Supporting Information 1.1

Capsule Endoscopy (CE) part

Summary documents of detailed literature searches for ESGE QIC Small bowel working group performed by:

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CPO
ıtro di Riferimento per l'Epidemiologia
ı Prevenzione Oncologica in Piemonte

% of examinations according to indications

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1.1 (St. 1.1-1.6) **Adherence to ESGE/ASGE recommendations OR Percentage of small bowel examinations procedures performed for an indication that is included in a published standard list of appropriate indications approved by an internationally recognized endoscopy professional society and the indication is documented.**

P: Patients having CE
I: indications for CE
C:
O: compliance with indication
Note: descriptive

1.2 (St. 2.1)**Overall detection rate**

P: Patients having CE
I: positive significant findings
C:
O: diagnostic yield
Note: descriptive

1.3 (St. 3.1-3.7) **Detection rate by indication**

P: Patients having CE
I: lesions detections rates
C: minimum published diagnostic yield per indication
O: improved lesion detection rates /reduced missed rates
Notes: descriptive. Do individual endoscopist lesion detection rates by indication predict reading quality in capsule endoscopy?

1.4 (St. 4.1) **Colonic visualization**

P: Patients having CE
I: colonic visualization CE
C:
O: cecum visualization
Note: descriptive

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 15/2/2016 separately for systematic reviews and primary studies using the following two different search strategies:

Search strategy n 1

Systematic reviews and meta-analysis

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** (indication[Title/Abstract] OR indications[Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** (indication:ab,ti OR indications:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

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

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Intestine, Small] explode all trees
#5 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
#7 indication:ti,ab,kw (Word variations have been searched)
#8 #3 and #6 and #7 Publication Year from 2000 to 2016

Primary studies

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** (indication[Title/Abstract] OR indications[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** (indication:ab,ti OR indications:ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Intestine, Small] explode all trees
#5 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
#7 indication:ti,ab,kw (Word variations have been searched)
#8 #3 and #6 and #7 Publication Year from 2000 to 2016

Search strategy n 2

Systematic reviews and meta-analysis

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** (((caecum[Title/Abstract] OR cecum[Title/Abstract] OR colon*[Title/Abstract]) AND (visualiz*[Title/Abstract] OR reach*[Title/Abstract])) OR complet*[Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** (((visualiz*:ab,ti OR reach*:ab,ti) AND ('caecum'/exp OR caecum:ab,ti OR cecum:ab,ti OR colon*:ab,ti)) OR complet*:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

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

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#5 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
#7 (cecum or colonic) and (visualization or reach):ti,ab,kw (Word variations have been searched)
#8 completeness or complete:ti,ab,kw (Word variations have been searched)
#9 #7 or #8
#10 #3 and #6 and #9 Publication Year from 2000 to 2016

Primary studies

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** (((caecum[Title/Abstract] OR cecum[Title/Abstract] OR colon*[Title/Abstract]) AND (visualiz*[Title/Abstract] OR reach*[Title/Abstract])) OR complet*[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta

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

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** (((visualiz*:ab,ti OR reach*:ab,ti) AND ('caecum'/exp OR caecum:ab,ti OR cecum:ab,ti OR colon*:ab,ti)) OR complet*:ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
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#8 completeness or complete:ti,ab,kw (Word variations have been searched)
#9 #7 or #8
#10 #3 and #6 and #9 Publication Year from 2000 to 2016

Results

Results of the bibliographic searches

Results of the two search strategies were combined and considered together.
After removing duplicates, 1444 articles (48 SRs, 1396 primary studies) were found.
Only full publications reporting data of at least 100 procedures were considered for inclusion.
45 studies were considered potentially relevant and acquired in full text for more detailed evaluation. Six further studies with useful data were found within results of search strategies performed for other questions.

Excluded studies

Three studies were excluded: two because they sere narrative reviews (Rosa 2015, Aerts 2010), one because analyzed only a subgroup of patients who received CE prior to single balloon Enteroscopy (Sethi 2014).

