National Institute for Health and Clinical Excellence

Cholelithiasis and cholecystitis
Scope Consultation Table
23rd November 2012 – 17th January 2013

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	AABGI	1	1	The AABGI has no comment.	Thank you for your comment.
SH	BAPES	1	4.1.1 Is the population to be covered in section 4.1.1 appropriate and correct?	4.1.2 Groups that will not be covered a) Children and young people, as cholelithiasis and cholecystitis in this group are rare and have a different aetiology to the adult condition. As a Paediatric surgeon most of the dozen or so cases a year that I operate on are obese adolescents. This is increasingly more common in the under 18 yrs age group. Perhaps the scope should include young people and adolescents?. See J Pediatr Gastroenterol Nutr. 2012 Sep;55(3):328-33. doi: 10.1097/MPG.0b013e31824d256f. Pediatric obesity and gallstone disease. Koebnick C, Smith N, Black MH, Porter AH, Richie BA, Hudson S, Gililland D, Jacobsen SJ, Longstreth GF. Abstract OBJECTIVES:	Thank you for your comment. Although cholelithiasis in children and young people is important and a potentially increasing problem, it is relatively rare and therefore will not be included in the guideline.

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				The aim of the present study was to investigate the association between childhood and adolescent obesity, the risk of gallstones, and the potential effect modification by oral contraceptive use in girls. METHODS: For this population-based cross-sectional study, measured weight and height, oral contraceptive use, and diagnosis of cholelithiasis or choledocholithiasis were extracted from the electronic medical records of 510,816 patients ages 10 to 19 years enrolled in an integrated health plan, 2007-2009. RESULTS: We identified 766 patients with gallstones. The adjusted odds ratios (95% CI) of gallstones for under-/normal-weight (reference), overweight, moderate obesity, and extreme obesity in boys were 1.00, 1.46 (0.94%-2.27%), 1.83 (1.17%-2.85%), and 3.10 (1.99%-4.83%) and in girls were 1.00, 2.73 (2.18%-3.42%), 5.75 (4.62%-7.17%), and 7.71 (6.13%-9.71%), respectively (P for interaction sex × weight class <0.001). Among girls, oral contraceptive use was associated with higher odds for gallstones (odds	

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				ratio 2.00, 95% CI 1.66%-2.40%). Girls who used oral contraceptives were at higher odds for gallstones than their counterparts in the same weight class who did not use oral contraceptives (P for interaction weight class × oral contraceptive use 0.023). CONCLUSIONS: Due to the shift toward extreme childhood obesity, especially in minority children, pediatricians can expect to face increasing numbers of children and adolescents affected by gallstone disease.	
SH	Boston Scientific	1	4.3.1 Are the key issues to be covered in section 4.3.1(a-d) appropriate and correct?	We can include difficult stone management requiring repeat ERCP, or persistent stone disease that has been previously treated with standard lithotripsy methods and failed.	Thank you for your comment. This issue will be covered in the review questions about diagnosis and interventions.
SH	Boston Scientific	2	4.3.1 What interventions for the management of cholelithiasis and cholecystitis should be included in the guideline? See section 4.3.1 (c)	Single Operator Cholangioscopy (with SpyGlass) with the use of Laser or EHL for Lithotripsy should be considered as a step in the patient pathway in patients with prior failed ductal stone clearance at ERCP.	Thank you for your comment. This will be included in the guideline if published evidence on the intervention is available during guideline development.
SH	Boston	3	4.4	Symptomatic stones remaining post	Thank you for your comment.

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	Scientific		Are the outcomes in section 4.4.appropriate and correct?	cholecystectomy or stones migrated to the CBD after the elective LC. They will require ERCP and few of them will fail by conventional lithotripsy and will need single operator cholangioscopy (SpyGlass) with EHL or laser	Stones remaining post cholecystectomy or migrated stones will be included as an outcome if studies report them. The scope has been amended to make this clearer. It is not possible to recommend how to deal with remaining or migrated stones without first reviewing the evidence. Recommendations about specific interventions may or may not be made, depending on the evidence available.
SH	Boston Scientific	4	4.5 Are the review questions in section 4.5 appropriate and correct?	4.5.3. b What is the relative effectiveness of different types of interventions? Single Operator Cholangioscopy with EHL or laser lithotripsy should be included in the list. Evidence in available from an international registry, single-center case-series and UK NHS experience	Thank you for your comment. This will be included in the guideline if published evidence is available during guideline development.
SH	British Infection Association		4.3.1 Are the key issues to be covered in section 4.3.1(a-d) appropriate and correct?	We would like to see the following included: 1. prevalence of infection 2. type of organisms involved 3. choice of therapeutic (including IV vs PO) as well as prophylactic antibiotics 4. duration of antibiotic treatment or prophylaxis There is limited literature to guide clinicians on duration of antibiotics in many types of	Thank you for your comment. Specific guidance about organisms, duration and choice of antibiotics will not be included in this guideline. However, infection as an adverse event relating to a therapeutic intervention and prophylactic use of antibiotics will be included in the guideline.

