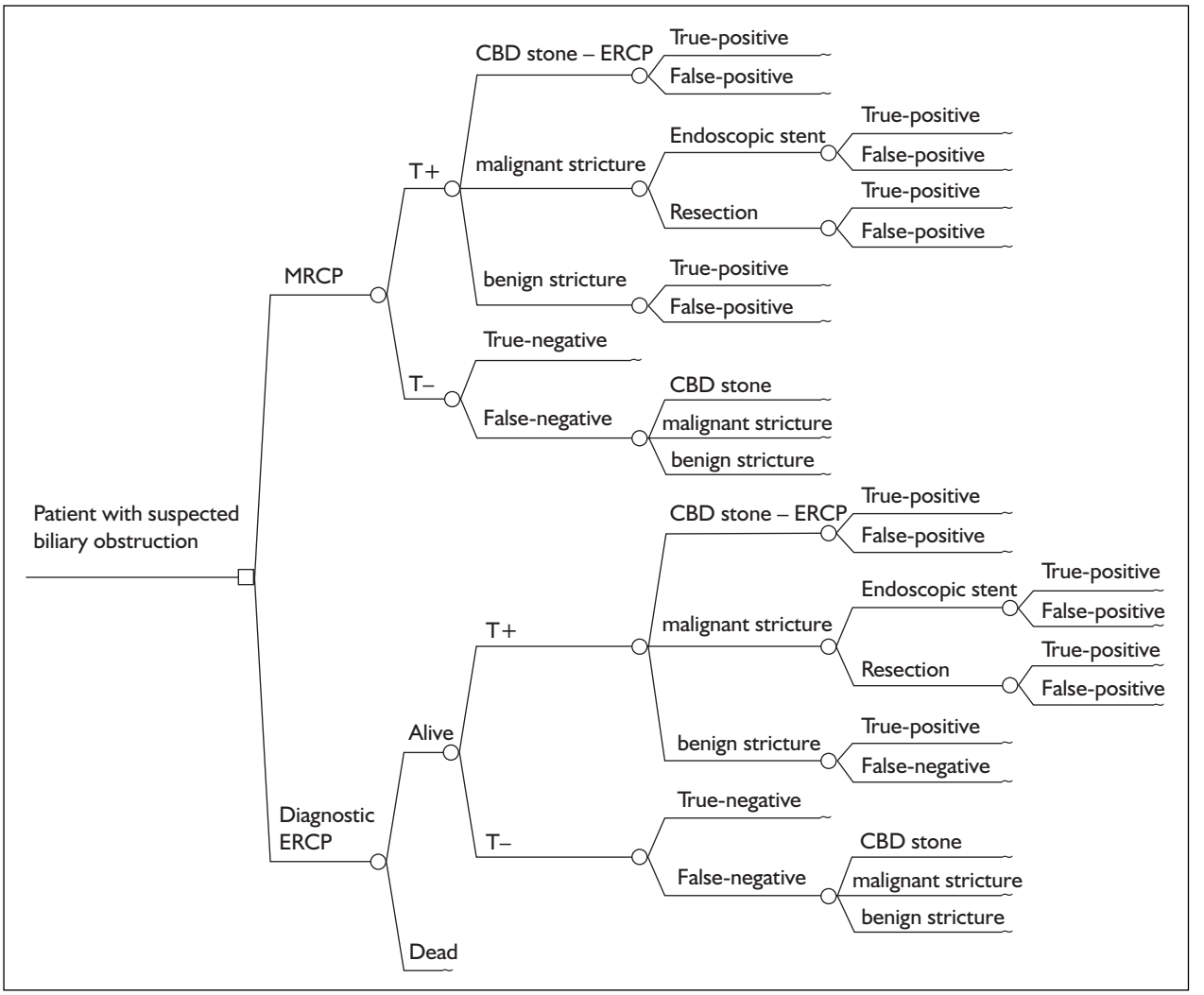


FIGURE 13 *Basic decision tree*

incidence; for example, only a proportion of potential patients with biliary disorders are admitted to hospital, and there may be more than one record for the same person, depending on the number of transfers or multiple visits during the year. However, following consultation with the College of the British Society of Gastroenterology and the Royal College of Radiologists (RCR), and in the absence of a better source of information, this is the best estimate available. These estimates were validated with data from GP patient consulting[9] for new and first ever episode rates for biliary tree and pancreatic lesions (*Table 10*). Given that the approximate population in England and Wales is 50 million people, based on the overall annual incidence rate presented in *Table 10* (12 per 10,000 person-years at risk) this gives a total annual incidence of 60,000 for biliary tree and pancreatic lesions. This figure is very similar to the total of 52,617 annual incidence based on FCE estimates.

Probabilities of events

Proportions for the different disorders were estimated using FCE records (see *Table 9*) and validated by estimates from the literature reviewed and by clinical judgement.

The probabilities of death and overall complications after diagnostic and therapeutic ERCP were estimated from the literature review and checked with estimates from local data.

The clinical-effectiveness review did not provide any useful data regarding the proportion of patients with malignant strictures who undergo open surgery or palliative treatment. Estimates were based on local data and clinical judgement according to the type of cancer, ranging between 10 and 30%. However, given that the most common cancer affecting bile duct obstruction is the head of the pancreas, and that its chances of

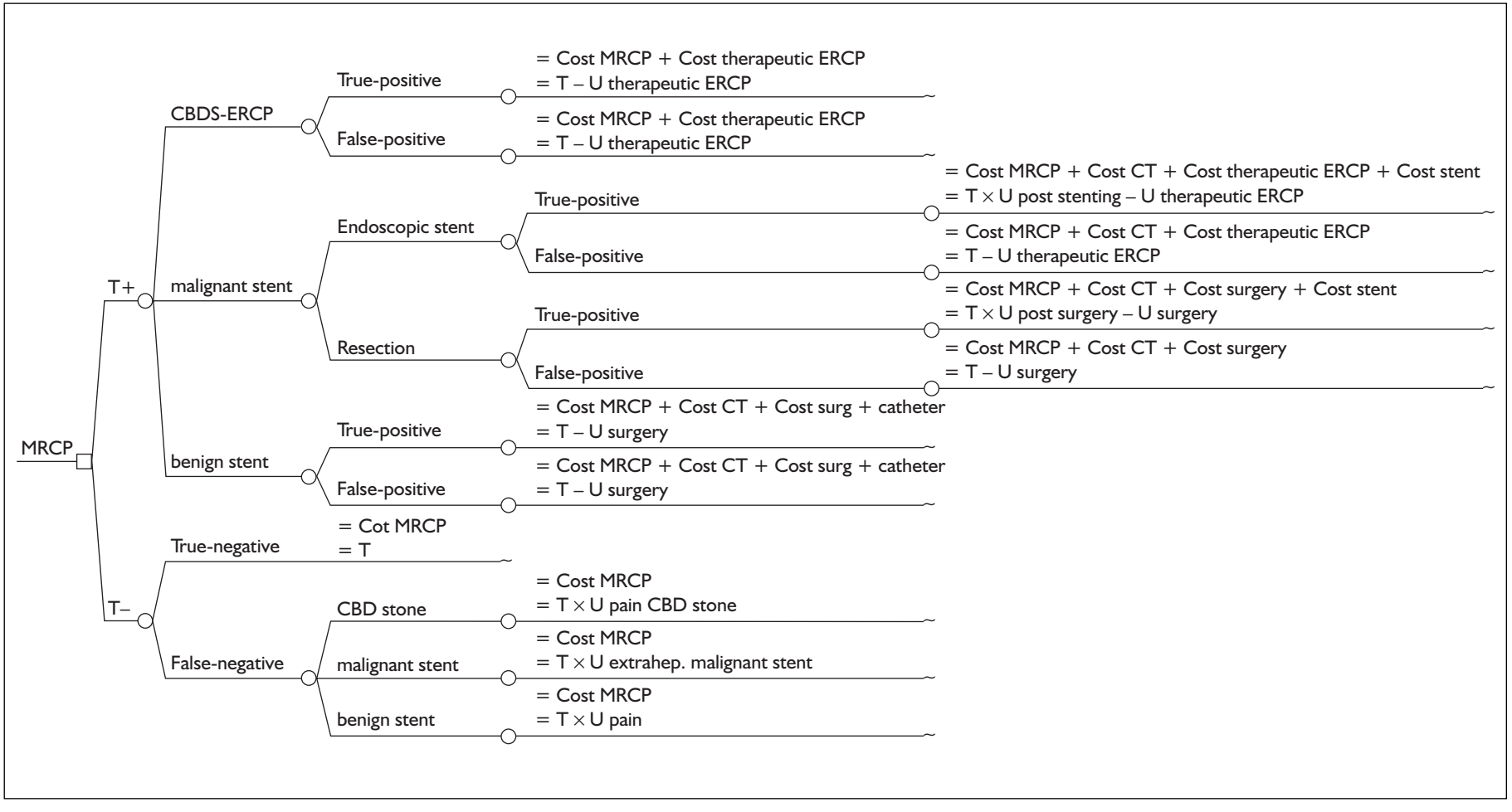


FIGURE 14 *Model: MRCP and ERCP sections with costs and utilities calculation*

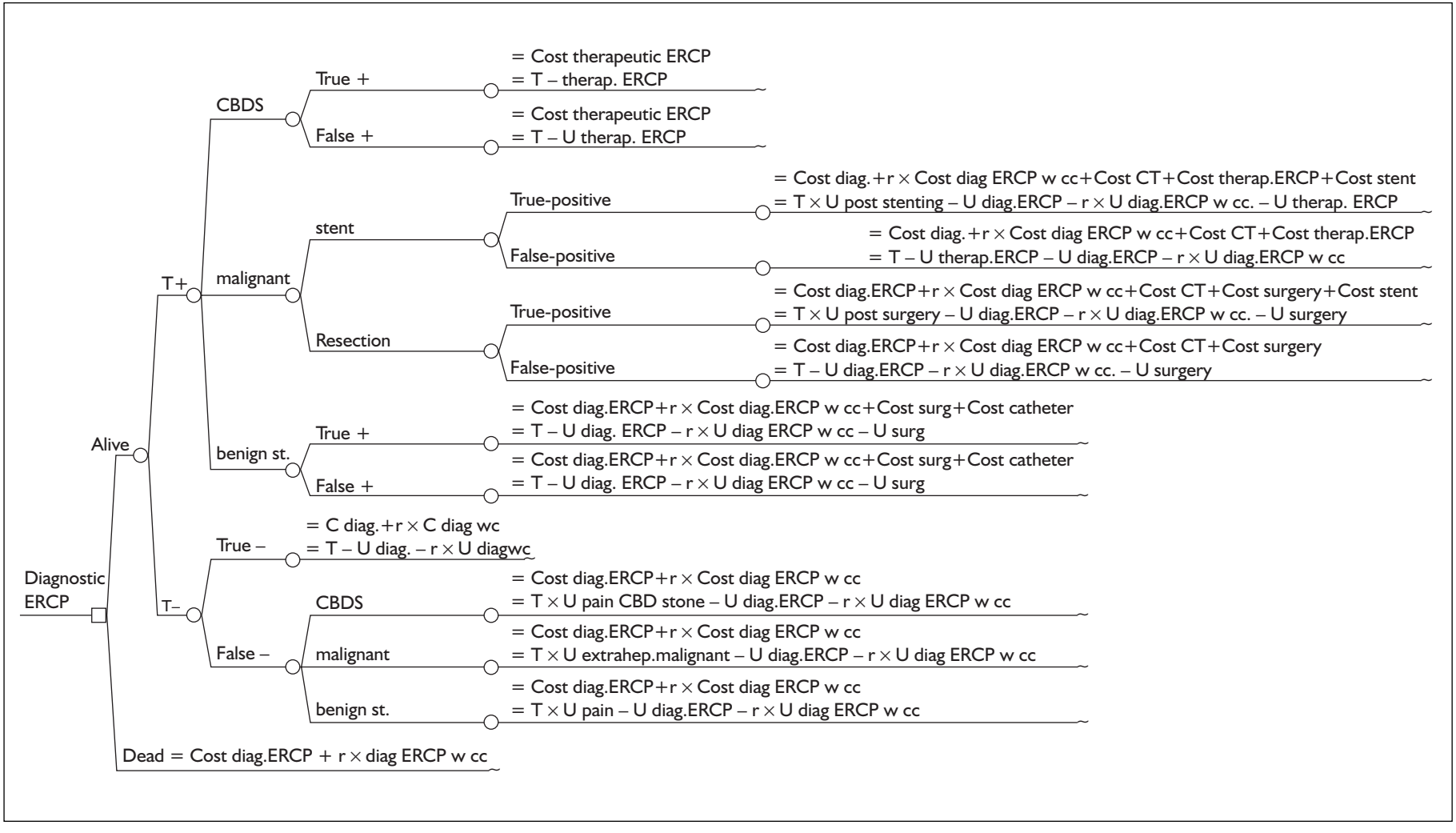


FIGURE 14 *Model: MRCP and ERCP sections with costs and utilities calculation (cont'd)*

TABLE 8 *Prior information and sources for key parameters*

	Mean value	SD	Range	Distribution	Source
Probabilities[a]					
Probability of CBD stones	0.37			Beta	HES
Probability of malignant stricture	0.17			Beta	HES
Probability of benign stricture	0.15			Beta	HES
Death after diagnostic ERCP (%)	0.085	0.005	0.07–0.1	Beta	Cotton *et al.*, 1994[27]
Overall complications after diagnostic ERCP (%)	5.5	0.16	5–6	Beta	Cotton *et al.*, 1994[27]
Resection open surgery for malignant stricture	0.10			Fixed parameter	Clinical judgement
Endoscopic stent placement for malignant stricture	0.90			Fixed parameter	Clinical judgement
Utilities					
Health-related quality of life general population	1				
MRCP examination	1				
Chest and back pain relating to CBD stones and strictures in the extrahepatic bile duct[b]	0.89	0.003	0.88–0.90	Normal. Range: severe (periodical) pain, moderate pain	Cook *et al.*, 1994[86]; Community, TTO
Diagnostic ERCP procedure only	0.9904			Beta (*a* 1, *b* 99)	Gregor *et al.*, 1996[87]; Clinicians, TTO
Therapeutic ERCP with sphincterotomy gamble	0.95			Beta (*a* 4, *b* 96)	Bass *et al.*, 1993[88]; patients, standard
Biliary stricture surgery	0.884	0.038	0.77–0.998	Normal. Range: complication of surgery, surgical scar	Bass *et al.*, 1993[88]; patients, standard gamble
ERCP papillotomy/other complications	0.759	0.016	0.7115–0.808	Normal. Range: papillotomy complication, other complication	Gregor *et al.*, 1996[87]; Clinicians, TTO
Patient with extrahepatic malignant stricture	0.37	0.041	0.25–0.50	Normal	Luman *et al.*, 1997[89]; EORTC QLQ-30
Postintervention for extrahepatic malignant biliary stricture	0.61	0.041	0.50–0.75	Normal	Luman *et al.*, 1997[89]; EORTC QLQ-30

continued

TABLE 8 *Prior information and sources for key parameters (cont'd)*

	Mean value	SD	Range	Distribution	Source
Costs (£ 2002)[c]					
MRI: medical gastroenterology[d]	£454	£26	£376–532	Normal	HRGs 2002 (F03op)
CT: medical gastroenterology[d]	£4340	£20.16	£279–400	Normal	HRGs 2002 (F04op)
Diagnostic ERCP examination of bile duct	£846	£100.83	£514–1119	Normal	HRGs 2002 (G17)Diagnostic ERCP
with complications	£1113	£139.83	£570–1409	Normal	HRGs 2002 (G16)
Therapeutic ERCP, extraction of CBD stones	£1108	£130.83	£750–1535	Normal	HRGs 2002 (G15)
Surgery malignant neoplasm of extrahepatic bile ducts > 69 years or with complications	£2004	£134.33	£1649–2455	Normal	HRGs 2002 (G13)
Memotherm biliary stent: palliative, malignant stricture	£800	£10		Normal	Sheffield Northern General Hospital and Bradford Royal Infirmary
Bilioplasty balloon catheter	£80	£10		Normal	Data from suppliers

[a] Sensitivity and specificity for diagnosing the cause of the biliary obstruction. Obtained against final diagnosis, made on the basis of surgical findings, percutaneous biopsy, clinical follow-up and others.
[b] Approximated same discomfort relating to gallbladder, according to clinical judgement.
[c] Elective procedures, relating to Hepato-biliary and Pancreatic System HRGs section. HRG codes in parentheses. Reporting range for 50% of NHS Trusts.
[d] Primary Care Trusts Outpatient HRG Data, 2001/2. Reporting range for 50% of NHS Trusts.
EORTC QLQ-30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-30.

TABLE 9 *FCEs for Primary Diagnosis biliary tree and pancreatic head lesions*

Primary diagnosis	ICD-10[a]	All NHS Trusts in England[b]	All NHS Trusts in Wales[c]
Malignant neoplasm of extrahepatic bile duct	C240	562	32
Malignant neoplasm of ampulla of Vater	C241	1,059	30
Malignant neoplasm of biliary tract, unspecified	C248–C249	235	3
Malignant neoplasm of head of pancreas	C250	6,652	325
Benign neoplasm of extrahepatic bile duct	D135	152	17
Obstruction of bile duct	K831	4,431	136
Other specified diseases of biliary tract	K838	2,432	146
Disease of biliary tract, unspecified	K839	348	19
Calculus of bile duct with cholangitis	K803	1,502	52
Calculus of bile duct with cholecystitis	K804	1,292	81
Calculus of bile duct without cholangitis or cholecystitis	K805	15,860	768
Other cholelithiasis	K808	667	93
Acute cholecystitis	K810	4,902	52
Chronic cholecystitis	K811	5,008	1,376
Other cholecystitis	K818	80	7
Cholecystitis, unspecified	K819	3,991	185
Perforation of bile duct	K832	24	1
Fistula of bile duct	K833	49	2
Spasm of sphincter of Oddi	K834	27	1
Biliary cyst	K835	17	1
Total disorders of the biliary tree and pancreatic head lesions		49,290	3,327
% Patients with malignant stricture		17.26	11.72
% Patients with benign stricture		14.93	9.55
% Patients with CBD stones		37.84	27.08
% Cholelithiasis, cholecystitis or other		35.59	56.59

[a] FCEs are grouped by four character ICD-10 codes.
[b] 2001/2 figures.
[c] 2000/1 figures.

TABLE 10 *Summary table: annual incidence estimates for biliary tree and pancreatic head lesions*

New and first ever episode rates[a]	
Cholelithiasis	8 per 10,000 person-years at risk
Other disorders of the biliary tract	2 per 10,000 person-years at risk
Diseases of the pancreas	2 per 10,000 person-years at risk
Hospital Episode Statistics[b]	
Total disorders of the biliary tree and pancreatic head lesions (England and Wales): primary diagnosis	52,617
Patients with malignant stricture	17%
Patients with benign stricture	15%
Patients with CBD stones	37%
Cholelithiasis, cholecystitis or other	37%

[a] Source OPCS (1992).[9]
[b] HES England figures for 2001/2; Wales figures for 2000/1.

resectability are around 10%, this figure was used as a general simplification. FCE records of main operations affecting the hepatobiliary organs (i.e. normally the most resource-intensive procedure performed during a theatre session) provide an overview of the proportions of this type of intervention (*Table 11*).