Awaiting assessment

One systematic review was classified as awaiting assessment because did not report the references of the included studies; we wrote to the author asking for data, but he didn't reply (Liao 2010).
Two other studies were classified as awaiting classification because they are written in Chinese (Ren 2009, Lu 2009).

Included studies

39 studies with 18035 procedures analyzed were finally included. All were retrospective or prospective analyses of registries of single or multiple centres experiences.

Authors, year of publication	N procedures setting	Indications							Cecum visualization	Overall detection rate
		Obscure bleeding	Abdominal pain or diarrhoea	Anemia	Polyposis (Familial adenomatous polyposis, Peutz–Jeghers syndrome)	Suspected IBD (Crohn disease)	Suspected small bowell tumors	Other		
Calabrese 2013	481 procedures Single centre experience Italy May 2006 to May 2011	346/481 (71.9%): Overt bleeding 137/346 Occult bleeding 209/346							NR	NR
Carey 2007	260 procedures Single centre experience USA 2001 to October 2003	Obscure-Overt: 126/260 Obscure-Occult: 134/260							74%	52.7%
Carlo 2005	702 procedures Single centre experience USA January 2002 to September 2004	532/702 (75.8%)	pain (including suspected Crohn's disease): 81/702 (11.3%) Diarrhea: 22/702 (3.1%)					history of GI malignancy, suspected fistula, malabsorption syndromes, or other indications 67/702 (9.5%)	95.6%	51.3%

Cobrin 2006	562 procedures Single centre experience USA August 2001 to November 2003	Obscure GI bleeding 443/562 (78.8%)	Chronic abdominal pain: 26/562 (4.6%) Diarrhea: 6/562 (1.1%)			Crohn disease (suspected or known): 12/562 (2.1%)	Carcinoid primary: 23/562 (4.1%)	Abnormal imaging: 14/562 (2.5%) Cancer surveillance: 11/562 (1.9%) IBS: 7/562 (1.2%) Other: 20/562 (3.5%)		49.3%
Cuyle 2011	120 procedures Single centre experience Belgium July 2008-March 2010	120 (overt: 27.5% and occult: 72.5%)							82.5%	50%
Enns 2004	226 procedures Single centre experience Canada December 2001-February 2004	(overt :n 88 and occult n:79): 167/226 (74%)	pain: 19/226 (8.4%)	Anemia: 14/226 (6%)	Familial adenomatous polyposis, Peutz–Jeghers syndrome 10/226 (4%)	12/226 (5%)		Radiological abnormalities (4/226 (1.76%)	NR	47%
Estevez 2006	100 procedures Single centre experience Spain February 2002 and December 2003	obscure–overt bleeding: 52/100 (52%) obscure–occult bleeding: 48/100							79%	68%

		(48%)								
Fidder 2007	112 procedures Single centre experience Israel December 2001 and December 2005		Abdominal pain: 13/112 (11.6%) Diarrhea: 11/112 (9.8%) Diarrhea plus abdominal pain: 12/112 (10.7%)	76/112 (67.9%)						6.2%
Firema n 2004	160 procedures 4 centres experience Israel August 2001 and 30 November 2002	(overt :n 8 and occult n:70): 78/160 (48.7%)	Pain: 24/160 (15%)		familial adenomatous polyps syndrome:2/160: 1.25%	21/160 (13%)		Malabsorption: 4/160 (2.5%) Miscellaneous (e.g. unexplained diarrhoea, ulcerative colitis, collagenous colitis) : 31/160 (19.4%)	NR	40.6%
Goenka 2011	505 procedures Single centre experience India from August 2003 to December 2009	385/505 (76.2%):	Abdominal pain: 30/505 (5.9%) Chronic diarrhea: 76/505 (15%)					Other: 14/505 (2.8%)		NR