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				abdominal or surgical infections and we think there should be production of more in order to help consistency of practice across the country.	Guidance regarding surgical site infection is provided by the Surgical site infection guideline CG74.
SH	Department of Health	1	10 Please insert the section number that your comment relates to (e.g 3.1.1), or state 'general' if your comment is in relation to the whole document.	It will be very helpful to have guidance particularly on timing of cholecystectomy and also on when not to intervene e.g. for 'silent gallstone disease' and also some guidance for commissioners on how to tackle variation across the country which is significant (see Atlas of Variation vol 1). Some of the scope here is too narrow and will not help guide clinicians for some of the more common problems in this arena. Examples are: a) exclusion of children/teenagers: transition to adulthood is a clinical grey zone but as most of the expertise for this condition is in the adult services, they need some guidance on dealing with the older children or younger adults who may present. This most often occurs because of hemolytic syndromes (causing pigment gallstones) e.g. hereditary spherocytosis etc, and these most commonly present as teenagers and this should be included in the aetiology list. More frequently now we are also seeing gallstones in older children due to obesity and this needs to be addressed.	Thank you for your comments. With regarding to timing of cholecystectomy and when not to intervene- this will be covered in the guideline. With regards to children and teenagers- although cholelithiasis in children and young people is important and a potentially increasing problem, it is relatively rare and therefore will not be included in the guideline. With regards to comorbidity- this is included in the guideline in intervention review question. With regards to cholecystitis and choledocholithiasis- both are included in the guideline and relevant management

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				b) co-morbidity is a very significant problem in this group of patients - they frequently are obese or have diabetes or heart disease. Age is a particular concern because risks escalate but it would be helpful to have an evidence review to delineate the relative risk of age v co-morbidity to help with decisions; c) a distinction should be made between the different presentations and how they are dealt with - some are due to gall bladder symptoms (cholecystitis) and some are due to stones that have migrated to the bile duct (common bile duct stones or choledocholithiasis, cause jaundice, pancreatitis or cholangitis which stones otherwise do not do). These latter can be dealt with by surgery, endoscopy or a combination of both - see attached article; d) post-cholecystectomy syndromes are a significant problem for clinicians and some patients and there is a real lack of guidance on this - practice in USA where any evidence comes from is very different to UK practice. This includes sphincter of Oddi dysfunction (SOD) and I think should be included in the scope of this guidance; e) specific guidance on type of surgery (e.g.	strategies will be reviewed. With regards to post cholecystectomy syndrome- this will be included as part of the outcomes of surgical intervention, along with other adverse effects. With regards to open vs laparoscopic surgery- it is envisioned that this will be covered in the review question concerning surgical intervention.

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				laparoscopic v traditional) is very important.	
SH	Johnson & Johnson	1	4.1.1 Is the population to be covered in section 4.1.1 appropriate and correct?	Johnson & Johnson (J&J) agree that the population covered in section 4.1.1 is entirely appropriate and correct.	Thank you for your comment.
SH	Johnson & Johnson	2	4.1.1 Are there any other subgroups that should be added to section 4.1.1	J&J do not believe that there are additional subgroups to be added to section 4.1.1	Thank you for your comment.
SH	Johnson & Johnson	3	4.1.2 Are there any other populations that should be excluded in section 4.1.2?	J&J do not believe that there are additional populations to be added to section 4.1.2	Thank you for your comment.
SH	Johnson & Johnson	4	4.2 Are the settings to be covered in section 4.2 appropriate and correct?	J&J support all settings in which NHS care is received to be in the scope.	Thank you for your comment.