Probabilities of events are proportions, such as the percentage of patients suitable for curative treatment, so the beta distribution has been used.

Estimates of sensitivity and specificity taken from the review of clinical effectiveness are summarised in *Table 12*.

TABLE 11 *FCEs for main operations on the biliary tree and pancreatic head lesions*

Main operations	ICD-10[a]	All NHS Trusts in England[b]	All NHS Trusts in Wales[c]
Diagnostic ERCP examination of CBD and/or pancreatic duct	J431–J459	14,018	751
Excision of bile duct	J271–J279	27	–
Extirpation of lesion of bile duct	J281–J289	37	1
Connection of CBD	J301–J309	180	11
Open introduction of prosthesis into CBD	J312–J319	59	–
Reconstruction of CBD	J321–J329	55	–
Open removal of calculus from CBD	J331–J339	200	3
Operations on ampulla of Vater	J361–J368	19	2
Other open operations on CBD	J371–J379	101	4
Endoscopic incision of sphincter of Oddi	J381–J389	11,663	421
Other therapeutic endoscopic operations on ampulla of Vater	J391–J399	268	18
ERCP placement of prosthesis in CBD	J401–J409	5,122	165
Other therapeutic ERCP operations in CBD	J411–J419	1,308	110
Therapeutic PTC insertion operations into CBD	J461–J489	820	43
Other operations in bile duct	J491–J529	717	10
Excision of head of pancreas	J561–J569	618	33
Total main operations on the biliary tree and pancreatic head lesions		35,212	1,572
% Diagnostic ERCP		39.81	47.77
% Therapeutic ERCP		52.14	45.41
% Therapeutic PTC		2.32	2.73

[a] FCEs are grouped by four character ICD-10 codes.
[b] 2001/2 figure.
[c] 2000/1 figures.

Sensitivity and specificity of ERCP were assumed to be 100%. The sensitivity and specificity of MRCP were assumed to have beta distributions based upon means and standard errors drawn from the clinical review. No correlation was assumed between MRCP and ERCP; therefore, the estimates of the difference in sensitivity and specificity will have a greater uncertainty.

TABLE 12 *Diagnostic test performance characteristics used in the model*

	Mean	CI		Beta distribution	
		Lower 95%	Lower 95%	*a*	*b*
MRCP					
Sensitivity	93%	81%	100%	37	3
Specificity	94%	83%	99%	32	2
ERCP					
Sensitivity	100%	–	–	–	–
Specificity	100%	–	–	–	–

Estimation of costs

The costs of healthcare resources used as inputs to the diagnostic tests and subsequent treatment options were estimated using the National Schedule of Reference Costs (NSRC), in particular for NHS Trust Elective Inpatient Healthcare Resource Group (HRG) data (2002, v.3). HRGs are groups of inpatient FCEs which are purported to have similar healthcare resource requirements. Each individual record in the HES data set is assigned to a single HRG based on the data contained in the record.[90] The costs included in the NSRC reflect the actual costs incurred in the 2001/2 financial year and represent national figures for England.

Reported costs are averages, and they include overheads and capital costs. They correspond to elective procedures, relating to hepatobiliary and pancreatic system HRGs. Instead of reporting cost variation in all NHS Trusts, the 50% interquartile range has been included to improve the skewness normally present in this data set.

Depending on the type of procedure, complication costs are also included in the HRG estimation (see *Table 8*); however, the follow-up and treatment of complications are not included.

Where more than one estimate for each cost item was obtained (e.g. ERCP with or without

complications), the range of values was used to calculate the distribution based on the minimum, median and maximum values. The standard deviation was estimated based on an approximate 99% confidence interval between the minimum and maximum values of the range.

Local activity data from the Bradford Royal Infirmary and the Sheffield Teaching Hospital NHS Trust were used to check that there were no striking differences from the national cost database. Missing data for cost variables were obtained from suppliers (e.g. the current price of Memotherm metal stents).

Utility estimates

The tree structure combines very different types of possible biliary disorders in terms of severity and associated mortality, and for these reasons cost per case avoided or cost per life-year gained could not be used as outcome measures. Utility values for the health states were assigned as the end-points of the decision tree. The states of perfect health and death were used as anchor states, with values of 1 and 0, respectively. Utility scores for the different health states were obtained from the Harvard CUA database, with the exception of utilities related to biliary tree malignant neoplasms, which required an additional literature search. Those utilities reported by clinicians and calculated using the methodologies of standard gamble and time trade-off (TTO) were preferred to those reported as utility scores using a rating scale. The peculiarities of patient satisfaction with diagnostic ERCP and MRCP were discussed in Chapter 3 ('Patient satisfaction', p. 14).

The probability of ending in one of the health states included in the tree structure is determined by previous events. The predictive value of disease given a positive or negative test, the predictive value of no disease given a positive or negative test, and the different probabilities of biliary tree disorders play key roles in determining final outcomes.

Model uncertainty

An overall sensitivity analysis for a population of normal risk is presented using Monte-Carlo simulation, assigning a probabilistic structure (prior distribution) to each of the model inputs and generating a CEAC. The probabilistic sensitivity analysis was undertaken for all model parameters simultaneously, to determine the overall impact of uncertainty within the model.

The economic value of diagnostic MRCP, however, is dependent on the risks of disease in the population in question. At an individual patient level, the economic value of MRCP is directly related to the prior assessment of risk of CBD stones and/or malignancies. A sensitivity analysis has been undertaken to investigate the impact of prior risk assessment based on ultrasound and LFT results on the decision to opt for MRCP.

Synthesis of results

The key clinical and economic results, together with uncertainty estimates (based upon 1000 Monte-Carlo simulations) are shown in *Table 13*.

Cost-effectiveness results have been displayed on the cost-effectiveness plane (*Figure 15*), which plots incremental costs and incremental quality-adjusted life-years (QALYs) in a 2D plane. The cost-effectiveness plane from 1000 samples shows that the uncertainty in the cost difference between MRCP and ERCP is much larger than the uncertainty in the QALY difference. This result is not surprising: with a similar sensitivity and specificity to ERCP for the most common biliary tree disorders, and despite all of its recognised advantages over ERCP in terms of morbidity and mortality, the main criticism of this test has been that it may only add further to the cost of the diagnostic work-up in patients who need therapeutic intervention. This is especially true in the case of patients with CBD stones (see the opening section to this chapter).

As shown in *Table 13*, the probability of avoiding unnecessary diagnostic ERCP, that is, the probability of a true-negative MRCP, is estimated at 31% (95% CI 20 to 40%). These patients could avoid the unnecessary risk of complications and death associated with diagnostic ERCP. Furthermore, substantial cost saving would be gained: the overall expected cost saving associated with MRCP is £149 (£325 to –£15) and the overall expected QALY gain is estimated at 0.011 (0.000 to 0.030).

The probability that MRCP is cost saving is estimated at approximately 96.5%, with an expected cost saving of £149 (£325 to –£15). From this result, one can infer that the cost savings in terms of avoided unnecessary diagnostic ERCP, associated complications and deaths can compensate for the added diagnostic costs in those patients who need therapeutic intervention.

Table 14 presents the key clinical and economic results for populations at lower risk of CBD stones or strictures based on the results of ultrasound and

TABLE 13 *Key economic and clinical results*

	Mean	95%	
		Lower	Upper
Key clinical results			
Probability of true-negative MRCP (i.e. avoiding unnecessary diagnostic ERCP)	31%	20%	41%
Probability of true-positive MRCP CBD stones (i.e. necessary therapeutic ERCP)	34%	27%	42%
Probability of death diagnostic ERCP	0.1%	0.1%	0.1%
Key economic results MRCP vs ERCP			
Incremental QALYs	0.012	0.002	0.028
Incremental costs	–£163	–£340	£7
Incremental net benefit (threshold of £20,000 per QALY)	£400	£159	£755
Cost-effectiveness MRCP vs ERCP	Dominant	Dominant	£259.23
Probability of cost saving	0.970	–	–
Probability of incremental QALYs positive	0.993	0.002	0.028
Probability of cost-effectiveness better than £20,000 per QALY	1.000	–	–

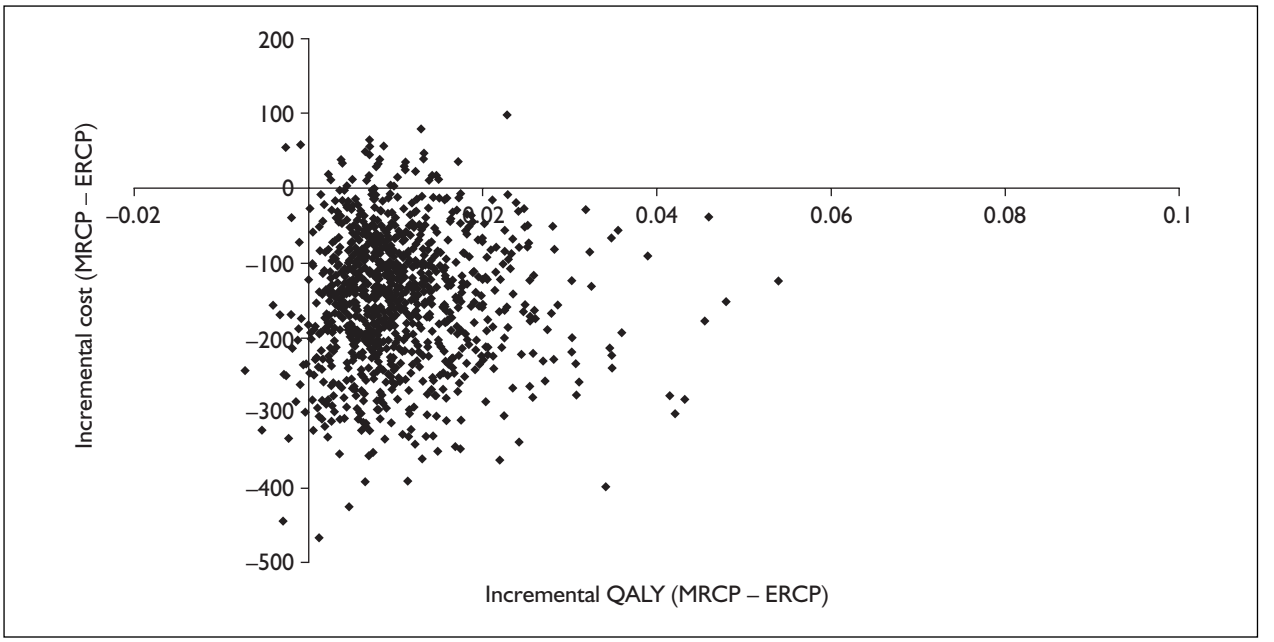


FIGURE 15 *Cost-effectiveness plane for MRCP versus diagnostic ERCP*

LFTs according to the classifications in the work by Everett and colleagues (unpublished). *Figure 17* presents the estimated cost savings from MRCP over a range of risks of CBD stones. It should be noted that these results assume that the risks of malignant and benign strictures are held constant at the values used in the baseline model.

Potential methodological strengths and limitations of the economic analysis

Strengths

This model used data from all published sources identified in the systematic review undertaken to compare sensitivity and specificity of both technologies, with diagnostic ERCP as a comparator. Additional searches were conducted to identify utilities related to biliary tree malignant neoplasms and costs of MRI technology. Data were cross-checked with clinical judgement and local hospital data where available. Literature recommended by clinicians in the field was read and analysed.

The basic tree structure and its main assumptions were discussed and checked by experts in the main disciplines related to biliary tree disorders and upper digestive organs in general: a consultant gastroenterologist, two consultant radiologists and a consultant biliary pancreatic surgeon.

TABLE 14 *Economic results with different probabilities of CBD stones or strictures associated with ultrasound and LFT results*[a]

	Ultrasound normal, LFTs abnormal	Ultrasound and LFTs abnormal	Ultrasound abnormal, LFTs abnormal
Probability of CBD stone or stricture	21%	32%	37%
Key clinical results			
Probability of true-negative MRCP (i.e. avoiding unnecessary diagnostic ERCP)	45%	34%	30%
Probability of true-positive MRCP CBD stones (i.e. necessary therapeutic ERCP)	19%	30%	34%
Key economic results MRCP vs ERCP			
Incremental QALYs	0.014	0.011	0.011
Incremental costs	–£250	–£185	–£149
Incremental net benefit (threshold of £20,000 per QALY)	£4524	£218	£364
Cost-effectiveness MRCP vs ERCP	Dominant	Dominant	£259.23
Probability of cost saving	0.991	0.980	0.965

[a] Estimations based on Everett *et al.* (Everett S, Hamlin J, Beckett C, Bzeizi K. MRCP – an important investigation in patients at low risk of pancretico-biliary disease. Conference abstract, UGW, 2002, unpublished).

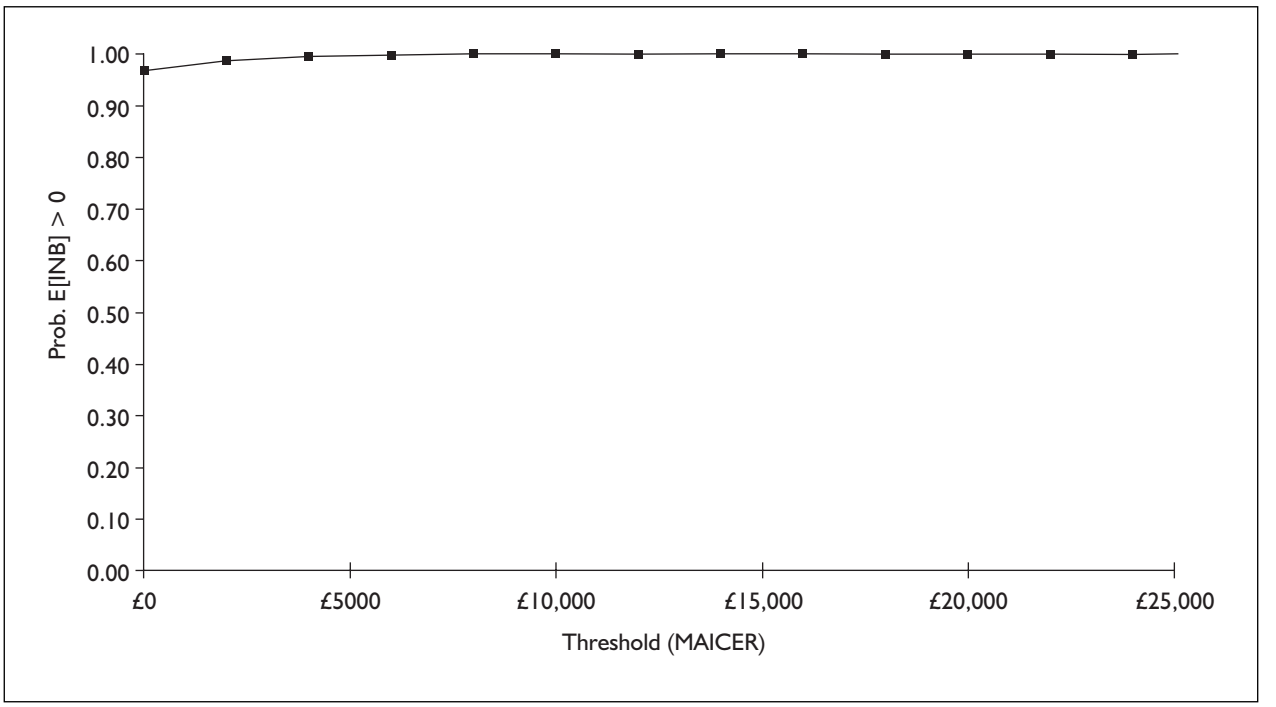


FIGURE 16 *Cost-effectiveness acceptability curve for MRCP. (MAICER, maximum acceptable incremental cost-effectiveness ratio.)*

Potential weaknesses

Missing information and unknown parameters

Many of the weaknesses in the technology assessment relate to the poor design of studies available, in particular on diagnostic test characteristics for final clinical outcomes and impact on clinical practice. Although these are primarily of clinical interest these impacts were only assessed within the decision analytical economic model. The clinical systematic review focused separately on the test characteristics for different disease types; although no significant differences were identified (sensitivities and specificity overlap for the different diseases), minor differences were found that were consistent with clinical judgement. It would, therefore, be preferable to model separately the test sensitivity and specificity for CBD stones and strictures. However, owing to the poor design of the studies, there is insufficient information to incorporate this separately within

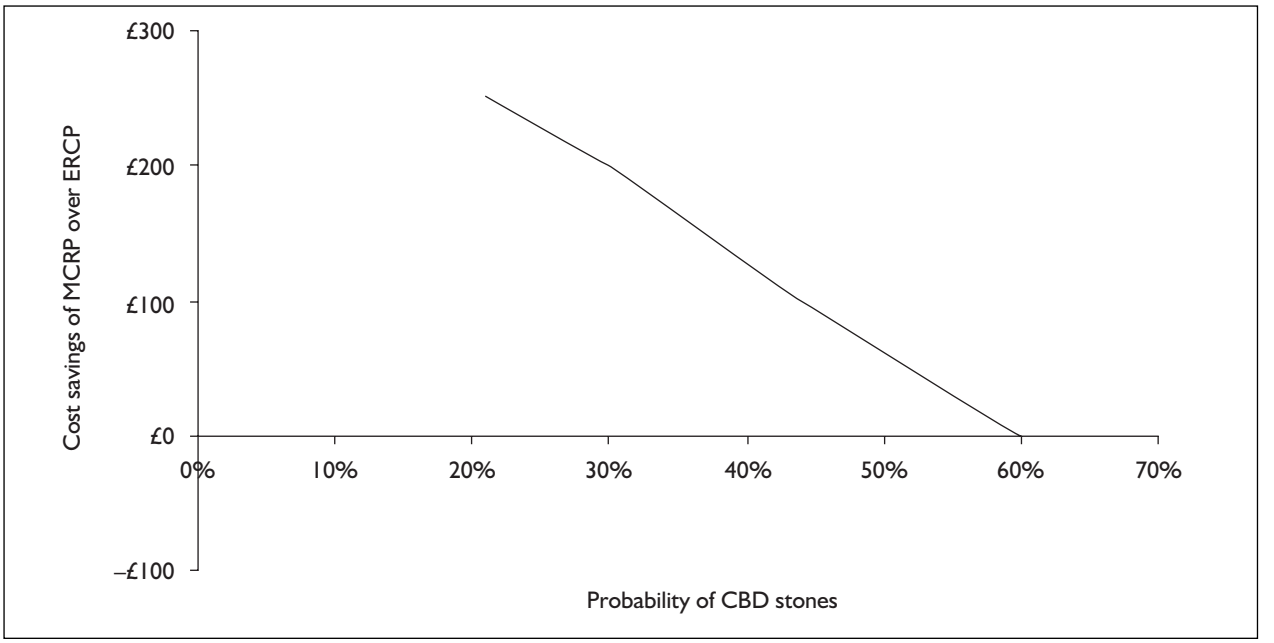


FIGURE 17 *Cost savings from MRCP for different risks of CBD stones*

the model. The model, therefore, uses the systematic review results for the most common disorder, CBD stones. The results for malignancies are prone to bias.

Ideally, the decision analytical model would use an ROC curve analysis of sensitivity and specificity to capture the impact of variation in diagnostic thresholds. Sensitivity and specificities should be handled similarly. Owing to the shortcomings in the design and/or reporting of the studies this is not captured fully in the model.