Hollera n 2013	309 procedures Single centre experience Ireland December 2009 to August 2011			93/309 (30.1%)						
Kalantz is 2005	193 procedures Single centre experience Grece June 2002 to December 2003	108/193 (55.9%)	Pain: 16/193 (8.3%) Diarrhea: 32/193 (16.6%)		3/193 (1.55%)	28/193 (14.5%) (Suspect ed: 22 Known:6)		Celiac disease: 4/193(2%) Other: 2/193 (1%)	83%	83%
Kalla 2013	315 procedures Single centre experience UK 2003 to 2009					Suspecte d Crohn's disease (CD), 265/315 (84.1%) establish ed CD. 50/315 (15.9%)				24.8% (Capsule suggestive of CD)
Katsine los 2010	101 procedures Single centre experience Greece May 2007 to	(overt :n 20 and occult n:36) 56/101 (55.4%)	Pain with/wit hout diarrhea: 23/101 (22.8%)		14/101 (13.8%)		Prior resected neuroendocr ine neoplasms:2 /101(2%)	Celiac disease: 5/101 (5%)	NR	47.5%

	February 2009						Fever of unknown origin, increased ESR and CRP:1/101 (1%)			
Kav 2009	125 procedures Single centre experience Turkey September 2003 to March 2009	70/125 (56%)	Pain: 9/125(7.2%) Diarrhea: 18/125 (14.4%)	10/125 (8%)		8/125 (6.4%)		10/125 (8%)	73.6%	77.6%
Khan 2013	122 procedures Single centre experience New Zealand December 2009 to December 2011	Overt bleeding: 33/122 (27%)	Pain: 10/122 (8.2%) Diarrhea: 18/122 (14.7%)	53 /122 (43.4%)				8/122 (6.5%)	NR	52%
Kim 2013	125 procedures Single centre experience Korea April 2007 to December 2009	Obscure bleeding: 125							74.4%	52%
Koulaouzidis 2012	221 procedures Single centre experience UK			Iron Deficiency Anemia (IDA)						30.7%

	March 2005 and June 2011			221/221 (100%)						
Liao 2010	2400 procedures 27 hospitals experience China	1232/2400 (51.3%)	Pain: 642/2400 (26.8%) Diarrhea _223/2400 (9.3%)	34 /2400 (1.4%)	10 /2400 (0.4%)	52/2400 (2.2%)	25/2400 (1%)	Health examination: 103/2400 (4.3%) Unexplained weight loss: 19/2400 (0.8%) Ileus:10/2400 (0.4%) Other: 50/2400 (2.0%)	86.8%	47.7%
Lim 2015	2914 procedures 24 hospitals experience Korea October 2002 to September 2012.	(overt :n 1311 and occult n:418): 1729/2914 (59.3%)	Pain:497 /2914 (17%) Diarrhea 102/2914 (3%)			105 /2914 (3.7%)	86/2914 (2.9%)	Ulcerative colitis, Behcet's disease, ischemic Enteritis; 15/2914 (0.5%) Weight loss:15/2914 (0.5%) Cancer of unknown primary; 4/2914 (0.14%) Healthy volunteer 158/2914 (5.8%) Protein losing enteropathy :3/2914 (0.1%) Others: 200/2914 (6.8%)	77%	63%

Maieron 2004	195 procedures Three centres experience Austria November 2001 to May 2003	Oscure bleeding or anemia: 151/195 (77.4%)			5/195 (2.5%)	25/195 (12.8%)		3/195(1.5%)	83.1%	48.7%
Matas 2006	416 procedures Single centre experience Spain November 2001 and January 2005	(overt :33% and occult 50%): 83.3%	Pain/diarrhea 4.6%		2.2%	7.5%		2.4%	NR	62.2%
Mehdizadeh 2010	146 procedures Single centre experience October 2001 and December 2005	overt or occult GI bleeding (GIB)+ iron deficiency anemia: 19/146 (13%) Abdominal pain plus GIB: 15/146 (10.3%)	Abdominal pain: 66/146(45.2%) Diarrhea: 22/146 (15.1%) Abdominal pain plus diarrhea: 13/146(8.9%) Weight loss _ abdominal pain: 5/146 (3.4%)					Combination: 6/146 (4.1%)	71.2%	51.8%