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SH	Johnson & Johnson	5	4.3.1 Are the key issues to be covered in section 4.3.1(a-d) appropriate and correct?	J&J agree that the key issues covered in section 4.3.1 (a-d) are appropriate and correct.	Thank you for your comment.
SH	Johnson & Johnson	6	4.3.1 What interventions for the management of cholelithiasis and cholecystitis should be included in the guideline? See section 4.3.1 (c)	J&J agree on the interventions to be included in the guideline for cholelithiasis and cholecystitis set out in section 4.3.1	Thank you for your comment.
SH	Johnson & Johnson	7	4.3.2 Are the clinical issues to be excluded in section 4.3.2 (a-d) appropriate and correct?	J&J agree with the clinical issues set to be excluded in section 4.3.2	Thank you for your comment.
SH	Johnson & Johnson	8	5 Should a distinction be made between	J&J do not wish to comment.	Thank you for your comment.

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			calculus cholecystitis (cholecystitis caused by cholelithiasis) and acalculous cholecystis (cholecystitis caused by acute illness, damage or infection, rather than cholelithiasis), and should patients with acalculous cholecystitis be excluded from the guideline, since this condition has a distinct aetiology, pathology and prognosis in comparison to calculous cholecystitis?		
SH	Johnson & Johnson	9	6 Is it appropriate to exclude comparisons of sub types of interventions (such as comparing different types of surgical	J&J seek further clarity on surgery guidance as set out in "Any Other Comments". Added below With regard to the role of cholecystectomy in the treatment guideline for cholelithiasis and	Thank you for your comment. It is envisioned that this will be covered in the review questions. We cannot advocate an approach without first reviewing the evidence. Only then can it be agreed whether laparoscopic surgery should be recommended.

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			management) from the guideline?	cholecystitis: J&J request NICE to recognise the system benefit of reduction in hospital stay associated with laparoscopic surgery and thus recommend a laparoscopic approach in the first instance when clinically appropriate. Additionally, J&J would ask that NICE does not contradict other areas of public policy such as hospital reimbursement through the established "best-practice" tariff for laparoscopic day case cholecystectomy set out in payment by results. **The Cochrane Collaboration review: Laparoscopic versus open cholecystectomy for patients with symptomatic cholecystolithiasis** comprising thirty-eight trials, randomised 2338 patients reported no significant differences were observed in mortality, complications and operative time between laparoscopic and open cholecystectomy. Laparoscopic cholecystectomy is associated with a significantly shorter hospital stay and a quicker convalescence compared with the classical open cholecystectomy.	
SH	Johnson & Johnson	10	4.4 Are the main outcomes to be reviewed in Section 4.4(a-g) appropriate and correct? Are	J&J agree that the main outcomes to be reviewed are appropriate and correct.	Thank you for your comment.

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			there any additional outcomes that should be included?		
SH	Johnson & Johnson	11	4.4 Are the outcomes in section 4.4.appropriate and correct?	J&J agree that the main outcomes to be reviewed are appropriate and correct.	Thank you for your comment.
SH	Johnson & Johnson	12	4.5 Are the review questions in section 4.5 appropriate and correct?	J&J believe the review questions to be appropriate and correct.	Thank you for your comment.
SH	Johnson & Johnson	13	7 Is it necessary to have review questions on suspecting and diagnosing cholelithiasis and cholecystitis? Is this an area needing guidance?	J&J do not wish to comment	Thank you for your comment.
SH	Johnson & Johnson	14	8	J&J do not wish to comment	Thank you for your comment.

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			Should there be an additional review question on how to identify people with cholecystitis for whom surgery is not appropriate?		
SH	Johnson & Johnson	15	9 Are there any additional review questions that should be covered by the guideline?	J&J do not wish to comment	Thank you for your comment.
SH	Johnson & Johnson	16	10 Please insert the section number that your comment relates to (e.g 3.1.1), or state 'general' if your comment is in relation to the whole document.	With regard to the role of cholecystectomy in the treatment guideline for cholelithiasis and cholecystitis: J&J request NICE to recognise the system benefit of reduction in hospital stay associated with laparoscopic surgery and thus recommend a laparoscopic approach in the first instance when clinically appropriate. Additionally, J&J would ask that NICE does not contradict other areas of public policy such as hospital reimbursement through the established "best-practice" tariff for laparoscopic day case cholecystectomy set out in payment by results. The Cochrane Collaboration review:	Thank you for your comment. It is envisioned that this will be covered in the review question concerning surgical intervention. We cannot advocate an approach without first reviewing the evidence. Only then can it be agreed whether laparoscopic surgery should be recommended.