Where standard deviations or confidence intervals were not given, the uncertainty surrounding the medians we estimated based on the minimum and maximum range, approximated as a 99% confidence interval.

The impact of the diagnostic technology on a wide range of types of malignancy made difficult the identification of appropriate utilities for the purpose of the modelling.

Some parameters (e.g. proportion of patients with malignant strictures who undergo palliative treatment) proved difficult to estimate based on a review of the available literature, so clinical judgement and local data were the only feasible alternatives.

Limitations of the model

In some cases, incomplete imaging may create confusion regarding ductal anatomy or disease, and repeat MRCP can help to avoid pitfalls in interpretation. However, for the sake of simplification, neither the possibility of pitfalls in MRCP interpretation nor the option of repeated MRCP was modelled. For the same reason, repeated diagnostic ERCP after cannulation failure was not modelled.

Conclusions on the economics of diagnostic MRCP versus ERCP

The estimated clinical and economic impacts of diagnostic MRCP versus diagnostic ERCP are very favourable. The baseline estimate is that MRCP would both be cost saving and result in improved quality of life outcomes compared with diagnostic ERCP. The uncertainty analysis, investigating the impact of parametric uncertainty within the model, indicates that this result is robust. It should be noted, however, that there are marked uncertainties in the structure and assumptions within the decision analytical model that are not captured within this parametric uncertainty analysis. The results presented in this assessment will thus overstate the robustness of the economic outcomes for MRCP.

Chapter 5

Factors relevant to the NHS

ERCP is often associated with significant morbidity and mortality.[1] Little information on adverse effects was provided in the studies, with only eight studies providing any data on adverse effects associated with ERCP. However, reports in the literature show diagnostic ERCP to have a complication rate of 5–6% and a mortality rate ranging from 0.01%[1] to 0.089%.[27] Therapeutic ERCP is reported to have a complication rate of 4–10%, although some authors put the rate as high as > 20%,[28] and a mortality rate ranging from 0.07%[1] to 0.3%.[91] If patients receive diagnostic ERCP when MRCP may have been more appropriate, legal issues may become important if complications arise from this unnecessary invasive procedure. This fact may be affecting the current provision of MRCP. In reality, following the British Society of Gastroenterology Working Party Report 2001,[92] it seems that the pattern of provision of ERCP is changing, with the provision moving away from surgeons and radiologists, and towards medical gastroenterologists.

The potential sources of economic benefit for MRCP compared with diagnostic ERCP are important but highly dependent on access to and waiting lists for adequate MRI technology at hospital level. Furthermore, the potential economic benefits of MRCP are affected by diagnostic ERCP operator ability and skills. However, MRCP is also a diagnostic technology highly dependent on skilful interpretation.

There has been a substantial increase in the workload of departments of clinical radiology over the past few years. Department of Health figures demonstrate an increase of 7.4% between 1996 and 1998. This overall rise in workload has been compounded by the increased complexity of the investigations and the increase in interventional work that has been required of departments of clinical radiology. During the same period, a large number of radiology posts have been advertised where an appointment has not been possible because of a lack of applicants (in 1999 this meant that over 40% of advertised consultant posts were not filled at the first attempt). The benchmarking figures produced by the RCR demonstrate that the individual consultant's workload is substantially higher than the RCR 1993 recommendations of 12,500 examinations per radiologist.[93]

In short, even in cases where MRCP is deemed to be the most appropriate diagnostic technique to undertake, it may not be possible to receive it. Some hospitals in the UK may not have the necessary MRI scanner and there may not be sufficient time set aside for MRCP investigations even in hospitals in possession of the appropriate scanners.

Taking into account the above infrastructure and professional limitations, protocols are needed to determine which patients are most suitable for MRCP. To present some illustrative figures: the utilisation rate of MRCP over all MRI scans carried out in the unit of radiology of the Royal Hallamshire Hospital, Sheffield, during the period April 2001 to April 2002 was 5.42%, in comparison with 41% for spine lesions, 9% for knee, 8% for brain and 4% for pelvis, among others.

This is where the real opportunity cost of performing MRCP on a routine basis could be identified, estimating MRI waiting lists by severity and type of condition and reinterpreting priorities. The elderly may be one group that may particularly benefit from MRCP, as invasive procedures are often avoided owing to frailty. This kind of estimation is well beyond the objective of this report.

Chapter 6
Discussion

Main results: clinical effectiveness

The median sensitivity (n = 13 studies) for choledocolithiasis was 93% (range 81–100%) and specificity 94% (range 83–99%). The median likelihood ratio for a positive value was 15.75 and for a negative value was 0.08. For malignancy, reported sensitivities were somewhat lower, ranging from 81 to 86%, and specificities ranged from 92 to 100%, with positive likelihood ratios ranging from 10.12 to 48 and negative likelihood ratios ranging from 0.15 to 0.21.

In the 28 studies in this review one positive likelihood ratio was less than 5[65] and four negative likelihood ratios were greater than 0.2.[57,67,77,80] No studies reported any adverse effects associated with MRCP, although six studies reported adverse effects associated with ERCP and two studies reported no adverse effects associated with ERCP. Twenty studies reported no information regarding adverse effects.

Main results: cost-effectiveness

For the general population with a probability of CBD stones of 37%, the probability of avoiding unnecessary diagnostic ERCP, that is, the probability of a true-negative MRCP, is estimated at 30% (95% CI 20% to 40%). These patients could avoid the unnecessary risk of complications and death associated with diagnostic ERCP. Furthermore, substantial cost saving would be gained: the overall expected cost saving associated with MRCP is £149 (£325 to –£15) and the overall expected QALY gain is estimated at 0.011 (0.000 to 0.030). It should be noted that uncertainties in the structural assumptions within the economic model are not captured within this parametric uncertainty analysis.

For populations with a lower risk of CBD stones the economics are further improved; for example, in a population with a 21% risk of CBD stones the estimated cost savings would be £250. For populations with a risk of CBD stones in the order of 60%, MRCP is approximately cost neutral when compared with ERCP.

Assumptions, limitations and uncertainties

The reporting in the studies was of moderate quality, with little information regarding patient characteristics and why some patients did not receive both tests. ERCP has been assumed to be the gold standard, although this test is imperfect.[22] It was often unclear whether those studies comparing MRCP with ERCP incorporated other tests as well.

Information on adverse effects was not reported in 20 of the 28 studies, making it difficult to determine the extent to which they occur.

Seven studies reported MRCP results compared with final diagnosis, one of which did not provide adequate data for calculations. Three of these studies provided results for both ERCP and MRCP. The remaining 21 studies reported results comparing MRCP versus ERCP. Thus, different types of study are being compared in the analysis. Sensitivities and specificities for those studies comparing MRCP with final diagnosis did not differ to any extent from those comparing MRCP with ERCP. Final diagnosis was not always clearly defined, but usually included ERCP and other components such as histological results.

There are several problems associated with using summary ROC curves. Although the production of a summary ROC curve allows the computation of a summary estimate of diagnostic performance, the results cannot be directly applied to clinical practice.[49] Many important aspects of study design were not provided in the studies and the standards of reporting were poor. There is little information as to what impact publication bias has on the results as there is no equivalent to the funnel plot for studies of diagnostic accuracy. The need to summarise information with a summary ROC technique, owing to variability and interdependence between the observed sensitivities and specificities, can be considered to indicate a problem with the application of a diagnostic technology. This is especially the case when an ROC-like relationship is observed for a test that purports not to have explicit variation in cut-points. Although the

summary ROC method allows for this variation, it does not attempt to characterise or explain it, so that the meta-analysis fails to provide information that will assist an operator in using the technology in the most accurate manner.[49]

Recent methodological research[94] has recommended that value of information approaches to analysing uncertainty should be used wherever possible in identifying research requirements in health technology assessment. This technique, however, only captures parametric uncertainty within a model, and caution should be exercised where there is marked uncertainty in the underlying structural assumptions. A value of information analysis has therefore not been presented and the further research requirements are based primarily on addressing the structural uncertainty within the assessment.

Need for further research

The following were identified as areas where further research is needed.

- Good quality studies are needed comparing MRCP and diagnostic ERCP to final diagnosis, stating inclusion/exclusion criteria and relevant patient characteristics. This would help to overcome some of the shortcomings of comparisons with diagnostic ERCP.
- Studies are needed comparing MRCP with diagnostic ERCP for the full range of target conditions, in particular differentiation of benign and malignant strictures and the impact on management and outcome.
- More research is needed in the area of patient satisfaction and ways to reduce problems with claustrophobia and make MRCP more acceptable to patients.
- Protocols, assessing prior risk, are needed to help to identify which patients with which suspected conditions would most benefit from MRCP and which would benefit from ERCP.
- To understand the real opportunity costs associated with MRCP, studies are needed to assess the relative need and urgency of patient access to MRI services.
- As the development of MRCP (a non-invasive test) may result in an increase in requests over what would be expected for ERCP (an invasive test), research is needed to determine how this will affect availability and potential cost savings.

Chapter 7
Conclusions

There is some evidence that MRCP is an accurate investigation in comparison to diagnostic ERCP. The quality of the studies was moderate. As MRCP provides diagnostic information only, there will always be cases where diagnostic ERCP is the preferred method as treatment can follow immediately.

The limited evidence on patient satisfaction showed that patients preferred MRCP to diagnostic ERCP; however, some patients had problems with MRCP, owing to claustrophobia and noise.

Many of the weaknesses in the economic analysis relate to the interpretation of the available information on diagnostic test characteristics for final clinical outcomes and impact on therapeutic interventions. Although these final outcomes are primarily of clinical interest, their impact can only been assessed within the decision analytical model presented within the economic section of this assessment.

The estimated clinical and economic impacts of diagnostic MRCP versus diagnostic ERCP are very favourable. The baseline estimate is that MRCP would both be cost saving and result in improved quality of life outcomes compared with diagnostic ERCP. The uncertainty analysis, investigating the impact of parametric uncertainty within the model, indicates that this result is robust. It should be noted, however, that there are marked uncertainties in the structure and assumptions within the decision analytical model that are not captured within this parametric uncertainty analysis. The results presented in this assessment will thus overstate the robustness of the economic outcomes for MRCP. The economic model indicated that MRCP remains potentially cost saving in populations with relatively high risks of CBD stones.

Acknowledgements

Andrea Shippam provided secretarial support. Catherine Beverley provided advice on the literature searching. Mr WEG Thomas (Consultant Biliary Pancreatic Surgeon and Clinical Director of Surgery for Sheffield Teaching Hospitals) and Dr Conrad Beckett (Consultant Gastroenterologist, Bradford Royal Infirmary) provided clinical advice. Dr MB Sheridan (Consultant Radiologist and Lead Clinician for Radiology Leeds East, Department of Clinical Radiology, St James's University Hospital, Leeds), Dr Jerry Healy (Consultant Radiologist, Department of Radiology, Chelsea and Westminster Hospital, London), Dr Karl P Claxton (Senior Lecturer, Centre for Health Economics, University of York) and Dr Marie Westwood (Reviewer, CRD, University of York) peer reviewed the report.

All responsibility for the contents of the report remains the authors.

Contributions of authors

Helen Bouchier undertook the electronic literature searches. Eva Kaltenthaler carried out the review of clinical effectiveness. Yolanda Bravo and Jim Chilcott carried out the economic analysis. Steven Thomas and Tony Blakeborough provided clinical advice.

About ScHARR

The School of Health and Related Research (ScHARR) is one of the four Schools that comprise the Faculty of Medicine at the University of Sheffield. ScHARR brings together a wide range of medical- and health-related disciplines including public health, general practice, mental health, epidemiology, health economics, management sciences, medical statistics, operational research and information science. It includes the Sheffield unit of the Trent Institute for Health Services Research, which is funded by NHS R&D to facilitate high-quality health services research and capacity development.

The ScHARR Technology Assessment Group (ScHARR-TAG) synthesises research on the effectiveness and cost-effectiveness of healthcare interventions for the NHS R&D Health Technology Assessment Programme on behalf of a range of policy makers, including the National Institute of Clinical Excellence. ScHARR-TAG is part of a wider collaboration of six units from other regions. The other units are: Southampton Health Technology Assessment Centre (SHTAC), University of Southampton; Aberdeen Health Technology Assessment Group (Aberdeen HTA Group), University of Aberdeen; Liverpool Reviews & Implementation Group (LRiG), University of Liverpool; Peninsular Technology Assessment Group (PenTAG), University of Exeter; NHS Centre for Reviews and Dissemination, University of York; and West Midlands Health Technology Assessment Collaboration (WMHTAC), University of Birmingham.

References

1. Misra SP, Dwivedi M. Complications of endoscopic retrograde cholangiopancreatography and endoscopic sphincterotomy: diagnosis, management and prevention. *Natl Med J India* 2002;**15**:27–31.
2. Medlineplus Medical Encyclopedia. Biliary Obstruction. MEDLINE 2003. www.nlm.nih.gov/medlineplus/ency/article/000263.htm
3. Kim JH, Kim MJ, Park SI, Chung JJ, Song S, Kim KS, *et al*. MR cholangiography in symptomatic gallstones: diagnostic accuracy according to clinical risk group. *Radiology* 2002;**224**:410–16.
4. Siegel JH, Kasmin FE. Biliary tract diseases in the elderly: management and outcomes. *Gut* 1997; **41**:433–5.
5. Vitellas KM, Keogan MT, Freed KS, Enns RA, Spritzer CE, Baillie JM, Nelson RC. Radiologic manifestations of sclerosing cholangitis with emphasis on MR cholangiopancreatography [review]. *Radiographics* 2000;**20**:959–75.
6. Textor HJ, Flacke S, Pauleit D, Keller E, Neubrand M, Terjung B, *et al*. Three-dimensional magnetic resonance cholangiopancreatography with respiratory triggering in the diagnosis of primary sclerosing cholangitis: comparison with endoscopic retrograde cholangiography. *Endoscopy* 2002;**34**:984–90.
7. Kalloo AN, Kantsevoy SV. Gallstones and biliary diseases. *Primary Care Clinics in Office Practice* 2001;**28**:591–606.
8. Diagnosis and treatment of common bile duct stones (CBDS). Results of a consensus development conference. Scientific Committee of the European Association for Endoscopic Surgery (E.A.E.S.). *Surg Endosc* 1998;**12**:856–64.
9. RCGP, OPCS, and DHSS Morbidity Statistics from General Practice. Fourth national study 1991–1992. Series MB5 No. 3; 1995. London: Office of Population, Censuses and Surveys, HMSO.
10. Mehta SN, Reinhold C, Barkun AN. Magnetic resonance cholangiopancreatography. *Gastrointest Endosc Clin North Am* 1997;**7**:247–70.
11. Anonymous National Statistics (England and Wales): Mortality Statistics Cause. National Statistics Series DH2, No. 26. London: Office of Population, Censuses and Surveys, HMSO.
12. Weaver SA, Stace, BSF, Hayward SJ, Taylor GJ, Rooney NI, Robertson DAF. Endoscopic palliation and survival in malignant biliary obstruction. *Dig Dis Sci* 2001;**46**:2147–53.
13. Doglietto GB, Alfieri S, Pacelli F, Mutignani M, Costamagna G, Carriero C, *et al*. Extrahepatic bile duct carcinoma: a western experience with 118 consecutive patients. *Hepato-Gastroenterology* 2000;**47**:349–54.
14. Hintze RE, Abou-Rebyeh H, Adler A, Veltzke-Schlieker W, Felix R, Wiedenmann B. Magnetic resonance cholangiopancreatography-guided unilateral endoscopic stent placement for Klatskin tumors. *Gastrointest Endosc* 2001;**53**:40–6.
15. Kim PN, Outwater EK, Mitchell DG. Mirizzi syndrome: evaluation by MRI imaging. *Am J Gastroenterol* 1999;**94**:2546–50.
16. Cancer Statistics Registrations 1995–1997 England. National Statistics Series, Series MB1, No. 28. London: The Stationery Office; 2001.
17. Baron TH, Fleischer DE. Past, present and future of endoscopic retrograde cholangiopancreatography: perspectives on the National Institutes of Health Consensus Conference. *Mayo Clin Proc* 2002;**77**:407–12.
18. Ahrendt SA, Cameron JL, Pitt HA. Current management of patients with perihilar cholangiocarcinoma [review]. *Adv Surg* 1996;**30**:427–52.
19. Tanner AR, Dwarakanath AD, Tait NP. The potential impact of high-quality MRI of the biliary tree on ERCP workload. *Eur J Gastroenterol Hepatology* 2000;**12**:773–6.
20. Sahai AV, Devonshire D, Yeoh KG. The decision-making value of magnetic resonance cholangiopancreatography in patients seen in a referral center with suspected biliary and pancreatic disease. *Am J Gastroenterol* 2001; **96**:207–80.
21. Demartines N, Eisne, L, Schnabel K, Fried R, Zuber M, Harder F. Evaluation of magnetic resonance cholangiography in the management of bile duct stones. *Arch Surg* 2000;**135**:148–52.
22. Sheridan MB. Endoscopic retrograde cholangiopancreatography should no longer be used as a diagnostic test: the case in favour. *Dig Liver Dis* 2002;**34**:370–4.
23. Farrell RJ, Noonan N, Mahmud N, Morrin MM, Kelleher D, Keeling PW. Potential impact of magnetic resonance cholangiopancreatography on endoscopic retrograde cholangiopancreatography workload and complication rate in patients referred because of abdominal pain. *Endoscopy* 2001;**33**:668–75.

24. Ponchon T, Pilleul F. Diagnostic ERCP. *Endoscopy* 2002;**34**:29–42.

25. Cotton PB. Endoscopic retrograde cholangiopancreatography and laparoscopic cholecystectomy. *Am J Surg* 1993;**165**:474–8.

26. Adamek HE, Weitz M, Breer H, Jakobs R, Schilling D, Riemann JF. Value of magnetic-resonance cholangio-pancreatography (MRCP) after unsuccessful endoscopic-retrograde cholangio-pancreatography (ERCP). *Endoscopy* 1997;**29**:741–4.

27. Cotton PB, Jowell PS, Baillie J. Spectrum of complications after diagnostic ERCP and effects of comorbidities [abstract]. *Gastrointest Endosc* 1994;**40** abs P18.

28. Baillie J. Predicting and preventing post-ERCP pancreatitis. *Curr Gastroenterol Rep* 2002;**4**:112–19.

29. Freeman ML, Nelson DB, Sherman S, Haber GB, Herman ME, Dorsher PJ, *et al*. Complications of endoscopic biliary sphincterotomy. *N Engl J Med* 1996;**335**:909–18.

30. Department of Health. Department of Health Reference Costs 2002. London: Department of Health; 2003.

31. Cohen SA, Siegel JH, Kasmin FE. Complications of diagnostic and therapeutic ERCP. *Abdom Imaging* 1996;**21**:385–94.

32. Coakley FV, Qayyum A. Magnetic resonance cholangiopancreatography. *Gastrointest Endosc* 2002;**55**:S2–12.

33. Pavone P, Laghi A, Catalano C, Panebianco V, Fabiano S, Passariello R. MRI of the biliary and pancreatic ducts [review]. *Eur Radiol* 1999; **9**:1513–22.

34. Fulcher AS. MRCP and ERCP in the diagnosis of common bile duct stones. *Gastrointest Endosc* 2002;**56**:S178–82.

35. Watanabe Y, Dohke M, Ishimori T, Amoh Y, Oda K, Okumura A, *et al*. High-resolution MR cholangiopancreatography. *Crit Reviews in Diagnostic Imaging* 1998;**39**:115–258.

36. Takehara Y. Can MRCP replace ERCP? *J Magn Reson Imaging* 1998;8:517–34.

37. Pavone P, Laghi A, Panebianco V, Catalano C, Lobina L, Passariello R. MR cholangiography: techniques and clinical applications. *Eur Radiol* 1998;**8**:901–10.

38. Czako L, Endes J, Takacs T, Boda K, Lonovics J. Evaluation of pancreatic exocrine function by secretin-enhanced magnetic resonance cholangiopancreatography. *Pancreas* 2001;**23**:323–8.

39. Barkum AN. Common bile duct stones: magnetic resonance cholangiopancreatography vs. endoscopic retrograde cholangiopancreatography for detection. *J Gastrointest Surg* 2000;**4**:332–3.

40. Jalan R, Sargentoni J, Coutts GA, Bell JD, Rolles K, Burroughs AK, Taylor Robinson SD. Hepatic phosphorus-31 magnetic resonance spectroscopy in primary biliary cirrhosis and its relation to prognostic models. *Gut* 1996;**39**:141–6.

41. Lomas DJ, Gimson A. Magnetic resonance cholangiopancreatography [review]. *Hosp Med* 2000**;61**:395–9.

42. Catalano C, Pavone P, Laghi A, Panebianco V, Scipioni A, Fanelli F, *et al*. Pancreatic adenocarcinoma: combination of MR imaging, MR angiography and MR cholangiopancreatography for the diagnosis and assessment of resectability. *Eur Radiol* 1998;**8**:428–34.

43. Kalra M, Sahani D, Ahmad A, Saini S. The role of magnetic resonance cholangiopancreatography in patients with suspected biliary obstruction [review]. *Cur Gastroenterol Rep* 2002;**4**:160–6.

44. Urakami A, Majima T, Tsunoda T. A pitfall of MRCP for preoperative cholangiography: report of a case. *Am J Gastroenterol* 2000;**95**:1601–2.

45. Fulcher AS, Turner MA. Pitfalls of MR cholangiopancreatography (MRCP). *J Comput Assist Tomogr* 1998;**22**:845–50.

46. Irie H, Honda H, Kuroiwa T, Yoshimitsu K, Aibe H, Shinozaki K, Masuda K. Pitfalls in MR cholangiopancreatographic interpretation. *Radiographics* 2001;**21**:23–37.

47. Lijmer JG, Mol BW, Heisterkamp S, Bonsel GJ, Prins MH, vanderMeulen JH, Bossuyt PM. Empirical evidence of design-related bias in studies of diagnostic tests. *JAMA* 1999;**282**:1061–6.

48. Greenhalgh T. How to read a paper: papers that report diagnostic or screening tests. *BMJ* 1997; **315**:540–3.

49. Deeks JJ. Systematic reviews of evaluations of diagnostic and screening tests. Eggers M, Davey Smith G, Altman DG editors. In *Systematic reviews in health care: meta-analysis in context*. London: BMJ Publishing Group; 2001. pp. 248–82.

50. Wilson EB. Probable inference, the law of succession, and statistical inference. *J Am Stat Assoc* 1927;**22**:209–12.

51. Newcombe RG, Altman DG, Machin D, Bryant TN, Gardner MJ, editors. In *Statistics with confidence. Confidence intervals and statistical guidelines*. 2nd ed. London: BMJ Books; 2000.

52. Moses LE, Littenberg B, Shapiro D. Combining independent studies of a diagnostic test into a summary ROC curve: data-analytical approaches and some additional considerations. *Stat Med* 1993;**12**:1293–316.

53. Littenberg B, Moses LE. Estimating diagnostic accuracy from multiple conflicting reports: a new meta-analytical method. *Med Decis Making* 1993;**13**:313–21.

54. Menon K, Barkun AN, Romagnuolo J, Friedman G, Mehta SN, Reinhold C, Bret PM. Patient satisfaction after MRCP and ERCP. *Am J Gastroenterol* 2001;**96**:2646–50.

55. Adamek HE, Albert J, Weitz M, Breer H, Schilling D, Riemann JF. A prospective evaluation of magnetic resonance cholangiopancreatography in patients with suspected bile duct obstruction. *Gut* 1998;**43**:680–3.

56. Alcaraz MJ, De la Morena EJ, Polo A, Ramos A, De la Cal MA, Gonzalez Mandly A. A comparative study of magnetic resonance cholangiography and direct cholangiography. *Revista Espanola de Enfermedades Digestivas* 2000;**92**:427–38.

57. Angulo P, Pearce DH, Johnson CD, Henr, JJ, LaRusso NF, Petersen BT, Lindor KD. Magnetic resonance cholangiography in patients with biliary disease: its role in primary sclerosing cholangitis. *J Hepatol* 2000;**33**:520–7.

58. Barish MA, Yucel EK, Soto JA, Chuttani R, Ferrucci JT. MR cholangiopancreatography: efficacy of three-dimensional turbo spin-echo technique. *AJR Am J Roentgenol* 1995;**165**:295–300.

59. Calvo MM, Bujanda L, Calderon A, Heras I, Cabriada JL, Bernal A, *et al*. Role of magnetic resonance cholangiopancreatography in patients with suspected choledocholithiasis. *Mayo Clin Proc* 2002;**77**:422–8.

60. Chan YL, Chan AC, Lam WW, Lee DW, Chung SS, Sung, JJ, *et al*. Choledocholithiasis: comparison of MR cholangiography and endoscopic retrograde cholangiography. *Radiology* 1996;**200**:85–9.

61. Dwerryhouse SJ, Brown E, Vipond MN. Prospective evaluation of magnetic resonance cholangiography to detect common bile duct stones before laparoscopic cholecystectomy. *Br J Surg* 1998;**85**:1364–6.

62. Feldman DR, Kulling DP, Kay CL, Cole DJ, Cunningham JT, Hawes RH, *et al*. Magnetic resonance cholangiopancreatography: a novel approach to the evaluation of suspected pancreaticobiliary neoplasms. *Ann Surg Oncol* 1997;**4**:634–8.

63. Guibaud L, Bret PM, Reinhold C, Atri M, Barkun AN. Bile duct obstruction and choledocholithiasis: diagnosis with MR cholangiography. *Radiology* 1995;**197**:109–15.

64. Hintze RE, Adler A, Veltzke W, Abou-Rebyeh H, Hammerstingl R, Vogl T, Felix R. Clinical significance of magnetic resonance cholangiopancreatography (MRCP) compared to endoscopic retrograde cholangiopancreatography (ERCP). *Endoscopy* 1997;**29**:182–7.

65. Holzknecht N, Gauger J, Sackmann M, Thoeni RF, Schurig J, Holl J, *et al*. Breath-hold MR cholangiography with snapshot techniques: prospective comparison with endoscopic retrograde cholangiography. *Radiology* 1998;**206**:657–64.

66. Laokpessi A, Bouillet P, Sautereau D, Cessot F, Desport JC, Le Sidaner A, Pillegand B. Value of magnetic resonance cholangiography in the preoperative diagnosis of common bile duct stones. *Am J Gastroenterol* 2001;**96**:2354–9.

67. Lee MG, Lee HJ, Kim MH, Kang EM, Kim YH, Lee SG, *et al*. Extrahepatic biliary diseases: 3D MR cholangiopancreatography compared with endoscopic retrograde cholangiopancreatography. *Radiology* 1997;**202**:663–9.

68. Lomanto D, Pavone P, Laghi A, Panebianco V, Mazzocchi P, Fiocca F, *et al*. Magnetic resonance-cholangiopancreatography in the diagnosis of biliopancreatic diseases. *Am J Surg* 1997; **174**:33–8.

69. Lomas DJ, Bearcroft PW, Gimson AE. MR cholangiopancreatography: prospective comparison of a breath-hold 2D projection technique with diagnostic ERCP. *Eur Radiol* 1999;**9**:1411–17.

70. Macaulay SE, Schulte SJ, Sekijima JH, Obregon RG, Simon HE, Rohrmann Jr CA, *et al*. Evaluation of a non-breath-hold MR cholangiography technique. *Radiology* 1995;**196**:1–232.

71. Regan F, Fradin J, Khazan R, Bohlman M, Magnuson T. Choledocholithiasis: evluation with MR cholangiography. *AJR Am J Roentgenol* 1996;**167**:1441–5.

72. Reinhold C, Taourel P, Bret PM, Cortas GA, Mehta SN, Barkun AN, *et al*. Choledocholithiasis: evaluation of MR cholangiography for diagnosis. *Radiology* 1998;**209**:435–42.

73. Soto JA, Barish MA, Yucel EK, Siegenberg D, Ferrucci JT, Chuttani R. Magnetic resonance cholangiography: comparison with endoscopic retrograde cholangiopancreatography. *Gastroenterology* 1996;**110**:589–97.

74. Soto JA, Barish MA, Alvarez O, Medina S. Detection of choledocholithiasis with MR cholangiography: comparison of three-dimensional fast spin-echo and single- and multisection half-Fourier rapid acquisition with relaxation enhancement sequences. *Radiology* 2000;**215**:737–45.

75. Soto JA, Alvarez O, Munera F, Velez SM, Valencia J, Ramirez N. Diagnosing bile duct stones: comparison of unenhanced helical CT, oral contrast-enhanced CT cholangiography, and MR cholangiography. *AJR Am J Roentgenol* 2000; **175**:1127–34.

76. Stiris MG, Tennoe B, Aadland E, Lunde OC. MR cholangiopancreaticography and endoscopic retrograde cholangiopancreaticography in patients with suspected common bile duct stones. *Acta Radiol* 2000;**41**:269–72.

77. Sugiyama M, Baba M, Atomi Y, Hanaoka H, Mizutani Y, Hachiya J. Diagnosis of anomalous

pancreaticobiliary junction: value of magnetic resonance cholangiopancreatography. *Surgery* 1998;**123**:391–7.

78. Taylor AC, Little AF., Hennessy OF, Banting SW, Smith PJ, Desmond PV. Prospective assessment of magnetic resonance cholangiopancreatography for noninvasive imaging of the biliary tree. *Gastrointest Endosc* 2002;**55**:17–22.

79. Varghese JC, Liddell RP, Farrell MA, Murray FE, Osborne DH, Lee MJ. Diagnostic accuracy of magnetic resonance cholangiopancreatography and ultrasound compared with direct cholangiography in the detection of choledocholithiasis. *Clin Radiol* 2000;**55**:25–35.

80. Zidi SH, Prat F, Le Guen O, Rondeau Y, Rocher L, Fritsch J, *et al*. Use of magnetic resonance cholangiography in the diagnosis of choledocholithiasis: prospective comparison with a reference imaging method. *Gut* 1999;**44**:118–22.

81. Pavone P, Laghi A, Passariello R. MR cholangiopancreatography in malignant biliary obstruction. *Semin Ultrasound CT MR* 1999;**20**:317–23.

82. Blackbourne LH, Earnhardt RC, Sistrom CL, Abbitt P, Jones RS. The sensitivity and role of ultrasound in the evaluation of biliary obstruction [review]. *Am Surg* 1994;**60**:683–90.

83. Luman W, Cull A, Palmer KR. Quality of life in patients stented for malignant biliary obstructions. *Eur J Gastroenterol Hepatol* 1997;**9**:481–4.

84. Robins TN, Stiegmann GV, Durham JD, Johnson SI, Wachs ME, Serra AD, Kumpe DA. Management of major bile duct injury associated with laparoscopic cholecystectomy. *Surg Endosc* 2001;**15**:1381–5.

85. NHS Executive Guidance on Commissioning Cancer Services. Improving outcomes in upper gastro-intestinal cancers. The manual. 2001. London: NHS Executive Health Services Directorate.

86. Cook J, Richardson J, Street A. A cost utility analysis of treatment options for gallstone disease: methodological issues and results. *Health Econ* 1994;**3**:157–68.

87. Gregor J, Ponich T, Detsky A. Should ERCP be routine after an episode of 'idiopathic' pancreatitis? A cost–utility analysis. *Gastrointest Endosc* 1996;**44**:118–23.

88. Bass E, Pitt HA, Lillemoe K. Cost-effectiveness of laparoscopic cholecystectomy versus open cholecystectomy. *Am J Surg* 1993;**165**:466–71.

89. Luman W, Cull A, Palmer KR. Quality of life in patients stented for malignant biliary obstructions. *Eur J Gastroenterol Hepatol* 1997;**9**:481–4.

90. Dawson D, Street A. Reference costs and the pursuit of efficiency in the 'new' NHS. University of York, CHE Discussion Paper; 1998. p. 161.

91. Freeman ML. Toward improving outcomes of ERCP: endoscopist's experience: does it make a difference? *Gastrointest Endosc* 1998;**48**:96–102.

92. British Society of Gastroenterology Endoscopy Committee. Provision of endoscopy related services in district general hospitals. London: BSG Working Party Report; 2001.

93. Royal College of Radiologists. Two national audits of radiographic reporting services. London: RCR; 2000.

94. Chilcott JB, Brennan A, Booth A, Karnon J, Tappenden P. The role of modelling in prioritising and planning clinical trials. *Health Technol Assess* 2003;**7**:23.

95. Arslan A, Geitung JT, Viktil E, Abdelnoor M, Osnes M. Pancreaticobiliary diseases. Comparison of 2D single-shot turbo spin-echo MR cholangiopancreatography with endoscopic retrograde cholangiopancreatography. *Acta Radiol* 2000;**41**:621–6.

96. Bearcroft PW, Gimson A, Lomas DJ. Non-invasive cholangio-pancreatography by breath-hold magnetic resonance imaging: preliminary results. *Clin Radiol* 1997;**52**:345–50.

97. Becker CD, Grossholz M, Becke, M, Mentha G, de Peyer R, Terrier F. Choledocholithiasis and bile duct stenosis: diagnostic accuracy of MR cholangiopancreatography. *Radiology* 1997;**205**:523–30.

98. Boraschi P, Neri E, Braccini G, Gigoni R, Caramella D, Perri G, Bartolozzi C. Choledocolithiasis: diagnostic accuracy of MR cholangiopancreatography. Three-year experience. *Magn Reson Imaging* 1999;**17**:1245–53.

99. Fulcher AS, Turne, MA, Capps GW, Zfass AM, Baker KM. Half-Fourier RARE MR cholangiopancreatography: experience in 300 subjects. *Radiology* 1998;**207**:21–32.

100. Fulcher, AS, Turner MA, Franklin KJ, Shiffman ML, Sterling RK, Luketic VA, Sanyal AJ. Primary sclerosing cholangitis: evaluation with MR cholangiography – a case–control study. *Radiology* 2000;**215**:71–80.

101. Georgopoulos SK, Schwartz LH, Jarnagin WR, Gerdes H, Breite I, Fong Y, *et al*. Comparison of magnetic resonance and endoscopic retrograde cholangiopancreatography in malignant pancreaticobiliary obstruction. *Arch Surg* 1999;**134**:1002–7.

102. Hall-Craggs MA, Allen CM, Owens CM, Theis BA, Donald JJ, Paley M, *et al*. MR cholangiography: clinical evaluation in 40 cases. *Radiology* 1993;**189**:423–7.

103. Hochwald SN, Dobryansky MBA, Rofsky NM, Naik KS, Shamamian P, Coppa G, Marcus SG. Magnetic resonance cholangiopancreatography

accurately predicts the presence or absence of choledocholithiasis. *J Gastrointest Surg* 1998; **2**:573–9.

104. Irie H, Honda H, Jimi M, Yokohat, K, Chijiiwa K, Kuroiwa T, *et al*. Value of MR cholangiopancreatography in evaluating choledochal cysts. *AJR Am J Roentgenol* 1998; **171**:1381–5.

105. Irie H, Honda H, Tajima T, Kuroiwa T, Yoshimitsu K, Makisumi K, Masuda K. Optimal MR cholangiopancreatographic sequence and its clinical application. *Radiology* 1998;**206**:379–87.

106. Ishizaki Y, Wakayama T, Okada Y, Kobayashi T. Magnetic resonance cholangiography for evaluation of obstructive jaundice. *Am J Gastroenterol* 1993;**88**:2072–7.

107. Laghi A, Pavone P, Catalano C, Messina A, Panebianco V, Passariell, R. Choledocholithiasis: a definite role for MR cholangiography. *Radiology* 1996;**201**:353, abs 1222.

108. Liu TH, Consorti ET, Kawashima A, Ernst RD, Black CT, Greger PH Jr, *et al*. The efficacy of magnetic resonance cholangiography for the evaluation of patients with suspected choledocholithiasis before laparoscopic cholecystectomy. *Am J Surg* 1999;**178**:480–4.

109. Magnuson TH, Bender JS, Duncan MD, Ahrendt SA, Harmon JW, Regan F. Utility of magnetic resonance cholangiography in the evaluation of biliary obstruction. *J Am Coll Surg* 1999;**189**:63–71.

110. Matos C, Nicaise N, Deviere J, Cassart M, Metens T, Struyven J, Cremer M. Choledochal cysts: comparison of findings at MR cholangiopancreatography and endoscopic retrograde cholangiopancreatography in eight patients. *Radiology* 1998;**209**:443–8.

111. Mendler MH, Bouillet P, Sautereau D, Chaumerliac P, Cessot F, Le Sidaner A, Pillegand B. Value of MR cholangiography in the diagnosis of obstructive diseases of the biliary tree: a study of 58 cases. *Am J Gastroenterol* 1998;**93**:2482–90.

112. Miyazaki T, Yamashita Y, Tsuchigame T, Yamamoto H, Urata J, Takahashi M. MR cholangiopancreatography using HASTE (half-Fourier acquisition single-shot turbo spin-echo) sequences. *AJR Am J Roentgenol* 1996;**166**:1297–303.

113. Musella M, Barbalace G, Capparelli G, Carrano A, Castaldo P, Tamburrini O, Musella S. Magnetic resonance imaging in evaluation of the common bile duct. *Br J Surg* 1998;**85**:16–19.

114. Ng KK, Wan YL, Lui KW, Wong HF, Hung CF, Kong MS, Chiu CT. Three-dimensional magnetic resonance cholangiopancreatography for evaluation of obstructive jaundice. *J Formos Med Assoc* 1997;**96**:586–92.

115. Pavone P, Laghi A, Catalano C, Broglia L, Messina A, Scipioni A, *et al*. MR cholangiopancreatography (MRCP) at 0.5 T: technique optimisation and preliminary results. *Eur Radiol* 1996;**6**:147–52.

116. Pavone P, Laghi A, Catalano C, Broglia L, Fiocca F, Passariello R. Non-invasive evaluation of the biliary tree with magnetic resonance cholangiopancreatography: initial clinical experience. *Ital J Gastroenterol* 1996;**28**:63–9.

117. Pavone P, Laghi A, Catalano C, Broglia L, Panebianco V, Messina A, *et al*. MR cholangiography in the examination of patients with biliary-enteric anastomoses. *AJR Am J Roentgenol* 1997;**169**:807–11.

118. Regan F, Smith D, Khazan R, Bohlman M, Schultze-Haakh H, Campion J, Magnuson TH. MR cholangiography in biliary obstruction using half-Fourier acquisition. *J Comput Assist Tomogr* 1996;**20**:627–32.