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				Laparoscopic versus open cholecystectomy for patients with symptomatic cholecystolithiasis comprising thirty-eight trials, randomised 2338 patients reported no significant differences were observed in mortality, complications and operative time between laparoscopic and open cholecystectomy. Laparoscopic cholecystectomy is associated with a significantly shorter hospital stay and a quicker convalescence compared with the classical open cholecystectomy.	
SH	RCN		4.1.1 Are there any other subgroups that should be added to section 4.1.1	No	Thank you for your comment.
SH	RCN		4.1.1 Is the population to be covered in section 4.1.1 appropriate and correct?	Yes, it seems appropriate	Thank you for your comment.
SH	RCN		4.1.2 Are there any other populations that should be excluded in	No	Thank you for your comment.

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			section 4.1.2?		
SH	RCN		4.2 Are the settings to be covered in section 4.2 appropriate and correct?	Yes	Thank you for your comment.
SH	RCN		4.3.1 What interventions for the management of cholelithiasis and cholecystitis should be included in the guideline? See section 4.3.1 (c)	None that we know of other than what is mentioned	Thank you for your comment.
SH	RCN		4.3.2 Are the clinical issues to be excluded in section 4.3.2 (a-d) appropriate and correct?	Yes, seems appropriate	Thank you for your comment.
SH	RCN		4.4 Are the main	Perhaps should include complications of endoscopic / radiological intervention	Thank you for your comment. Complications of any intervention are included in the guideline; the scope has

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			outcomes to be reviewed in Section 4.4(a-g) appropriate and correct? Are there any additional outcomes that should be included?		been amended to reflect this more clearly.
SH	RCN		4.4 Are the outcomes in section 4.4.appropriate and correct?	Perhaps should include complications of endoscopic / radiological intervention	Thank you for your comment. Complications of any intervention are included in the guideline. The scope has been amended to reflect this more clearly.
SH	RCN		4.5 Are the review questions in section 4.5 appropriate and correct?	Yes, seem appropriate	Thank you for your comment.
SH	RCN		5 Should a distinction be made between calculus cholecystitis (cholecystitis caused by cholelithiasis) and acalculous cholecystis	Yes, a distinction should be made and should be kept separate. Acalculous should not be excluded, just dealt with separately.	Thank you for your comment. Following comments from other stakeholders and discussion with clinical advisers a decision has been made to exclude cholecystitis that is secondary to another condition such as critical/traumatic illness. This is because this condition is rare and has a different aetiology to cholecystitis caused by cholelithiasis. We will include

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			(cholecystitis caused by acute illness, damage or infection, rather than cholelithiasis), and should patients with acalculous cholecystitis be excluded from the guideline, since this condition has a distinct aetiology, pathology and prognosis in comparison to calculous cholecystitis?		cholecystitis presumed to be caused by cholelithiasis regardless of whether cholelithiasis can be found during investigations.
SH	RCN		6 Is it appropriate to exclude comparisons of sub types of interventions (such as comparing different types of surgical management) from the guideline?	Yes	Thank you for your comment. After comments from other stakeholders and discussions with clinical experts, a decision has been made to include comparisons of different types of intervention (such as open vs laparascopic surgery or pharmacological vs percutaneous interventions). The guideline will not compare specific techniques or sub-types of interventions (such as single incision laparoscopic surgery vs robot assisted laparoscopic surgery or opioids vs non opioid pharmacological interventions).

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SH	RCN		7 Is it necessary to have review questions on suspecting and diagnosing cholelithiasis and cholecystitis? Is this an area needing guidance?	No, do not think so	Thank you for your comment.
SH	RCN		8 Should there be an additional review question on how to identify people with cholecystitis for whom surgery is not appropriate?	Yes, but should be included in Diagnosis (4.5.1) section	Thank you for your comment.
SH	RCN		9 Are there any additional review questions that should be covered by the guideline?	We do not know of any at this stage	Thank you for your comment.

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SH	RCN		10 Please insert the section number that your comment relates to (e.g 3.1.1), or state 'general' if your comment is in relation to the whole document.	No	Thank you for your comment.
SH	Royal College of General Practitioners	1	4.1.1 Are there any other subgroups that should be added to section 4.1.1	Non verbal patients, particularly those with learning disabilities may present with challenging behaviour rather than typical symptoms and signs Pregnant women with cholecystitis	Thank you for your comment. Treating and managing non verbal patients, particularly those with learning disabilities, is a challenge across all health conditions. This specific challenge should be dealt with in its entirety across the NHS rather than just specific to cholelithiasis and cholecystitis. Thank you for suggesting pregnant women as a potential subgroup. We will pay particular attention to all potential subgroups during the evidence reviews, and if supported by robust evidence, the GDG will make specific considerations for recommendations where appropriate.