119. Rösch T, Meining A, Fruhmorgen S, Zillinger C, Schusdziarra V, Hellerhoff K, *et al*. A prospective comparison of the diagnostic accuracy of ERCP, MRCP, CT, and EUS in biliary strictures. *Gastrointest Endosc* 2002;**55**:870–6.

120. Sarli L, Costi R, Gobbi S, Sansebastiano G, Roncoroni L. Asymptomatic bile duct stones: selection criteria for intravenous cholangiography and/or endoscopic retrograde cholangiography prior to laparoscopic cholecystectomy. *Eur J Gastroenterol Hepatol* 2000;**12**:1175–80.

121. Schwartz LH, Coakley FV, Sun Y, Blumgart LH, Fong Y, Panicek DM. Neoplastic pancreaticobiliary duct obstruction: evaluation with breath-hold MR cholangiopancreatography. *AJR Am J Roentgenol* 1998;**170**:1491–5.

122. Sugiyama M, Atomi Y, Hachiya J. Magnetic resonance cholangiography using half-Fourier acquisition for diagnosing choledocholithiasis. *Am J Gastroenterol* 1998;**93**:1886–90.

123. Taourel P, Bret PM, Reinhold C, Barkun AN, Atri M. Anatomic variants of the biliary tree: diagnosis with MR cholangiopancreatography. *Radiology* 1996;**199**:521–7.

124. Topal BV. The value of magnetic resonance cholangiopancreatography in predicting common bile duct stones in patients with gallstone disease. *Br J Surg* 2003;**90**:42–7.

125. Tripathi RP, Batra A, Kaushik S. Magnetic resonance cholangiopancreatography: evaluation in 150 patients. *Indian J Gastroenterol* 2002;**21**:105–9.

126. Varghese JC, Liddell RP, Farrell MA, Murray FE, Osborne H, Lee MJ. The diagnostic accuracy of magnetic resonance cholangiopancreatography and ultrasound compared with direct cholangiography in the detection of choledocholithiasis [comment]. [Published

erratum appears in *Clin Radiol* 2000;**55**:657.] *Clin Radiol* 1999;**54**:604–14.

127. Varghese JC, Farrell MA, Courtney G, Osborne H, Murray FE, Lee MJ. A prospective comparison of magnetic resonance cholangiopancreatography with endoscopic retrograde cholangiopancreatography in the evaluation of patients with suspected biliary tract disease. *Clin Radiol* 1999;**54**:513–20.

128. Vitellas KM, El Dieb A, Vaswani KK, Bennett WF, Tzalonikou M, Mabee C, *et al*. MR cholangiopancreatography in patients with primary sclerosing cholangitis: interobserver variability and comparison with endoscopic retrograde cholangiopancreatography. *AJR Am J Roentgenol* 2002;**179**:399–407.

129. Yamashita Y, Abe Y, Tang Y, Urata J, Sumi S, Takahashi M. In vitro and clinical studies of image acquisition in breath-hold MR cholangiopancreatography: single-shot projection technique versus multislice technique. *AJR Am J Roentgenol* 1997;**168**:1449–54.

130. Yeh TS, Jan YY, Tseng JH, Chiu CT, Chen TC, Hwang TL, Chen MF. Malignant perihilar biliary obstruction: magnetic resonance cholangiopancreatographic findings. *Am J Gastroenterol* 2000;**95**:432–40.

131. Zidi SH, Prat F, Le Guen O, Rondeau Y, Pelletier G. Performance characteristics of magnetic resonance cholangiography in the staging of malignant hilar strictures. *Gut* 2000;**46**:103–6.

Appendix 1

Search strategies

Electronic bibliographic databases searched

1. BIOSIS previews (the new online version of Biological Abstracts)
2. CCTR (Cochrane Controlled Trials Register)
3. CDSR (Cochrane Database of Systematic Reviews)
4. CINAHL
5. EMBASE
6. HEED (Health Economic Evaluations Database)
7. MEDLINE
8. NHS DARE (Database of Assessments of Reviews of Effectiveness)
9. NHS EED (Economic Evaluations Database)
10. NHS HTA
11. Pre-MEDLINE
12. Science Citation Index
13. Social Sciences Citation Index

Appendix 2

Other sources searched

1. AHRQ (Agency for Healthcare Research and Quality), USA
2. Bandolier
3. British Dietetic Association
   a. CCOHTA (Canadian Coordinating Office for Health Technology Assessment)
4. CenterWatch
5. CHE (Centre for Health Economics), York
6. *CliniWeb*
7. CMA (Canadian Medical Association) InfoBase
8. COIN (DoH)
9. Current Controlled Trials
10. Development and Evaluation Committee (Department of Health)
11. DES Reports (West Midlands Health Technology Assessment Collaboration)
12. DoH
13. eGuidelines
14. EMEA (The European Agency for the Evaluation of Medicinal Products)
15. Google
16. HSRU (Health Services Research Unit), Aberdeen
18. INAHTA (International Network of Agencies for Health Technology Assessment) Clearinghouse
19. Index to Theses (Sheffield University)
20. MDChoice
21. MeRec
22. MRC Trials Register
23. National Assembly for Wales
24. National Guidelines Clearinghouse
25. National Research Register (2002 Issue 2)
26. NCCHTA (National Co-ordinating Centre for Health Technology Assessment)
27. NHS CRD (Centre for Reviews and Dissemination), University of York
28. NeLH (National Electronic Library for Health)
29. New Zealand Health Technology Clearing House for Health Outcomes and Health Technology Assessment (NZHTA)
30. NICE (National Institute for Clinical Excellence)
31. OMNI
32. POINT (DoH)
33. RAND
34. ReFeR (Research Findings Register)
35. ScHARR Library catalogue
36. SIGN (Scottish Intercollegiate Guidelines Network)
37. TRIP (Turning Research into Practice) Database
38. TWGAP (Trent Institute Working Group on Acute Purchasing)
39. US FDA (Federal Food and Drug Administration)
40. WHO

Appendix 3

Search strategies used

BIOSIS Previews

1985–2003
SilverPlatter WebSPIRS
Search undertaken January 2003

#1 mri or mri scan* or mri imag*
#2 'nuclear-magnetic-resonance-imaging'
#3 #1 or #2
#4 biliary tract* or biliary tree* or biliary
#5 'hepatobiliary-system'
#6 #4 or #5
#7 #3 and #6

CDSR, CCTR and DARE

Ovid Online
Search undertaken January 2003

1 exp *magnetic resonance imaging/
2 mri.tw
3 magnetic resonance.tw
4 mrcp.tw
5 ((noninvasive$ or non-invasive$) adj3 (diagnos$ or imag$)).tw
6 or/1-5
7 bilary.tw
8 biliary.tw
9 exp *biliary tract/
10 exp *biliary tract diseases/
11 bile.ti
12 *bile/
13 gall bladder$.tw
14 cholestat$.tw
15 choledocholethias$.tw
16 cholangiopancreatography, endoscopic retrograde/
17 or/7-16
18 6 and 17

CINAHL

1982–2003
Ovid Online
Search undertaken January 2003

1 exp *magnetic resonance imaging//
2 mri.tw
3 magnetic resonance.tw
4 mrcp.tw
5 ((noninvasive$ or non-invasive$) adj3 (diagnos$ or imag$)).tw
6 or/1-5
7 bilary.tw
8 biliary.tw
9 exp *biliary tract/
10 exp *biliary tract diseases/
11 bile.ti
12 *bile/
13 gall bladder$.tw
14 cholestat$.tw
15 choledocholethias$.tw
16 cholangiopancreatography, endoscopic retrograde/
17 or/7-16
18 6 and 17

Citation Indexes (Science and Social Sciences)

1981–2003
Web of Science
Search undertaken January 2003

(Magnetic resonance imag* OR mri) AND biliary* AND (guideline* OR systematic review* OR trial* OR economic* OR pricing* OR cost*)

CRD databases (NHS DARE, EED, HTA)

CRD website: complete databases
Search undertaken January 2003

[(magnetic resonance imag OR mri) AND (bilary OR biliary)]/all fields

EMBASE

1980–2003
SilverPlatter WebSPIRS
Search undertaken January 2003

#1 mri
#2 'nuclear-magnetic-resonance-imaging'

#3 #1 or #2
#4 biliary tract* or biliary tree* or biliary
#5 'hepatobiliary-system'
#6 #4 or #5
#7 #3 and #6

HEED

CD ROM version
Search undertaken January 2003

Search terms

Biliary
Bilary
MRI
Magnetic resonance imag*

Fields searched

Quick search – All data

MEDLINE

1966–2003
Ovid Online
Search undertaken January 2003

1 exp *magnetic resonance imaging/
2 mri.tw
3 magnetic resonance.tw
4 mrcp.tw
5 ((noninvasive$ or non-invasive$) adj3 (diagnos$ or imag$)).tw
6 or/1-5
7 bilary.tw
8 biliary.tw
9 exp *biliary tract/
10 exp *biliary tract diseases/
11 bile.ti
12 *bile/
13 gall bladder$.tw
14 cholestat$.tw
15 choledocholethias$.tw
16 cholangiopancreatography, endoscopic retrograde/
17 or/7-16
18 6 and 17

Pre-MEDLINE

January 2003
Ovid Online
Search undertaken January 2003

1 mri.tw
2 magnetic resonance.tw
3 mrcp.tw
4 ((noninvasive$ or non-invasive$) adj3 (diagnos$ or imag$)).tw
5 or/1-4
6 bilary.tw
7 biliary.tw
8 bile.ti
9 gall bladder$.tw
10 cholestat$.tw
11 choledocholethias$.tw
12 or/6-11
13 5 and 12

Appendix 4

Methodological search filters used in Ovid MEDLINE

Guidelines

1 guideline.pt
2 practice guideline.pt
3 exp guidelines/
4 health planning guidelines/
5 or/1-4

Systematic reviews

1 meta-analysis/
2 exp review literature/
3 (meta-analy$ or meta analy$ or metaanaly$).tw
4 meta analysis.pt
5 review academic.pt
6 review literature.pt
7 letter.pt
8 review of reported cases.pt
9 historical article.pt
10 review multicase.pt
11 or/1-6
12 or/7-10
13 11 not 12

Clinical trials

1 Clinical.pt

Economic evaluations

1 economics/
2 exp "costs and cost analysis"/
3 economic value of life/
4 exp economics, hospital/
5 exp economics, medical/
6 economics, nursing/
7 economics, pharmaceutical/
8 exp models, economic/
9 exp "fees and charges"/
10 exp budgets/
11 ec.fs
12 cost$.ti
13 (economic$ or pharmacoeconomic$ or price$ or pricing).ti
14 or/1-13

Quality of life

1 exp quality of life/
2 quality of life.tw
3 life quality.tw
4 hql.tw
5 (sf 36 or sf36 or sf thirtysix or sf thirty six or short form 36 or short formthirty six or short form thirtysix or shortform 36).tw
6 qol.tw
7 (euroqol or eq5d or eq 5d).tw
8 qaly$.tw
9 quality adjusted life year$.tw
10 hye$.tw
11 health$ year$ equivalent$.tw
12 health utilit$.tw
13 hui.tw
14 quality of wellbeing$.tw
15 quality of well being.tw
16 qwb.tw
17 (qald$ or qale$ or qtime$).tw
18 or/1-17

Appendix 5

Excluded studies

Study	Reason for exclusion
Adamek *et al.*, 1997[26]	Comparison with failed ERCP
Arslan *et al.*, 2000[95]	Retrospective review
Bearcroft *et al.*, 1997[96]	Includes pancreatic duct abnormalities
Becker *et al.*, 1997[97]	Retrospective review
Boraschi *et al.*, 1999[98]	Multiple comparators, only subgroup had ERCP and almost half had no comparator at all
Fulcher *et al.*, 1998[99]	Multiple comparators, less than half had ERCP
Fulcher *et al.*, 2000[100]	Case–control design
Georgopoulos *et al.*, 1999[101]	Retrospective review
Hall-Craggs *et al.*, 1993[102]	Before 1995
Hochwald *et al.*, 1998[103]	Retrospective review
Irie *et al.*, 1998[104]	Retrospective review
Irie *et al.*, 1998[105]	Paper deals with diagnosing pancreatic abnormalities
Ishizaki *et al.*, 1993[106]	Before 1995
Laghi *et al.*, 1996[107]	Same data as Lomanto *et al.*[68]
Liu *et al.*, 1999[108]	MRCP results affected decision to proceed with ERCP
Magnuson *et al.*, 1999[109]	Unclear as to number of patients who had ERCP, multiple comparators
Matos *et al.*, 1998[110]	Paper dealt with pancreatitis
Mendler *et al.*, 1998[111]	Multiple comparators, less than half had ERCP
Miyazaki *et al.*, 1996[112]	Less than half had ERCP, main comparator was PTC
Musella *et al.*, 1998[113]	Patients separated into groups after MRCP, only one of which had ERCP. Small subset of patients ($n = 9$) had ERCP
Ng *et al.*, 1997[114]	Retrospective review
Pavone *et al.*, 1996[115]	Same data as Lomanto *et al.*[68]
Pavone *et al.*, 1996[116]	Same data as Lomanto *et al.*[68]
Pavone *et al.*, 1997[117]	Same data as Lomanto *et al.*[68]
Regan *et al.*, 1996[118]	Trial data repeated[71]
Rösch *et al.*, 2002[119]	Number of patients having ERCP is not stated separately from the ERCP/PTC group
Sarli *et al.*, 2000[120]	Case–control design
Schwartz *et al.*, 1998[121]	No data on ERCP reported
Sugiyama *et al.*, 1998[122]	No data comparing ERCP with MRCP
Taourel *et al.*, 1996[123]	Overlap with Reinhold *et al.*[72]
Topal *et al.*, 2003[124]	Retrospective review
Tripathi *et al.*, 2002[125]	Retrospective review
Varghese *et al.*, 1999[126]	Same data as Varghese *et al.*[79]
Varghese *et al.*, 1999[127]	Patient overlap with Varghese *et al.*[79]
Vitellas *et al.*, 2002[128]	Retrospective review
Yamashita *et al.*, 1997[129]	No results comparing MRCP and ERCP diagnosis are reported
Yeh *et al.*, 2000[130]	Retrospective review
Zidi *et al.*, 2000[131]	Patients referred for stenting rather than diagnosis

Appendix 6

Evidence tables

TABLE 15 *Study characteristics*

Study, country	Sample selection	Comparison (type of MRCP and reference tests used)	Description of patients and procedures; study period	Time between ERCP and MRCP
Adamek *et al.*, 1998[55]; Germany	Not reported	RARE and HASTE MRCP compared with ERCP	86 patients entered the study; 8 were excluded due to biliary–enteric anastomoses, of the remaining 78, 16 had unsatisfactory ERCP and 2 had unsatisfactory MRCP (claustrophobia), leaving 60 patients who had both January–December 1996	Not reported
Alcaraz *et al.*, 2000[56]; Spain	Not reported	T2-weighted HASTE and RARE MRCP compared with ERCP, PTC and surgery	81 patients had MRCP, 70 had ERCP, 7 had PTC and 4 had surgery October 1997–February 1998	Not reported
Angulo *et al.*, 2000[57]; USA	Not reported	FSE pulse sequence compared with ERCP and PTC	Initially 74; 1 did not receive MRCP owing to claustrophobia, 73 had MRCP, 68 had ERCP, 2 had PTC and 3 had neither Study period not stated	MRCP performed within 24 hours before the scheduled ERCP
Barish *et al.*, 1995[58]; USA	Random selection from referrals	3D TSE MRCP compared with ERCP and PTC	30 patients initially selected; 1 patient did not receive MRCP owing to the presence of ascitic fluid in the upper abdomen; 3 had PTC owing to failed ERCP, 8 of the 29 patients did not have ERCP or PTC Study period not reported	ERCP performed 8 hours after MRCP
Calvo *et al.*, 2002[59]; Spain	Not reported	Two HASTE sequences MRCP compared with ERCP	116 patients with suspected biliopancreatic pathology initially, of these 61 patients were selected with suspected choledocholithiasis, failure in 1 patient for ERCP November 1996–February 1998	MRCP within 72 hours before ERCP
Chan *et al.*, 1996[60]; Hong Kong	Consecutive sample	T2-weighted TSE sequence (non-breath-holding, fat-suppressed) MRCP compared with ERCP	47 had MRCP, 45 had ERCP (two failures) May–August 1995	ERCP within 5 hours after MRCP
Demartines *et al.*, 2000[21]; Switzerland	Not reported	3 acquisition techniques of MRCP used, including T2/T1 weighted, single-shot TSE and HASTE heavy sequence compared with ERCP (high-risk patients) or IOC (moderate-risk patients)	40 patients received ERCP and MRCP, and 30 received IOC and MRCP April 1997–September 1998	Not reported

continued

TABLE 15 *Study characteristics (cont'd)*

Study, country	Sample selection	Comparison (type of MRCP and reference tests used)	Description of patients and procedures; study period	Time between ERCP and MRCP
Dwerryhouse *et al.*, 1998[61]; UK	Not reported	T2-weighted TSE with non-breath-holding MRCP compared with ERCP and PTC	Initially 405 patients who underwent laparoscopic cholecystectomy; 278 had no known risk factors for CBD stones, 87 underwent early ERCP and were excluded. 40 patients with risk factors for CBD stones underwent MRCP. 2 patients had failed MRCP owing to claustrophobia, ERCP was unsuccessful in 4 patients, who then had perioperative cholangiography February 1996–January 1998	All patients underwent ERCP within 1 week after ERCP
Feldman *et al.*, 1997[62]; USA	Not reported	Fat-saturated heavily T2-weighted FSE MRCP compared with ERCP	20 patients had MRCP and 17 had ERCP Study period not reported	MRCP either before or after ERCP, but time between the two not reported
Guibaud *et al.*, 1995[63]; Canada	Consecutive	2D FSE MRCP compared with ERCP, PTC, T-tube cholangiography, surgery and autopsy	Initially 198 patients; 72 were excluded owing to no proof of bile duct obstruction (n = 42), unsuccessful ERCP (n = 12), unsuccessful MRCP owing to claustrophobia (n = 6), inadequate ERCP (n = 10) or MRCP (n = 2), leaving 126 patients September 1992–March 1993	Time between MRCP and final diagnosis < 6 hours in 105 cases, < 1 week in 15 cases and > 1 week in six cases
Hintze *et al.*, 1997[64]; Germany	Not reported	T2-weighted and fat-suppressed MRCP compared with ERCP	78 patients examined with both MRCP and ERCP; 1 patient excluded because of claustrophobia making MRCP impossible, and did not have ERCP owing to a malignant duodenal stenosis; of the 78 patients, 55 had examination of the biliary duct systems (the other 36 had examination of the pancreatic duct systems) September 1995–September 1996	ERCP within 24 hours after MRCP
Holzknecht *et al.*, 1998[65]; Germany	Consecutive	RARE and half-Fourier RARE MRCP compared with ERCP	66 patients were eligible, 2 were excluded because of pacemakers, 3 had failed ERCP after MRCP, leaving 61 patients who had both MRCP and ERCP June 1995–April 1996	MRCP performed before ERCP (patients were due to have ERCP within the next 2 days)

continued

TABLE 15 *Study characteristics (cont'd)*

Study, country	Sample selection	Comparison (type of MRCP and reference tests used)	Description of patients and procedures; study period	Time between ERCP and MRCP
Laokpessi *et al.*, 2001[66]; France	Consecutive	FSE and heavily T2-weighted single-shot FSE sequences with fat-suppression MRCP compared with ERCP or IOC	Initially 166 inpatients, but only 147 patients had MRCP; of these 101 had ERCP and 45 had IOC and cholecystectomy. Those in the group receiving ERCP had a past history of cholecystectomy or a high surgical or anaesthetic risk. 21 removed from study for refusal to sign protocol ($n = 3$), refusal to undergo MRCP ($n = 4$) or ERCP ($n = 7$), or excessive time between MRCP and final diagnosis ($n = 7$) November 1997–December 1999	Average time between MRCP and final diagnosis 10 hours (range 3–48 hours); if > 48 hours between MRCP and final diagnosis, patients were removed from the study
Lee *et al.*, 1997[67]; South Korea	Consecutive	3D steady-state free-precession MRCP compared with ERCP	71 patients; 25 were excluded (8 because ERCP was not performed, 15 who were evaluated for intrahepatic stones, 1 for peripheral type of intrahepatic cholangiocarcinoma, 1 suspected mucinous ductal ectasia of the pancreas), leaving 46 patients who had both MRCP and ERCP January–March 1995	33 patients had MRCP before ERCP, ranging from 6 hours to 5 days. The remaining 31 patients had ERCP first, ranging from 3 to 16 days
Lomanto *et al.*, 1997[68]; Italy	Not reported	T2-weighted TSE sequence MRCP compared with ERCP and PTC	136 patients referred for MRCP, 62 had MRCP for choledocholithiasis (the other 74 were: 48 for stenosis of the biliary tract, 15 with previous hepaticojejunostomy and choledochojejunostomy, and 11 with chronic pancreatitis), 60 of these patients had ERCP and 2 had PTC September 1994–October 1995	Not reported
Lomas *et al.*, 1999[69]; UK	Not reported	Hybrid four-shot RARE (FSE) sequence and single-shot half-Fourier RARE sequence compared with ERCP	76 referrals, 2 did not have MRCP (1 was obese and 1 was claustrophobic), 5 did not have ERCP (1 died, 1 refused and in 3 patients the operator was unable to cannulate the CBD), leaving 69 referrals in 66 patients 18-month period, dates not stated	MRCP took place first within 4 hours of ERCP
Macaulay, *et al.*, 1995[70]; USA	Sequential	T2-weighted TSE MRCP (non-breath-holding) compared with ERCP, PTC and IOC	28 patients initially had MRCP, 24 patients had 28 direct cholangiographic studies (21 had ERCP, 6 had PTC and 1 had IOC) Study period not reported	ERCP took place within 1–4 hours in 15 patients, 4 were within 5–7 days after MRCP, 1 was 11 days before and 1 was 109 days before MRCP, all PTC studies were within 2 days after MRCP and the 1 IOC preceded MRCP by 5 days

continued

TABLE 15 *Study characteristics (cont'd)*

Study, country	Sample selection	Comparison (type of MRCP and reference tests used)	Description of patients and procedures; study period	Time between ERCP and MRCP
Regan *et al.*, 1996[71]; USA	Not reported	HASTE MRCP compared with ERCP and sonography	26 patients; 2 had unsuccessful ERCP and 1 did not have MRCP owing to claustrophobia, leaving 23 patients	MRCP performed just before ERCP in 18 patients and within 24 hours in 5 patients
Reinhold *et al.*, 1998[72]; Canada	Consecutive	FSE MRCP compared with ERCP, IOC and surgery	Initially 159 patients; 49 were excluded for the following reasons: 34 lack of diagnosis, 10 unsuccessful ERCP, 3 unsuccessful MRCP claustrophobia ($n = 1$), inadequate ERCP ($n = 1$) or MRCP ($n = 1$), leaving a sample of 110 patients. 101 patients had ERCP, 2 had IOC and 7 had surgery 5-month study period, dates not reported	MRCP performed first and ERP or equivalent was ≤ 6 hours later in 97 patients, < 1 week in 7 patients and > 1 week in 6 patients
Soto *et al.*, 1996[73]; USA	Randomly recruited	3D FSE MRCP compared with ERCP and PTC	46 patients, 7 of whom were included in Barish *et al.*, 1995[58]; 45 had ERCP and 1 had PTC May 1994–April 1995	ERCP/PTC within 24 hours after MRCP
Soto *et al.*, 2000[74]; Columbia	Not reported	3D FSE, single-section half-Fourier RARE and multisection half-Fourier RARE MRCP compared with ERCP	Initially 59 patients, 10 were excluded for the following reasons: 2 owing to MRCP contraindications, 4 because 1 or more of the 3 MRCP sequences could not be completed, and 4 because ERCP could not be completed August 1997–May 1998	MRCP before ERCP, within 72 hours
Soto *et al.*, 2000[75]; Columbia	Not reported	Breath-hold, single-shot half-Fourier rapid acquisition and non-breath-holding 3D FSE MRCP compared with ERCP, CT and oral contrast-enhanced CT cholangiography	Initially 68 patients; 12 did not meet inclusion or exclusion criteria, 2 did not have MRCP because of claustrophobia, in 3 ERCP was not attempted or completed, leaving 51 patients who had all 4 studies April 1998–March 1999	MRCP within 48 hours before ERCP
Stiris *et al.*, 2000[76]; Norway	Consecutive	HASTE fat-suppressed breath-holding MRCP compared with ERCP	50; all patients had both techniques Study period not stated	MRCP performed first, followed by ERCP within 12 hours
Sugiyama *et al.*, 1998[77]; Japan	Non-consecutive	HASTE MRCP compared with ERCP	187 patients were recruited; 19 underwent only cholangiography or pancreatography on ERCP, in 8 the common channel could not be identified clearly and there was failure of cannulation in 2 patients, leaving 159 patients with CBD, main pancreatic duct and common channel depicted June 1994–August 1996	MRCP 0–14 days before ERCP

continued

TABLE 15 *Study characteristics (cont'd)*

Study, country	Sample selection	Comparison (type of MRCP and reference tests used)	Description of patients and procedures; study period	Time between ERCP and MRCP
Taylor *et al.*, 2002[78]; Australia	Consecutive	HASTE MRCP compared with ERCP, PTC or surgery	Initially 149 procedures (146 patients); MRCP unsuccessful in 8 owing to claustrophobia and in 1 patient owing to poor image quality, 5 were excluded because MRCP was more than 24 hours before ERCP, in 20 ERCP was unsuccessful (3 had subsequent ERCP, 2 had surgery and 2 had PTC and were included). In 2 patients ERCP and MRCP were both unsuccessful, leaving 129 patients who had both MRCP and ERCP (or equivalent) November 1998–December 1999	MRCP performed within 24 hours before ERCP
Textor *et al.*, 2002[6]; Germany	Consecutive	3D T2-weighted FSE MRCP compared with ERCP	150 patients initially; 146 had successful MRCP, 3 patients with PSC had unsuccessful ERCP and 1 failed owing to a bilidigestive anastomosis January 1996–December 2000	ERCP performed 1–14 days before MRCP (mean 3.2 days)
Varghese *et al.*, 2000[79]; Ireland	Consecutive	T2-weighted 2D multislice FSE MRCP compared with ERCP, PTC or IOC	256 patients initially; 64 excluded because ultrasound report or ERCP hard-copy images were not available ($n = 30$), direct cholangiography was not performed after failed ERCP ($n = 22$), MRCP not performed owing to contraindications ($n = 5$) or MRCP images were of non-diagnostic quality ($n = 7$), resulting in 191 patients [of these 34 had choledocholithiasis diagnosed by ERCP ($n = 29$), IOC ($n = 3$) and PTC ($n = 2$)] 18-month period, dates not stated	MRCP performed before ERCP, within 4 hours to 2 weeks (mean 18 hours)
Zidi *et al.*, 1999[80]; France	Consecutive	Non-breath-holding fat-suppressed TSE MRCP compared with ERCP (with or without sphincterotomy), endosonography or IOC	70 inpatients were included, 63 had ERCP, 5 had sonography and 2 had IOC 12-month period, dates not reported	MRCP performed within 12 hours before ERCP

TABLE 16 *Patient characteristics*

Study	Age (years)	Gender (male/female)	Suspected condition	Patient inclusion criteria	Exclusions
Adamek *et al.*, 1998[55]	Mean 64.4 (range 11–78)	31/29	CBD obstruction	Raised alkaline phosphatase or γ-glutamyltranspeptidase more than twice normal value and serum bilirubin > 2 μg/dl or morphological features on abdominal ultrasonography	8 of the original 86 patients were excluded owing to former operations with bilary–enteric anastomosis (Roux-en-Y gastrojejunostomy or Whipple's procedure)
Alcaraz *et al.*, 2000[56]	Mean not reported (range 40–90)	25/56	Obstruction of the biliary tree	Obstruction of the biliary tree based on clinical, laboratory and/or ultrasound findings	Not reported
Angulo *et al.*, 2000[57]	Mean 56 (range 19–94)	33/40	Symptoms consistent with biliary disease (cholestasis)	Males and females, age ≥ 18 years; clinical and/or biochemical evidence of cholestasis	Usual contraindications to MR scanning
Barish *et al.*, 1995[58]	Mean 51.5 (range 17–97)	8/22	Suspected biliary or pancreatic disease (reported separately)	ERCP referrals	MRI contraindicated
Calvo *et al.*, 2002[59]	Mean 67 years (range not reported) (in original 116 patients)	Ratio 1.08:1 (in original 116 patients)	Choledocholithiasis	Patients with suspected bilipancreatic pathology requiring ERCP between November 1996 and February 1998; age > 18 years; all patients in whom ERCP was started were included; all patients in whom MRCP was started were included; informed written consent	Patients with at least 1 absolute contraindication to either technique; patients with degenerative or ankylotic conditions, senile dementia or impossibility of patient cooperation in MRCP; patients with severe clinical conditions with urgent therapeutic requirements
Chan *et al.*, 1996[60]	Mean 65 (range 32–86)	27/20	Choledocholithiasis	Hospital inpatients referred for endoscopy because of right upper quadrant or epigastric pain, jaundice or dark-coloured urine, fever or biochemical jaundice	Not reported
Demartines *et al.*, 2000[21]	Mean 59.6 ± 15.4 (for all 70 patients in the study), 62.6 ± 18.2 (high-risk group who had ERCP) (range not reported)	Ratio 3:1 (for all 70 patients in the study), ratio 6:1 (for high-risk group who had ERCP)	Symptomatic cholelithiasis and suspected CBD stones	Elevation of bilirubin level ≥ 26 μmol/l (<1.5 mg/dl); alkaline phosphatase level > 216 U/l; CBDS demonstrated by any imaging modality; CBD diameter ≥ 8 mm (sonography); biliary pancreatitis	3 patients excluded because ERCP was technically not possible (1 each with duodenal stenosis, papillary oedema and large duodenal diverticulum)

continued

TABLE 16 *Patient characteristics (cont'd)*

Study	Age (years)	Gender (male/female)	Suspected condition	Patient inclusion criteria	Exclusions
Dwerryhouse *et al.*, 1998[61]	Not reported	Not reported	CBD stones	Abnormal LFT results, previous mild gallstone pancreatitis, dilated CBD of 7 mm or more, previous jaundice	Patients with jaundice, cholangitis or severe acute gallstone pancreatitis
Feldman *et al.*, 1997[62]	Not reported	Not reported	Pancreaticobiliary neoplasm	Clinical diagnosis of suspected pancreaticobiliary neoplasm	Not reported
Guibaud *et al.*, 1995[63]	Mean 57 (range 12–91)	50/76	Bile duct obstruction	Patients presented with clinical symptoms and/or results of biochemical studies consistent with bile duct obstruction	As stated in Description of patients (Table 15)
Hintze *et al.*, 1997[64]	Mean 52 (range 5–75)	38/40	Disorder affecting biliary or pancreatic duct system	Not previously undergone MRCP or ERCP and no definite diagnosis	Not reported
Holzknecht *et al.*, 1998[65]	Mean 55.8 ± 17.9 (range 14–84)	30/31	Not reported	Patients due to have ERCP within the next 2 days	Patients with contraindications for MRI
Laokpessi *et al.*, 2001[66]	Mean 59.8 (range 18–94) for whole group	67/80 for whole group	Choledocholithiasis	Past history of cholecystectomy or those with a high surgical or anaesthetic risk in group receiving ERCP and MRCP	Absolute contraindications to MRI, time span of greater than 48 hours between MRCP and final diagnosis; refusal to sign protocol, refusal to undergo MRCP or ERCP
Lee *et al.*, 1997[67]	Mean 62 (range 31–95)	22/24	Biliary disease	Suspected biliary disease	As stated in Description of patients (Table 15)
Lomanto *et al.*, 1997[68]	Mean 56.3 ± 6 (range 20–83)	24/38	Choledocholithiasis	Recurrent episodes of jaundice, pain, elevation in bilirubin, alanine transaminase, aspartate transaminase, alkaline phosphatase, γ-glutamytranspeptidase, amylase, ultrasonographic finding of dilated bile ducts (> 6 mm) or suspicion of CBD stones	Not reported

continued

TABLE 16 *Patient characteristics (cont'd)*

Study	Age (years)	Gender (male/female)	Suspected condition	Patient inclusion criteria	Exclusions
Lomas *et al.*, 1999[69]	Mean not reported (range: 21–92)	33/33	Biliary strictures or choledocholithiasis	Sonographic evidence of calculi within the gallbladder combined with a dilated common bile duct, history of prior jaundice with known gallbladder calculi, known gallbladder calculi and abnormal biochemical liver function (other causes excluded), recurrent pain or dilated CBD or abnormal liver function after cholecystectomy; strictures suspected in patients with dilatation with or without evidence of a mass lesion or abnormal LFTs	Patients were excluded if the diagnosis was known and therapeutic interventions were planned. Also excluded were those patients with the usual contraindications for MRI
Macaulay, *et al.*, 1995[70]	Mean 66 (range 32–93)	27/1	Biliary obstruction	Patients with suspected biliary obstruction scheduled to undergo ERCP	Not reported
Regan *et al.*, 1996[71]	Mean 68 (range 42–89)	10/13	CBD stones	Clinical suspicion or sonographic evidence of CBD stones	Not reported
Reinhold *et al.*, 1998[72]	Mean 55 ± 10.5 (range 11–89)	47/63	CBD obstruction	Clinical symptoms and/or biochemical study results consistent with CBD obstruction	As stated in Description of patients (Table 15)
Soto *et al.*, 1996[73]	Mean 51.4 (range 17–97)	Not reported	Not reported	Patients referred for elective ERCP	Not reported
Soto *et al.*, 2000[74]	Mean 52 (range 17–89)	14/35	Choledocholithiasis	Patients with suspected choledocholithiasis referred for ERCP	As stated in Description of patients (Table 15)
Soto *et al.*, 2000[75]	Mean 53 (range 18–84)	19/32	Choledocholithiasis	18 years or older	Bilirubin > 5 mg/dl, known hyperuricaemia, creatinine level > 1.3 mg/dl, contraindications for MRCP
Stiris *et al.*, 2000[76]	Mean 60 (range 19–94)	13/37	CBD stones	Patients with clinically and laboratory suspected CBD stone disease	Not reported

continued

TABLE 16 *Patient characteristics (cont'd)*

Study	Age (years)	Gender (male/female)	Suspected condition	Patient inclusion criteria	Exclusions
Sugiyama *et al.*, 1998[77]	Mean 58.5 (range 16–92)	90/97	Pancreatobiliary disease	Not reported	Not reported
Taylor *et al.*, 2002[78]	Mean 60 (range 17–94	60/69	Biliary tract disease in 96% (the other 4% had pancreatic duct disease)	Patients scheduled for ERCP	Less than 16 years old, inability to give informed consent, contraindication to MRCP, patients unable to follow instructions or hold breath for 20 seconds in supine position
Textor *et al.*, 2002[6]	Mean 48.6 (range not reported)	67/83	PSC	Progressive fatigue, pruritus followed by icterus and/or elevated values for alkaline phosphatase and serum aspartate transaminase and occasionally an elevated serum concentration of bilirubin	Not reported
Varghese *et al.*, 2000[79]	Mean 66 (range 24–92)	76/115	Patients referred for diagnostic ERCP	Not reported	As stated in Description of patients (Table 15)
Zidi *et al.*, 1999[80]	Mean 71 ± 15.5 (range 30–93)	34/36	Inpatients with suspected CBD stones	Not reported	Not reported

TABLE 17 *Quality assessment*

Study	Appropriate spectrum of patients	Work-up bias (all patients had both tests)	Expectation bias (blinded assessment)	Reproducibility	CIs reported	Placed in context of other tests
Adamek *et al.*, 1998[55]	Yes	No, of the 78 original patients 16 had unsuccessful ERCP and 2 had unsuccessful MRCP	Results of ultrasound examination were known, but operators were unaware of each other's findings or clinical diagnosis when MRCP images were interpreted	Not reported	No	Yes, other tests mentioned
Alcaraz *et al.*, 2000[56]	Yes	No, 70 of 81 had ERCP, 7 had PTC and 4 had surgery	Yes, examinations were read independently by 2 radiologists unaware of the patients' clinical information	Yes, kappa values reported for dilatation ($\kappa = 0.79$), location ($\kappa = 0.80$) and cause ($\kappa = 0.74$)	No	No other tests mentioned
Angulo *et al.*, 2000[57]	Yes	No, 68 of 73 patients had ERCP, 2 had PTC but not clear what happened to the other 3	Yes, unaware of clinical and biochemical data and other results	Not reported	No	Yes, other tests mentioned
Barish *et al.*, 1995[58]	Yes	No, only 21 of 29 had ERCP	Yes, 2 clinicians evaluated images without clinical or radiological information	Not reported	No	No other tests reported
Calvo *et al.*, 2002[59]	Yes, although no mention of other 55 patients without suspected choledocholithiasis	No, 60 out of 61 had ERCP	Radiologists were blinded to ERCP results, but not to relevant clinical data and results of other imaging studies such as ultrasonography	Not reported	No	Yes, other tests mentioned
Chan *et al.*, 1996[60]	Yes	No, 2 out of 47 did not have ERCP	Radiologists who performed and interpreted MRCP results were blinded to all clinical, biochemical and imaging findings	Not reported	Yes	Yes, other tests mentioned
Demartines *et al.*, 2000[21]	Yes	No, 3 were excluded because ERCP was technically not possible	Yes, radiologists were unaware of laboratory and ERCP results	Not reported	No	Yes, other test results reported