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					Please note that the Patient experience guideline (CG138) will support this guideline.
SH	Royal College of General Practitioners	2	4.3.1 What interventions for the management of cholelithiasis and cholecystitis should be included in the guideline? See section 4.3.1 (c)	Lifestyle issues in preventing recurrence in patients treated conservatively. The increased use of CT in acute abdominal pain in admissions to hospital is not as sensitive or specific diagnostically as ultrasound and may miss cholecystitis in acalculous cholecystitis. There are concerns about the high level of radiation in young people	Thank you for your comment. A new review question has been added which will focus on identifying the information and education needs of patients diagnosed with cholelithiasis and cholecystitis. It is anticipated that evidence relating to preventive lifestyle factors will be reviewed here. Diagnostic outcomes were not specifically listed in the scope, but they will be included in the relevant evidence reviews. The scope has been amended to reflect this more clearly.
SH	Royal College of General Practitioners	3	5 Should a distinction be made between calculus cholecystitis (cholecystitis caused by cholelithiasis) and acalculous cholecystis	Both should be included in the guideline	Thank you for your comment. Following comments from other stakeholders and discussion with clinical advisers a decision has been made to exclude cholecystitis that is secondary to another condition such as critical/traumatic illness. This is because this condition is rare and has a different aetiology to cholecystitis caused by cholelithiasis. We will include

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			(cholecystitis caused by acute illness, damage or infection, rather than cholelithiasis), and should patients with acalculous cholecystitis be excluded from the guideline, since this condition has a distinct aetiology, pathology and prognosis in comparison to calculous cholecystitis?		cholecystitis presumed to be caused by cholelithiasis regardless of whether cholelithiasis can be found during investigations.
SH	Royal College of General Practitioners	4	6 Is it appropriate to exclude comparisons of sub types of interventions (such as comparing different types of surgical management) from the guideline?	No	Thank you for your comment. After comments from other stakeholders and discussions with clinical experts, a decision has been made to include comparisons of different types of intervention (such as open vs laparascopic surgery or pharmacological vs percutaneous interventions). The guideline will not compare specific techniques or sub-types of interventions (such as single incision laparoscopic surgery vs robot assisted laparoscopic surgery or opioids vs non opioid pharmacological interventions).

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SH	Royal College of General Practitioners	5	4.4 Are the main outcomes to be reviewed in Section 4.4(a-g) appropriate and correct? Are there any additional outcomes that should be included?	Recovery time, postoperative care and time to return to work	Thank you for your comment. Outcomes relating to recovery time and postoperative care will be included in the guideline and these outcomes have been added to the scope. Return to work will not be included as an outcome in this guideline. This is because this measure is related to other outcomes that are already included (i.e. recovery time) and also NICE does not consider costs to the individual in the health economic evaluation of an intervention.
SH	Royal College of General Practitioners	6	7 Is it necessary to have review questions on suspecting and diagnosing cholelithiasis and cholecystitis? Is this an area needing guidance?	Yes particularly in people with learning disability	Thank you for your comment. A review question on suspecting and diagnosing cholelithiasis and cholecystitis will be included in the guideline.
SH	Salford Royal NHS Foundation	1	4.1.1	4.1.1 a: Yes. Does cholelithiasis refers to stone disease of the	Thank you for your comment. Following comments from other

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	Trust		Is the population to be covered in section 4.1.1 appropriate and correct?	entire biliary tree (bile ducts and gallbladder) or just the gallbladder? I am not convinced that acalculous cholecystitis should be included. See comment to question 5. Added I personally believe that acalculous cholecystitis should be excluded as it is separate disease. Concentrating on stone disease of the biliary tree and its management would allow for a more focused guideline. Potentially worth considering a distinctly separate guideline on the topic of acalculous cholecystitis?	stakeholders and discussion with clinical advisers, a decision has been made to include stone disease of the entire biliary tree, and the scope has been amended to reflect this. The guideline will not cover cholecystitis that is caused by illness, injury or infection as this condition is rare and has a different aetiology to cholecystitis caused by cholelithiasis.
SH	Salford Royal NHS Foundation Trust	2	4.1.1 Are there any other subgroups that should be added to section 4.1.1	No	Thank you for your comment.
SH	Salford Royal NHS Foundation Trust	3	4.1.2 Are there any other populations that should be excluded in	No	Thank you for your comment.