continued

TABLE 17 *Quality assessment (cont'd)*

Study	Appropriate spectrum of patients	Work-up bias (all patients had both tests)	Expectation bias (blinded assessment)	Reproducibility	CIs reported	Placed in context of other tests
Dwerryhouse *et al.*, 1998[61]	Yes, although a large number of patients was excluded	No, of the 40 chosen for ERCP, 2 did not have MRCP and 4 did not have ERCP	Yes, the ERCP operator was unaware of the MRCP result, but no mention of clinical or other imaging findings	Not reported	No	Yes, other tests mentioned
Feldman *et al.*, 1997[62]	Yes	No, 3 did not have ERCP, reasons not stated	Yes, radiologists were blinded to the results of the other tests	Not reported	No	No other tests mentioned
Guibaud *et al.*, 1995[63]	Yes	No, of the original sample, 22 did not have ERCP results and 8 did not have MRCP results	Yes, reviewers were blinded to clinical parameters, results of other imaging tests and the final diagnosis	Yes, kappa values reported for diagnosis of bile duct obstruction ($\kappa = 0.90$), choledocholithiasis ($\kappa = 0.77$), malignant obstruction ($\kappa = 0.82$) and all causes ($\kappa = 0.82$)	Yes	Yes, other tests mentioned
Hintze *et al.*, 1997[64]	Not clear but all had suspected disorder of pancreatic/biliary system	No of the original 78 patients, 1 did not have MRCP and 1 did not have ERCP	Yes, radiologists interpreted results on a blinded basis, but not clear whether blinded to clinical information	Not reported	No	Yes, other tests mentioned
Holzknecht *et al.*, 1998[65]	Not clear as suspected condition not reported	No, 2 of the original sample did not have both MRCP and 3 did not have ERCP	Yes, radiologists and endoscopists were blinded to each others reports	Yes, an off-site radiologist read all 61 MRCP images	No	No other tests reported
Laokpessi *et al.*, 2001[66]	Only patients with past history of cholecystectomy or high surgical or anaesthetic risk included	No, 147 had MRCP and only 101 had ERCP out of original 166 patients	Yes, MRCP results were read without knowledge of ERCP results, but no information regarding blinding of clinical data	Not reported	Yes	Yes, other tests mentioned

continued

TABLE 17 *Quality assessment (cont'd)*

Study	Appropriate spectrum of patients	Work-up bias (all patients had both tests)	Expectation bias (blinded assessment)	Reproducibility	CIs reported	Placed in context of other tests
Lee *et al.*, 1997[67]	Yes	No, 25 of the original sample were excluded	Yes, radiologists were blinded to ERCP results, and gastroenterologist and radiologist were blinded to MRCP results, but no mention of clinical data	Yes, 2 readers interpreted MRCP and ERCP results and agreement was good (κ = 0.487 for MRCP, κ = 0.702 for ERCP)	No	No other tests reported
Lomanto *et al.*, 1997[68]	Yes	No, 2 of 62 had PTC	Not reported	Not reported	No	Yes, other tests mentioned
Lomas *et al.*, 1999[69]	Yes	No, of the original 76 patients only 66 had both tests	Not clear, results were assessed 'independently' but investigators were aware of clinical presentation, prior imaging and laboratory studies	Not reported, although a κ-value was reported for agreement between MRCP and ERCP; κ = 0.88 (CI 0.82 to 0.94)	Yes	Yes, other tests mentioned
Macaulay, *et al.*, 1995[70]	Yes	No, of the original 28 patients, only 291 underwent ERCP	Yes, ERCP, PTC and IOC were read by 2 radiologists blinded to patient history and diagnosis, MRCP images were read by 2 radiologists blinded to diagnosis; clinical history and findings of other imaging studies	No, 2 readers, but inter-rater agreement was not reported	No	No other tests reported
Regan *et al.*, 1996[71]	Yes	No, 26 initially, of whom 2 did not have ERCP and 1 did not have MRCP	Radiologists were unaware of the results of the ERCP and each other's results, but no information about other tests	2 readers disagreed on 3 cases	Yes	Yes, tests used for final diagnoses mentioned, as well as sonography
Reinhold *et al.*, 1998[72]	Yes	No, of 159 initial patients, 101 had ERCP	One reviewer was blinded to clinical findings and other results. The other reviewer was blinded to the results of the direct cholangiography, but had access to clinical findings	Kappa values were reported for choledocholithiasis (κ = 0.82)	Yes	Yes, other tests mentioned

continued

TABLE 17 *Quality assessment (cont'd)*

Study	Appropriate spectrum of patients	Work-up bias (all patients had both tests)	Expectation bias (blinded assessment)	Reproducibility	CIs reported	Placed in context of other tests
Soto *et al.*, 1996[73]	No, not clear what suspected condition was	No, 1 had PTC, not clear whether patients were excluded from initial sample	Yes, radiologists did not have access to clinical information or other imaging studies	2 radiologists, but no information on inter-rater agreement	No	No other tests reported
Soto *et al.*, 2000[74]	Yes	No, only 49 of initial 59 patients had both tests	Yes, radiologists were blinded to clinical and laboratory data and results of other imaging tests	Yes, kappa values reported for 3D FSE sequence $\kappa = 0.92$, multisection half-Fourier RARE sequence ($\kappa = 0.84$) and single-section half-Fourier RARE sequence ($\kappa = 0.80$). ROC curves for both radiologists also reported and diagnostic performance of the 3 sequences for both radiologists was reported to be excellent	Yes	No other tests mentioned
Soto *et al.*, 2000[75]	Yes	No, of initial 68 patients only 51 had both tests	Yes, radiologists were blinded to results of other diagnostic studies and clinical information. The sequence of interpretation of studies was randomised	Not reported	Yes	Yes, other test results reported
Stiris *et al.*, 2000[76]	Yes	Yes	Yes, those performing ERCP were unaware of MRCP results, but no mention of blinding to clinical data	Not reported	No	Yes, other tests mentioned
Sugiyama *et al.*, 1998[77]	Yes, but included any pancreatobiliary disease	No, only 159 of original 187 patients had both tests	No, although the endoscopist interpreting the ERCP images was not aware of the MRCP results, the radiologists were aware of clinical information and other imaging findings	Not reported	No	No other test results mentioned

continued

TABLE 17 *Quality assessment (cont'd)*

Study	Appropriate spectrum of patients	Work-up bias (all patients had both tests)	Expectation bias (blinded assessment)	Reproducibility	CIs reported	Placed in context of other tests
Taylor *et al.*, 2002[78]	Yes	No, only 129 of original 146 patients had both tests	Yes, the radiologist interpreting MRCP images was blinded to ERCP findings, but no mention of other images and clinical information	Not reported	Yes	Yes, other test results reported
Textor *et al.*, 2002[6]	Yes	No, of 150 patients only 146 had both tests	Yes, radiologists were blinded to patients' gender, age, clinical and medical history	Yes, kappa values reported for bile duct abnormalities (κ = 0.98 and 0.978)	No	Yes, other tests mentioned
Varghese *et al.*, 2000[79]	Not clear what suspected diagnosis was	No, 64 of the original 256 patients were excluded from the study, resulting in a final sample of 191 patients; not clear who had ERCP or IOC or PTC, apart from those diagnosed with choledocholithiasis	Patient clinical information and ultrasound findings were available to the endoscopists, but they were unaware of the MRCP findings at the time of ERCP	Not reported	No	Yes, other tests, such as ultrasound, reported
Zidi *et al.*, 1999[80]	Yes	No, only 63 of original 70 had ERCP	Yes, radiologists were blinded to ERCP results and previous investigations	Not reported	No	Yes, other tests mentioned

TABLE 18 *Results*

Study	Diagnosis		Sensitivity		Specificity		Adverse effects
Adamek *et al.*, 1998[55]	**Final diagnosis**	**No. of patients**	**Compared with final diagnosis (ERCP plus histological findings or follow-up)**		**Compared with final diagnosis**		3 patients had mild acute pancreatitis after ERCP
	Normal	13	Any abnormality	42/47 (89%)	Any abnormality	12/13 (92%)	
	Benign stricture	15	Detection of malignancy	22/27 (81%)	Detection of malignancy	33/33 (100%)	
	Choledocholithiasis	3					
	Hepatolithiasis	1					
	Choledochal cyst	1	**ERCP**		**ERCP**		
	Malignant stricture	23	Any abnormality	91%	Any abnormality	92%	
	Cholangiocarcinoma	4	Malignancy	93%	Malignancy	94%	
Alcaraz *et al.*, 2000[56]	**Diagnosis**		**Compared with ERCP (with histological examination)**		**Compared to ERCP (with histological examination)**		No complications occurred during the procedures
	Normal	11	**Location of obstruction**		**Location of obstruction**		
	Choledocholithiasis	20	Intrahepatic/hilar	100%	Intrahepatic/hilar	100%	
	Neoplasms	15	Suprapancreatic	92%	Suprapancreatic	94%	
	Benign biliary stricture	23	Ampullary	86%	Ampullary	91%	
	Chronic pancreatitis	8	Intrapancreatic	69%	Intrapancreatic	92%	
	Other	4	**Cause of obstruction**		**Cause of obstruction**		
			Choledocolithiasis	89%	Choledocholithiasis	90%	
			Malignant obstruction	92%	Malignant obstruction	88%	
			Benign stricture	63%	Benign stricture	90%	
			Pancreatitis	50%	Pancreatitis	99%	
Angulo *et al.*, 2000[57]	**Diagnosis**		**Compared with ERCP**		**Compared with ERCP**		6 of 68 patients who underwent ERCP (8.8%) developed complications such as abdominal pain ($n = 3$) requiring hospitalisation for at least 24 hours, pancreatitis ($n = 2$) and perforation of the CBD ($n = 1$)
	Benign biliary disease	45 (58%)	Normal ducts	19/22 (86%)	Normal ducts	46/48 (96%)	
	including PSC	23 (32%)	Dilatation:		Dilatation:		
	Malignant biliary disease	9 (12%)	Hepatic ducts	40/42 (95%)	Hepatic ducts	24/28 (86%)	
	Normal biliary tree	22 (30%)	CBD	38/41 (93%)	CBD	27/29 (93%)	
			Obstruction	37/37 (100%)	Obstruction	30/33 (91%)	
			Biliary stones*	5/10 (50%)	Biliary stones	59/60 (98%)	
			PSC	19/23 (83%)	PSC	46/47 (98%)	
			*Sensitivity of MRCP in detection of bile duct stones was greater in patients without PSC (80%) than in patients with PSC (20%)				

continued

TABLE 18 *Results (cont'd)*

Study	Diagnosis		Sensitivity		Specificity		Adverse effects
Barish *et al.*, 1995[58]	**Diagnosis according to MRCP**		**Compared with ERCP**		**Compared with ERCP**	6/6 (100%)	Not reported
	Normal	6	Diagnosis of CBD	19/21 (90%)	Dilatation of the CBD		
	Periampullary stricture	5	Dilatation of the CBD	13/15 (87%)			
	Calculous obstruction	3					
	Structural duct anomaly (Caroli's disease)	1					
	Solitary stricture:						
	(chronic pancreatitis)	2					
	hepaticojejunostomy stricture	1					
	cystic lesion (biliary cystadenocarcinoma)	1					
Calvo *et al.*, 2002[59]	**High-probability patients (n = 49)**		**Compared with ERCP**	91%	**Compared with ERCP**	84%	No morbidity associated with diagnostic ERCP, but those undergoing therapeutic ERCP had a morbidity of 4% (2 of 49 patients), which consisted of mild acute pancreatitis and digestive tract bleeding secondary to sphincterotomy that required endoscopic sclerotherapy
		ERCP **MRCP**					
	Gallstones	32 29					
	Normal	1					
	Diagnostic doubt between gallstone and aerobilia	1					
	Diagnostic doubt between gallstone lodged in papilla and ampulloma	1					
	Papillitis	4 2					
	Diagnostic doubt	2					
	Ampulloma	2 1					
	Diagnostic doubt between ampulloma and obstructive choledocholithiasis	1					
	Cholangiocarcinoma	1 1					
	Normal	10 8					
	Diagnostic doubt with aerobilia	2					
	Intermediate-probability patients (n = 9)						
	Gallstones	3 3					
	Papillitis	2 1					
	Diagnostic doubt	1					
	Normal	4 4					

continued

TABLE 18 *Results (cont'd)*

Study	Diagnosis			Sensitivity		Specificity		Adverse effects
Chan *et al.*, 1996[60]		**ERCP**	**MRCP**	**Compared with ERCP**		**Compared with ERCP**		Not reported
	Absence of ductal dilatation	16	16	95% (CI 0.8449 to 1.000)		85% (CI 0.7046 to, 0.9877)		
	CBD dilatation	29	28					
	Choledocholithiasis	19	18					
	Without choledocholithiasis	26	22					
Demartines *et al.*, 2000[21]		**ERCP**	**MRCP**	**Compared with ERCP**		**Compared with ERCP**		No complications
	CBD stones	19	21	19/19 (100%)		19/21 (calculated 90.5%)		
Dwerryhouse *et al.*, 1998[61]	8 patients with CBD stones			**Compared with ERCP**		**Compared with ERCP**		Not reported
				7/8 (88%)		28/30 (93%)		
Feldman *et al.*, 1997[62]		**ERCP**	**MRCP**	**Compared with final diagnosis (ERCP plus pathological diagnosis)**				Not reported
	Bile duct dilatation	14	14					
	Normal ducts	3	3	Dilatation	14/14 (100%)			
	Malignancy			Malignancy	17/18			
	18 malignant pancreaticobiliary neoplasms				(calculated 94.4%)			
Guibaud *et al.*, 1995[63]	**Diagnosis**			**Compared with ERCP**		**Compared with ERCP**		Not reported
	Bile duct obstruction	79		Bile duct obstruction	72/79 (91%) (CI 85 to 100%)	Bile duct obstruction	100%	
	Choledocholithiasis	32				Choledocholithiasis	98% (CI 95 to 100%)	
	Malignant obstruction	14		Choledocholithiasis	26/32 (81%) (CI 68 to 95%)			
						Malignant obstruction	98% (CI 96 to 100%)	
				Malignant obstruction	12/14 (86%) (CI 67 to 100%)			
Hintze *et al.*, 1997[64]	**Final diagnosis**			**Compared with ERCP**		**Compared with ERCP**		Not reported
	Cholangiocarcinoma (Klatskin)		14	Normal duct	5/7 (71%)	Overall	78%	
	Papillary stenosis		7	Recognition of dilatation	20/24 (83%)			
	Normal		7	Recognition of stricture	22/26 (85%)			
	Choledocholithiasis		6	Correct stricture location	20/26 (77%)			
	Liver metastasis		6	Diagnosis of benign stricture	6/12 (50%)			
	Juxtapapillary duodenal diverticulum		6	Diagnosis of malignant stricture	8/10 (80%)			
	Liver cirrhosis		4	Diagnosis of stones	4/5 (80%)			
	Primary sclerosising cholangitis		3	Overall	89%			
	Surgical ligation of bile duct		2					
	Caroli syndrome		1					
	Ischaemic type biliary lesion		1					

continued

TABLE 18 *Results (cont'd)*

Study	Diagnosis			Sensitivity		Specificity		Adverse effects
Holzknecht *et al.*, 1998[65]	**Diagnosis**	**ERCP**	**MRCP**	**Compared with ERCP**		**Compared with ERCP**		Not reported
	Cholangiolithiasis	13	12	Cholangiolithiasis		Cholangiolithiasis		
	Dilatation	34	32	on-site	12/13 (92.3%)	on-site	46/48 (95.8%)	
	Stenosis	36	32	off-site	11/13 (84.6%)	off-site	45/48 (93.7%)	
				Dilatation		Dilatation		
				on-site	32/34 (94.1%)	on-site	25/27 (92.6%)	
				off-site	32/34 (94.1%)	off-site	26/27 (96.3%)	
				Stenosis		Stenosis		
				on-site	32/36 (88.9%)	on-site	22/25 (84%)	
				off-site	30/36 (83.3%)	off-site	22/25 (84%)	
				Overall		Overall		
				on-site	42/46 (91.3%)	on-site	12/15 (80%)	
				off-site	43/46 (93.5%)	off-site	12/15 (80%)	
Laokpessi *et al.*, 2001[66]	**Diagnosis**			**Compared with final diagnosis (stone extraction with ERCP or IOC)**		**Compared with final diagnosis**		Not reported
	CBD free of obstruction		15	MRCP	93% (CI 86.1 to 96.7)	MRCP	100% (CI 87.4 to 100)	
	CBD stones (including stones < 3 mm)		113 (15)	ERCP	95% (CI 87.3 to 98.4)	ERCP	100% (CI 79.1 to 100)	
	Malignant strictures of the papilla		5					
	Cystic lesions of CBD		1					
	Adenocarcinoma of head of pancreas		2					
	Papillary stenosis		7					
	Hilum cholangiocarcinoma		2					
	Benign strictures of CBD		2					
Lee *et al.*, 1997[67]	**Diagnosis (*n* = 46)**			**Compared with final diagnosis (ERCP plus surgical findings)**		**Compared with final diagnosis**		Not reported
	Normal		1	MRCP	17/21 (81%)	MRCP	23/25 (92%)	
	Choledocholithiasis		11	ERCP	15/21 (71%)	ERCP	23/25 (92%)	
	Choledochal cyst		1					
	Non-specific biliary dilitation		12					
	Klatskin tumour		4					
	Proximal CBD carcinoma		1					
	Ampullary carcinoma		8					
	Pancreatic head carcinoma		5					
	Hepatoma with biliary tumour emboli		3					

continued

TABLE 18 *Results (cont'd)*

Study	Diagnosis	Sensitivity	Specificity	Adverse effects
Lomanto *et al.*, 1997[68]	24 of 62 patients were positive for stones	**Compared with ERCP** 22/24 (91.6%)	**Compared with ERCP** 100%	Not reported
Lomas *et al.*, 1999[69]	**Diagnosis** Strictures 20 Choledocholithiasis 11 Other 12 Normal 25 Chronic pancreatitis 1	**Compared with ERCP** Strictures 19/19 100% Choledocholithiasis 9/9 100%	**Compared with ERCP** Strictures 98% (CI 94 to 100%) Choledocholithiasis 97% (CI 93 to 100%)	Not reported
Macaulay *et al.*, 1995[70]	**Diagnosis** Obstruction 14 Duct stones or sludge 7 Intrahepatic ducts Dilated 18 Non-dilated 11 All 4 hepatic segments Dilated 18 Non-dilated 11	**Compared with final diagnosis (direct cholangiography plus endoscopic or fluoroscopic observation)** Obstruction 14/14 100% Duct stones or sludge 5/7 (calculated 71.4%)	**Compared with final diagnosis** (91%)	Not reported
Regan *et al.*, 1996[71]	**Diagnosis** CBD stones 15 CBD dilatation 12	**Compared with final diagnosis (ERCP, endoscopic balloon or basket extraction or surgical removal of stones)** Choledocholithiasis **ERCP** **MRCP** No. of patients 15 14 100% 93% (CI 70 to 100%) Dilatation MRCP 100%	**Compared with ERCP** Choledocholithiasis ERCP 100% MRCP 89% (CI 52 to 100%) Dilatation MRCP 100%	Not reported