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			section 4.1.2?		
SH	Salford Royal NHS Foundation Trust	4	4.2 Are the settings to be covered in section 4.2 appropriate and correct?	Yes	Thank you for your comment.
SH	Salford Royal NHS Foundation Trust	5	4.3.1 Are the key issues to be covered in section 4.3.1(a-d) appropriate and correct?	Yes	Thank you for your comment.
SH	Salford Royal NHS Foundation Trust	6	4.3.1 What interventions for the management of cholelithiasis and cholecystitis should be included in the guideline? See section 4.3.1 (c)	• Surgical: cholecystectomy and bile duct exploration • Merits of on table cholangiogram and laparoscopic ultrasound at time of cholecystectomy? • Therapeutic ERCP, including discussion of various therapeutic interventions: o balloon sphincteroplasty o mechanical lithotripsy o electrohydraulic lithotripsy o Role of ERCP in management of post cholecystectomy bile leaks? o Discuss role of transampullary	Thank you for your comment. The interventions listed will be included in the guideline if published evidence is available during guideline development.

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				stenting of the gallbladder? • Explore relative merits of laparoscopic bile duct exploration vs ERCP • Radiological percutaneous cholecystotomy • Percutaneous biliary interventions	
SH	Salford Royal NHS Foundation Trust	7	4.3.2 Are the clinical issues to be excluded in section 4.3.2 (a-d) appropriate and correct?	4.3.2a I assume the remit does include the management of choledocholithiasis (stones in the bile duct) however?	Thank you for your comment. Following comments from other stakeholders and discussions with clinical advisers, a decision has been made to include choledocholithiasis. The scope has been amended to reflect this.
SH	Salford Royal NHS Foundation Trust	8	5 Should a distinction be made between calculus cholecystitis (cholecystitis caused by cholelithiasis) and acalculous cholecystis (cholecystitis caused by acute illness, damage or infection,	I personally believe that acalculous cholecystitis should be excluded as it is separate disease. Concentrating on stone disease of the biliary tree and its management would allow for a more focused guideline. Potentially worth considering a distinctly separate guideline on the topic of acalculous cholecystitis?	Thank you for your comment. Following comments from other stakeholders and discussion with clinical advisers a decision has been made to exclude cholecystitis that is secondary to another condition such as critical/traumatic illness This is because this condition is rare and has a different aetiology to cholecystitis caused by cholelithiasis. We will include cholecystitis presumed to be caused by cholelithiasis regardless of whether cholelithiasis can be found during

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			rather than cholelithiasis), and should patients with acalculous cholecystitis be excluded from the guideline, since this condition has a distinct aetiology, pathology and prognosis in comparison to calculous cholecystitis?		investigations.
SH	Salford Royal NHS Foundation Trust	9	6 Is it appropriate to exclude comparisons of sub types of interventions (such as comparing different types of surgical management) from the guideline?	Sub types of interventions should be compared in my opinion. For example: • Comparisons of imaging modalities for diagnosis(transabdominal ultrasound, CT, MRCP, endoscopic ultrasound, radionuclide studies) • cholecystectomy vs percutaneous cholecystotomy in medically unfit patients • relative merits of ERCP + interval cholecystectomy vs combined laparosocopic cholecystectomy and bile duct exploration (if management of choledocholithiasis to be explored).	Thank you for your comment. After comments from other stakeholders and discussions with clinical experts, it is expected that comparisons of imaging modalities will be included in the guideline (as part of a diagnostic review question), and a comparison of surgical and non-surgical interventions will also be included in the guideline. Combinations of interventions (such as combined laparoscopic cholecystectomy with bile duct exploration) will be included if evidence is found about the combinations.

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SH	Salford Royal NHS Foundation Trust	11	4.4 Are the outcomes in section 4.4.appropriate and correct?	Yes.	Thank you for your comment.
SH	Salford Royal NHS Foundation Trust	12	4.5 Are the review questions in section 4.5 appropriate and correct?	yes	Thank you for your comment.
SH	Salford Royal NHS Foundation Trust	13	7 Is it necessary to have review questions on suspecting and diagnosing cholelithiasis and cholecystitis? Is this an area needing guidance?	yes	Thank you for your comment. A review question on suspecting and diagnosing cholelithiasis and cholecystitis will be included in the guideline.
SH	Salford Royal NHS Foundation Trust	14	8 Should there be an additional review	yes	Thank you for your comment. After comments from other stakeholders and discussions with clinical experts, a decision has been made not to include a

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			question on how to identify people with cholecystitis for whom surgery is not appropriate?		specific question on identifying people for whom surgery is not appropriate. This is because there are many reasons why surgery may not be appropriate, and these reasons are not specific to the issue of cholecystitis. Therefore recommendations about identifying people for whom surgery is inappropriate will not be made if no evidence is found. However, if on searching the evidence it is highlighted that people with cholecystitis have specific factors that impact on the decision to operate or not, these will be discussed by the GDG who will decide if recommendations should be made.
SH	Salford Royal NHS Foundation Trust	15	9 Are there any additional review questions that should be covered by the guideline?	Management of bile duct calculi?	Thank you for your comment. Patients with asymptomatic stones in their bile duct are included in the guideline and will be covered by all review questions. Therefore it is not necessary to have a specific review question for this patient group.
SH	Salford Royal NHS Foundation Trust	16	10 Please insert the section number that your comment relates to (e.g 3.1.1), or state 'general' if your comment is in relation	General. It is unclear whether the scope of this review includes the management of stones in the bile duct, in addition to stones in the gallbladder. It would seem a missed opportunity if it does not include management of choledocholithiasis.	Thank you for your comment. Following comments from other stakeholders and discussions with clinical advisers, a decision has been made to include choledocholithiasis. The scope has been amended to reflect this.

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			to the whole document.		
SH	University Hospitals Leicester	1	4.1.1 Is the population to be covered in section 4.1.1 appropriate and correct?	Yes	Thank you for your comment.
SH	University Hospitals Leicester	2	4.1.1 Are there any other subgroups that should be added to section 4.1.1	Yes – some patients present with jaundice	Thank you for your comment. Jaundice is a presenting feature rather than a patient subgroup. This group will not be added to the scope, but this group of patients will be included in the evidence review.
SH	University Hospitals Leicester	3	4.1.2 Are there any other populations that should be excluded in section 4.1.2?	Yes – patients with stones in the common bile duct	Thank you for your comment. Following comments from other stakeholders and discussion with clinical advisers, a decision has been made to include stone disease of the entire biliary tree, and the scope has been amended to reflect this.
SH	University Hospitals Leicester	4	4.2 Are the settings to be covered in section 4.2	Yes	Thank you for your comment.

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			appropriate and correct?		
SH	University Hospitals Leicester	5	4.3.1 Are the key issues to be covered in section 4.3.1(a-d) appropriate and correct?	Yes	Thank you for your comment.
SH	University Hospitals Leicester	6	4.3.1 What interventions for the management of cholelithiasis and cholecystitis should be included in the guideline? See section 4.3.1 (c)	About 10% - 15% of patients with acute cholecytitis present with jaundice which may be due to oedema around the bile duct but also may be due to stones in the bile duct. The latter group have to have an ERCP. These could be excluded from this study.	Thank you for your comment. Following comments from other stakeholders and discussion with clinical advisers, a decision has been made to include stone disease of the entire biliary tree, and the scope has been amended to reflect this.
SH	University Hospitals Leicester	7	4.3.2 Are the clinical issues to be excluded in section 4.3.2 (a-d) appropriate and correct?	Yes	Thank you for your comment.
SH	University Hospitals Leicester	8	5 Should a distinction be made between calculus cholecystitis	Yes. Acalculous cholecystitis should be assessed separately because the aetiology is different but also because surgeons are more reluctant to operate in the absence of gall stones.	Thank you for your comment. Following comments from other stakeholders and discussion with clinical advisers a decision has been made to exclude cholecystitis that is secondary to

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			(cholecystitis caused by cholelithiasis) and acalculous cholecystis (cholecystitis caused by acute illness, damage or infection, rather than cholelithiasis), and should patients with acalculous cholecystitis be excluded from the guideline, since this condition has a distinct aetiology, pathology and prognosis in comparison to calculous cholecystitis?		another condition such as critical/traumatic illness. This is because this condition is rare and has a different aetiology to cholecystitis caused by cholelithiasis. We will include cholecystitis presumed to be caused by cholelithiasis regardless of whether cholelithiasis can be found during investigations.
SH	University Hospitals Leicester	9	6 Is it appropriate to exclude comparisons of sub types of interventions (such as comparing different types of surgical management) from	Yes	Thank you for your comment. After comments from other stakeholders and discussions with clinical experts, a decision has been made to include comparisons of different types of intervention (such as open vs laparascopic surgery or pharmacological vs percutaneous interventions). The guideline