continued

TABLE 18 *Results (cont'd)*

Study	Diagnosis		Sensitivity	Specificity	Adverse effects
Reinhold *et al.*, 1998[72]	**Diagnosis**		**Compared with ERCP**	**Compared with ERCP**	3 of 28 patients with choledocholithiasis developed complications (11%) (2 with pancreatitis and 1 with postsphincter bleeding), among those negative for choledocholithiasis 4 of 80 (5%) developed complications (pancreatitis in all 4)
	Choledocholithiasis	30	Choledocholithiasis	Choledocholithiasis	
	Normal biliary tract	32	Reviewer 1 90% (CI 79 to 100%)	Reviewer 1 100%	
	Postcholecystectomy dilatation or oddities	27	Reviewer 2 90% (CI 70 to 100%)	Reviewer 2 93% (CI 87 to 98%)	
	Pancreatic carcinoma	14	Bile duct obstruction 91% (CI 84 to 97%)	Bile duct obstruction 100%	
	Ampullary carcinoma	2			
	Cholangiocarcinoma	1			
	Metastases	2			
	Chronic pancreatitis	2			
Soto *et al.*, 1996[73]	**Diagnosis**		**Compared with ERCP**	**Compared with ERCP**	Not reported
	Normal	17	Bile duct dilatation 26/27 (96.3%)	Normal bile ducts 16/17 (94.1%)	
	Ampullary stenosis	12	Bilary strictures 9/10 (90%)		
	Choledocholithiasis	6	Intraductal abnormalities 7/7 (100%)		
	Chronic pancreatitis with stricture	4			
	Pancreatic head adenocarcinoma with stricture	2			
	Mid-CBD cholangiocarcinoma	1			
	Periportal adenopathy	1			
	Sclerosing cholangitis	1			
	Common bile duct polyp	1			
	Intrahepatic cholangiocarcinoma	1			
Soto *et al.*, 2000[74]	**Diagnosis**		**Compared with ERCP**	**Compared with ERCP**	Not reported
	Bile duct dilatation with only choledocholithiasis	18	3D FSE	3D fast SE	
	Bile duct dilatation with choledocholithiasis and hepatolithiasis	4	Radiologist 1 96% (CI 90 to 100%) Radiologist 2 92% (CI 84 to 99%)	Radiologist 1 96% (CI 90 to 100%) Radiologist 2 100% (CI 99 to 100%)	
	Choledocholithiasis with normal-calibre ducts	2	Single-section half-Fourier RARE	Single-section half-Fourier RARE	
	Bile duct dilatation without stones	19	Radiologist 1 100% (CI 99 to 100%) Radiologist 2 92% (CI 84 to 99%)	Radiologist 1 96% (CI 90 to 100%) Radiologist 2 96% (CI 90 to 100%)	
	Normal biliary ductal system	6	Multi-section half-Fourier RARE	Multi-section half-Fourier RARE	
			Radiologist 1 92% (CI 84 to 99%) Radiologist 2 96% (CI 90 to 100%)	Radiologist 1 92% (CI 84 to 99%) Radiologist 2 92% (CI 84 to 99%)	

continued

TABLE 18 *Results (cont'd)*

Study	Diagnosis			Sensitivity	Specificity	Adverse effects
Soto *et al.*, 2000[75]	**Diagnosis**			**Compared with ERCP**	**Compared with ERCP**	Not reported for ERCP or MRCP
	Bile duct stones		26	96% (CI 78 to 99%)	100% (CI 84 to100%)	
Stiris *et al.*, 2000[76]	CBD stones		32	**Compared with ERCP** 28/32 (87.5%)	**Compared with ERCP** 17/18 (94.4%)	1 of 50 patients developed moderate pancreatitis (2%)
Sugiyama *et al.*, 1998[77]	**Diagnosis**			**Compared with ERCP**	**Compared with ERCP**	Not reported
		No. of patients	**No. detected with MRCP**	Anomalous PBJ 82%	Anomalous PBJ 100%	
	Anomalous PBJ	11	9	Without PBJ:		
	Congenital choledochal cyst	7	7	Pancreatobiliary lesions in pancreatic carcinoma 22/24 (92%)		
	Mucosal hyperplasia of gallbladder	5	0	Pancreatic cystic disease 13/13 (100%)		
	Carcinoma of gallbladder	1	0	Chronic pancreatitis 13/15 (87%)		
	Gallbladder stone	1	1	Bile duct carcinoma 11/12 (92%)		
	CBD stone	2	1	Polypoid gallbladder lesions 5/7 (71%)		
				Gallbladder stones 23/27 (85%)		
				Choledocholithiasis 20/21 (95%)		
Taylor *et al.*, 2002[78]	**Diagnosis**			**Compared with ERCP**	**Compared with ERCP**	Not reported
	Choledocholithiasis		46	45/46 (97.8%) (CI 88.5 to 99.9%)	74/83 (89.1%) (CI 80.4 to 94.9%)	
	Stricture		12			
	Normal		47			
	Dilated biliary tree		22			
	Other		4			

continued

TABLE 18 *Results (cont'd)*

Study	Diagnosis				Sensitivity	Specificity	Adverse effects
Textor *et al.*, 2002[6]	**Diagnosis**	**MRCP**	**Final**		**Compared with final diagnosis (clinical presentation and biochemical tests)**	**Compared with final diagnosis**	1 patient had mild pancreatitis following ERCP
	Normal	71 (47.3%)	72 (48.0%)		For diagnosing PSC 29/33 (88%)	For diagnosing PSC 108/109 (99%)	
	Choledocholithiasis	3 (2.0%)	5 (3.3%)				
	Cholangiocellular carcinoma	36 (24.0%)	39 (26.0%)				
	Primary sclerosing cholangitis	29 (19.3%)	34 (22.7%)				
Varghese *et al.*, 2000[79]	**Diagnosis**	**Final**	**ERCP**	**MRCP**	**Compared with ERCP**	**Compared with final diagnosis**	Not reported
	Choledocholithiasis	34	29	31	Choledocholithiasis (3 false positives and 3 false negatives for choledocholithiasis) 31/34 (91%)	Choledocholithiasis 98%	
	Strictures	47					
	Normal ducts	100					
Zidi *et al.*, 1999[80]	**Diagnosis**				**Compared with ERCP**	**Compared with ERCP**	Not reported
	Undilated CBD			24	Choledocholithiasis 28/49 (57.1%)	Choledocholithiasis 21/21 (100%)	
	Dilated CBD			46			
	CBD stones			49			

Health Technology Assessment Programme

Prioritisation Strategy Group

Members

Chair,
Professor Tom Walley, Director, NHS HTA Programme & Professor of Clinical Pharmacology, University of Liverpool

Professor Bruce Campbell, Consultant Vascular & General Surgeon, Royal Devon & Exeter Hospital

Professor Shah Ebrahim, Professor in Epidemiology of Ageing, University of Bristol

Dr John Reynolds, Clinical Director, Acute General Medicine SDU, Radcliffe Hospital, Oxford

Dr Ron Zimmern, Director, Public Health Genetics Unit, Strangeways Research Laboratories, Cambridge

HTA Commissioning Board

Members

Programme Director,
Professor Tom Walley, Director, NHS HTA Programme & Professor of Clinical Pharmacology, University of Liverpool

Chair,
Professor Shah Ebrahim, Professor in Epidemiology of Ageing, Department of Social Medicine, University of Bristol, Canynge Hall, Whiteladies Road, Bristol

Deputy Chair,
Professor Jenny Hewison, Professor of Health Care Psychology, Academic Unit of Psychiatry and Behavioural Sciences, University of Leeds School of Medicine, Leeds

Professor Douglas Altman, Professor of Statistics in Medicine, Centre for Statistics in Medicine, Oxford University, Institute of Health Sciences, Cancer Research UK Medical Statistics Group, Headington, Oxford

Professor John Bond, Professor of Health Services Research, Centre for Health Services Research, University of Newcastle, School of Health Sciences, Newcastle upon Tyne

Professor John Brazier, Director of Health Economics, Sheffield Health Economics Group, School of Health & Related Research, University of Sheffield, ScHARR Regent Court, Sheffield

Dr Andrew Briggs, Public Health Career Scientist, Health Economics Research Centre, University of Oxford, Institute of Health Sciences, Oxford

Dr Christine Clark, Medical Writer & Consultant Pharmacist, Cloudside, Rossendale, Lancs
and
Principal Research Fellow, Clinical Therapeutics in the School of Pharmacy, Bradford University, Bradford

Professor Nicky Cullum, Director of Centre for Evidence Based Nursing, Department of Health Sciences, University of York, Research Section, Seebohm Rowntree Building, Heslington, York

Dr Andrew Farmer, Senior Lecturer in General Practice, Department of Primary Health Care, University of Oxford, Institute of Health Sciences, Headington, Oxford

Professor Fiona J Gilbert, Professor of Radiology, Department of Radiology, University of Aberdeen, Lilian Sutton Building, Foresterhill, Aberdeen

Professor Adrian Grant, Director, Health Services Research Unit, University of Aberdeen, Drew Kay Wing, Polwarth Building, Foresterhill, Aberdeen

Professor Alastair Gray, Director, Health Economics Research Centre, University of Oxford, Institute of Health Sciences, Headington, Oxford

Professor Mark Haggard, Director, MRC ESS Team, CBU Elsworth House, Addenbrooke's Hospital, Cambridge

Professor F D Richard Hobbs, Professor of Primary Care & General Practice, Department of Primary Care & General Practice, University of Birmingham, Primary Care and Clinical Sciences Building, Edgbaston, Birmingham

Professor Peter Jones, Head of Department, University Department of Psychiatry, University of Cambridge, Addenbrooke's Hospital, Cambridge

Professor Sallie Lamb, Research Professor in Physiotherapy/Co-Director, Interdisciplinary Research Centre in Health, Coventry University, Coventry

Dr Donna Lamping, Senior Lecturer, Health Services Research Unit, Public Health and Policy, London School of Hygiene and Tropical Medicine, London

Professor David Neal, Professor of Surgical Oncology, Oncology Centre, Addenbrooke's Hospital, Cambridge

Professor Tim Peters, Professor of Primary Care Health Services Research, Division of Primary Health Care, University of Bristol, Cotham House, Cotham Hill, Bristol

Professor Ian Roberts, Professor of Epidemiology & Public Health, Intervention Research Unit, London School of Hygiene and Tropical Medicine, London

Professor Peter Sandercock, Professor of Medical Neurology, Department of Clinical Neurosciences, University of Edinburgh, Western General Hospital NHS Trust, Bramwell Dott Building, Edinburgh

Professor Martin Severs, Professor in Elderly Health Care, Portsmouth Institute of Medicine, Health & Social Care, St George's Building, Portsmouth

Dr Jonathan Shapiro, Senior Fellow, Health Services Management Centre, Park House, Birmingham

Current and past membership details of all HTA 'committees' are available from the HTA website (www.ncchta.org)

Diagnostic Technologies & Screening Panel

Members

Chair,
Dr Ron Zimmern, Director of the Public Health Genetics Unit, Strangeways Research Laboratories, Cambridge

Dr Paul Cockcroft, Consultant Medical Microbiologist/ Laboratory Director, Public Health Laboratory, St Mary's Hospital, Portsmouth

Professor Adrian K Dixon, Professor of Radiology, Addenbrooke's Hospital, Cambridge

Dr David Elliman, Consultant in Community Child Health, London

Dr Andrew Farmer, Senior Lecturer in General Practice, Institute of Health Sciences, University of Oxford

Dr Karen N Foster, Clinical Lecturer, Dept of General Practice & Primary Care, University of Aberdeen

Professor Jane Franklyn, Professor of Medicine, University of Birmingham

Professor Antony J Franks, Deputy Medical Director, The Leeds Teaching Hospitals NHS Trust

Mr Tam Fry, Honorary Chairman, Child Growth Foundation, London

Dr Susanne M Ludgate, Medical Director, Medical Devices Agency, London

Dr William Rosenberg, Senior Lecturer and Consultant in Medicine, University of Southampton

Dr Susan Schonfield, CPHM Specialised Services Commissioning, Croydon Primary Care Trust

Dr Margaret Somerville, Director of Public Health, Teignbridge Primary Care Trust, Devon

Mr Tony Tester, Chief Officer, South Bedfordshire Community Health Council, Luton

Dr Andrew Walker, Senior Lecturer in Health Economics, University of Glasgow

Professor Martin J Whittle, Head of Division of Reproductive & Child Health, University of Birmingham

Dr Dennis Wright, Consultant Biochemist & Clinical Director, Pathology & The Kennedy Galton Centre, Northwick Park & St Mark's Hospitals, Harrow

Pharmaceuticals Panel

Members

Chair,
Dr John Reynolds, Clinical Director, Acute General Medicine SDU, Oxford Radcliffe Hospital

Professor Tony Avery, Professor of Primary Health Care, University of Nottingham

Professor Iain T Cameron, Professor of Obstetrics & Gynaecology, University of Southampton

Mr Peter Cardy, Chief Executive, Macmillan Cancer Relief, London

Dr Christopher Cates, GP and Cochrane Editor, Bushey Health Centre, Bushey, Herts.

Mr Charles Dobson, Special Projects Adviser, Department of Health

Dr Robin Ferner, Consultant Physician and Director, West Midlands Centre for Adverse Drug Reactions, City Hospital NHS Trust, Birmingham

Dr Karen A Fitzgerald, Pharmaceutical Adviser, Bro Taf Health Authority, Cardiff

Professor Alastair Gray, Professor of Health Economics, Institute of Health Sciences, University of Oxford

Mrs Sharon Hart, Managing Editor, *Drug & Therapeutics Bulletin*, London

Dr Christine Hine, Consultant in Public Health Medicine, Bristol South & West Primary Care Trust

Professor Robert Peveler, Professor of Liaison Psychiatry, Royal South Hants Hospital, Southampton

Dr Frances Rotblat, CPMP Delegate, Medicines Control Agency, London

Mrs Katrina Simister, New Products Manager, National Prescribing Centre, Liverpool

Dr Ken Stein, Senior Lecturer in Public Health, University of Exeter

Professor Terence Stephenson, Professor of Child Health, University of Nottingham

Dr Richard Tiner, Medical Director, Association of the British Pharmaceutical Industry, London

Professor Dame Jenifer Wilson-Barnett, Head of Florence Nightingale School of Nursing & Midwifery, King's College, London

Therapeutic Procedures Panel

Members

Chair,
Professor Bruce Campbell,
Consultant Vascular and General Surgeon, Royal Devon & Exeter Hospital

Dr Mahmood Adil, Head of Clinical Support & Health Protection, Directorate of Health and Social Care (North), Department of Health, Manchester

Professor John Bond, Head of Centre for Health Services Research, University of Newcastle upon Tyne

Mr Michael Clancy, Consultant in A & E Medicine, Southampton General Hospital

Dr Carl E Counsell, Senior Lecturer in Neurology, University of Aberdeen

Dr Keith Dodd, Consultant Paediatrician, Derbyshire Children's Hospital, Derby

Professor Gene Feder, Professor of Primary Care R&D, Barts & the London, Queen Mary's School of Medicine and Dentistry, University of London

Ms Bec Hanley, Freelance Consumer Advocate, Hurstpierpoint, West Sussex

Professor Alan Horwich, Director of Clinical R&D, The Institute of Cancer Research, London

Dr Phillip Leech, Principal Medical Officer for Primary Care, Department of Health, London

Mr George Levvy, Chief Executive, Motor Neurone Disease Association, Northampton

Professor James Lindesay, Professor of Psychiatry for the Elderly, University of Leicester

Dr Mike McGovern, Senior Medical Officer, Heart Team, Department of Health, London

Dr John C Pounsford, Consultant Physician, North Bristol NHS Trust

Professor Mark Sculpher, Professor of Health Economics, Institute for Research in the Social Services, University of York

Dr L David Smith, Consultant Cardiologist, Royal Devon & Exeter Hospital

Professor Norman Waugh, Professor of Public Health, University of Aberdeen

Expert Advisory Network

Members

Mr Gordon Aylward,
Chief Executive,
Association of British Health-Care Industries, London

Ms Judith Brodie,
Head of Cancer Support Service, Cancer BACUP, London

Mr Shaun Brogan,
Chief Executive, Ridgeway Primary Care Group, Aylesbury, Bucks

Ms Tracy Bury,
Project Manager, World Confederation for Physical Therapy, London

Mr John A Cairns,
Professor of Health Economics, Health Economics Research Unit, University of Aberdeen

Professor Howard Stephen Cuckle,
Professor of Reproductive Epidemiology, Department of Paediatrics, Obstetrics & Gynaecology, University of Leeds

Professor Nicky Cullum,
Director of Centre for Evidence Based Nursing, University of York

Dr Katherine Darton,
Information Unit, MIND – The Mental Health Charity, London

Professor Carol Dezateux,
Professor of Paediatric Epidemiology, London

Professor Martin Eccles,
Professor of Clinical Effectiveness, Centre for Health Services Research, University of Newcastle upon Tyne

Professor Pam Enderby,
Professor of Community Rehabilitation, Institute of General Practice and Primary Care, University of Sheffield

Mr Leonard R Fenwick,
Chief Executive, Newcastle upon Tyne Hospitals NHS Trust

Professor David Field,
Professor of Neonatal Medicine, Child Health, The Leicester Royal Infirmary NHS Trust

Mrs Gillian Fletcher,
Antenatal Teacher & Tutor and President, National Childbirth Trust, Henfield, West Sussex

Ms Grace Gibbs,
Deputy Chief Executive, Director for Nursing, Midwifery & Clinical Support Servs., West Middlesex University Hospital, Isleworth, Middlesex

Dr Neville Goodman,
Consultant Anaesthetist, Southmead Hospital, Bristol

Professor Robert E Hawkins,
CRC Professor and Director of Medical Oncology, Christie CRC Research Centre, Christie Hospital NHS Trust, Manchester

Professor F D Richard Hobbs,
Professor of Primary Care & General Practice, Department of Primary Care & General Practice, University of Birmingham

Professor Allen Hutchinson,
Director of Public Health & Deputy Dean of ScHARR, Department of Public Health, University of Sheffield

Professor Rajan Madhok,
Medical Director & Director of Public Health, Directorate of Clinical Strategy & Public Health, North & East Yorkshire & Northern Lincolnshire Health Authority, York

Professor David Mant,
Professor of General Practice, Department of Primary Care, University of Oxford

Professor Alexander Markham,
Director, Molecular Medicine Unit, St James's University Hospital, Leeds

Dr Chris McCall,
General Practitioner, The Hadleigh Practice, Castle Mullen, Dorset

Professor Alistair McGuire,
Professor of Health Economics, London School of Economics

Dr Peter Moore,
Freelance Science Writer, Ashtead, Surrey

Dr Andrew Mortimore,
Consultant in Public Health Medicine, Southampton City Primary Care Trust

Dr Sue Moss,
Associate Director, Cancer Screening Evaluation Unit, Institute of Cancer Research, Sutton, Surrey

Professor Jon Nicholl,
Director of Medical Care Research Unit, School of Health and Related Research, University of Sheffield

Mrs Julietta Patnick,
National Co-ordinator, NHS Cancer Screening Programmes, Sheffield

Professor Chris Price,
Visiting Chair – Oxford, Clinical Research, Bayer Diagnostics Europe, Cirencester

Ms Marianne Rigge,
Director, College of Health, London

Professor Sarah Stewart-Brown,
Director HSRU/Honorary Consultant in PH Medicine, Department of Public Health, University of Oxford

Professor Ala Szczepura,
Professor of Health Service Research, Centre for Health Services Studies, University of Warwick

Dr Ross Taylor,
Senior Lecturer, Department of General Practice and Primary Care, University of Aberdeen

Mrs Joan Webster,
Consumer member, HTA – Expert Advisory Network

Feedback

The HTA Programme and the authors would like to know your views about this report.

The Correspondence Page on the HTA website (http://www.ncchta.org) is a convenient way to publish your comments. If you prefer, you can send your comments to the address below, telling us whether you would like us to transfer them to the website.

We look forward to hearing from you.

The National Coordinating Centre for Health Technology Assessment,
Mailpoint 728, Boldrewood,
University of Southampton,
Southampton, SO16 7PX, UK.
Fax: +44 (0) 23 8059 5639 Email: hta@soton.ac.uk
http://www.ncchta.org

ISSN 1366-5278