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			the guideline?		will not compare specific techniques or sub-types of interventions (such as single incision laparoscopic surgery vs robot assisted laparoscopic surgery or opioids vs non opioid pharmacological interventions).
SH	University Hospitals Leicester	10	4.4 Are the main outcomes to be reviewed in Section 4.4(a-g) appropriate and correct? Are there any additional outcomes that should be included?	Outcomes are acceptable	Thank you for your comment.
SH	University Hospitals Leicester	11	7 Is it necessary to have review questions on suspecting and diagnosing cholelithiasis and cholecystitis? Is this an area needing guidance?	Yes. Because many patients have asymptomatic gallstones this group is different from those with cholecytitis. Also some patients have stones in the bile duct – another separate group which needs identifying.	Thank you for your comment. A review question on suspecting and diagnosing cholelithiasis (in the gallbladder and/or bile duct) and cholecystitis will be included in the guideline.
SH	University Hospitals Leicester	12	8	Yes – although this could be brief.	Thank you for your comment. After comments from other stakeholders

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			Should there be an additional review question on how to identify people with cholecystitis for whom surgery is not appropriate?		and discussions with clinical experts, a decision has been made not to include a specific question on identifying people for whom surgery is not appropriate. This is because there are many reasons why surgery may not be appropriate, and these reasons are not specific to the issue of cholecystitis. Therefore recommendations about identifying people for whom surgery is inappropriate will not be made if no evidence is found. However, if on searching the evidence it is highlighted that people with cholecystitis have specific factors that impact on the decision to operate or not, these will be discussed by the GDG who will decide if recommendations should be made.
SH	University Hospitals Leicester	13	9 Are there any additional review questions that should be covered by the guideline?	As I have mentioned – patients with asymptomatic stones in their bile duct.	Thank you for your comment. Patients with asymptomatic stones in their bile duct are included in the guideline and will be covered by all review questions. Therefore it is not necessary to have a specific review question for this patient group.

These organisations were approached but did not respond:

Aintree University Hospital NHS Foundation Trust
Airedale NHS Trust
Allocate Software PLC
Association of Anaesthetists of Great Britain and Ireland
Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland
Barnsley Hospital NHS Foundation Trust
British Association of Day Surgery
British Medical Association
British Medical Journal
British National Formulary
British Nuclear Cardiology Society
British Psychological Society
Cambridge University Hospitals NHS Foundation Trust
Care Quality Commission (CQC)
Department of Health, Social Services and Public Safety - Northern Ireland
Dr Falk Pharma UK Ltd
East and North Hertfordshire NHS Trust
Gloucestershire Hospitals NHS Foundation Trust
Health Quality Improvement Partnership
Healthcare Improvement Scotland
Healthcare Infection Society
Institute of Biomedical Science
Maidstone Hospital
Medicines and Healthcare products Regulatory Agency
Ministry of Defence
National Clinical Guideline Centre
National Collaborating Centre for Cancer

National Collaborating Centre for Mental Health
National Collaborating Centre for Women's and Children's Health
National Institute for Health Research Health Technology Assessment Programme
National Patient Safety Agency
National Treatment Agency for Substance Misuse
NHS Connecting for Health
NHS Direct
NHS Plus
NHS Sheffield
NICE technical lead
NICE TLOC GDG
Parenteral and Enteral Nutrition Group
Public Health Wales NHS Trust
Public Health Wales NHS Trust
Royal College of General Practitioners in Wales
Royal College of Midwives
Royal College of Obstetricians and Gynaecologists
Royal College of Paediatrics and Child Health
Royal College of Pathologists
Royal College of Physicians
Royal College of Psychiatrists
Royal College of Radiologists
Royal College of Surgeons of England
Royal Pharmaceutical Society
Scottish Intercollegiate Guidelines Network
Sheffield Childrens Hospital
Social Care Institute for Excellence

South London & Maudsley NHS Trust
South West Yorkshire Partnership NHS Foundation Trust
St Mary's Hospital
Walsall Local Involvement Network
Welsh Government
Welsh Scientific Advisory Committee