Muhammad 2009	652 procedures Single centre experience USA 2002 to 2007	Obscure gastrointestinal bleeding without IDA: 93/652 (14.3%)	Unexplained abdominal pain: 100/652 (15.3) Chronic diarrhea 61/652 (9.3)	Iron Deficiency Anemia (IDA): 424/652 (65%)	Suspected polyposis syndrome: 5/652 (0.8%)	Suspected Crohn disease: 68/652 (10.4%)		Suspected Celiac disease: 5/652 (0.8%)		NR
Mussetto 2012	118 procedures Single centre experience Italy March 2009 and March 2011	Occult obscure bleeding: 118							96%	57.6%
Pongprasobchai 2013	103 procedures Single centre experience Thailand 2005 to 2009	Obscure bleeding: 103							74%	51%
Qvigstad 2006	195 (167 pz) procedures Single centre experience Norway January 2003 and 31 December 2004	Gastrointestinal bleeding: 50/167 (29.9%)	Abdominal pain: 25/167 (15%) Diarrhoea: 21/167 (12.6)	40/167 (23.9%)		Crohn's disease: 20/167 (12%)		Other (lymphoma, familial adenomatous polyposis, coeliac disease, weight loss, carcinoid tumour, nausea,	83%	27.5%

								hypoalbuminaemia and cobalamine deficiency): 11/167 (6.6%)		
Riccioni 2010	650 procedures Single centre experience Italy from 2002 to 2007			138/650 (21.2%)					NR	NR
Rondonotti 2010	2921 procedures 23 centres experience procedures Italy 2001 and 2008	1268/2921 (43.3%)	Pain:155 /2921 (5.3%) diarrhea :140/2921 (4.8%)	698 /2921 (23.9%)	90/2921 (3.1%)	336/2921 (11.5%) (Suspected 7.8%, Known 3.7%	101/2921 (3.4%)	Celiac disease: 94/2921 (3.2%) Other:39/2921 (1.4%)	81.2%	50.6%
Saul, 2010	187 procedures Single centre experience Recruitment period not reported	64/187 (34.2%)	Pain: 11/187 (5.8%) Diarrhea: 12 /187(6.4%)	68 /187(36.3%)	13/187 (6.9%)		Neoplasia: 4/187 (2.1%)	Celiac disease: 7/187 (3.7%)	NR	54%
Sturniolo 2006	314 procedures Two centres experience Italy September 2001 to November 2004	203/314 (64.6%) (overt :106 and occult 97)	Pain 12/314 (3.8%) Diarrhea: 16 /314 (5%)		18 /314 (5.7%) (13 of whom had familial adenomatous polyposis)	35/314 (16.8%)	13/314(4.1%)	Malabsorption: 11/314 (3.5%) Intestinal lymphangectasia :3/314 (0.9%) Vascular abnormalities: 3/314(0.9%)	80%	45.8%

Tatar 2006	200 procedures Single centre experience USA September 2003 and January 2005	62/200 (31%)	Pain:41/200 (21%) Diarrhea: 22/200 (11%)	132/200 (66%)				abnormal radiographic findings or surveillance of inflammatory bowel disease: 17/200 (9%)	87%	54%
Toy 208	145 procedures Single centre experience USA March 2003 to July 2005	88/145 (60.6%) (overt 55, occult 32)	Pain 30/145 (20.7%)	4/145 (2.7%)		18/145 (12.4%)		4/145 (2.7%)	80%	69%
Tukey 2009	105 procedures Single centre experience Israel before May 2007					Suspected Crohn disease: 100%			64%	37.1%
van Turenhout 2010	592 procedures Single centre experience The Netherlands February 2003 until June 2007	382/592 (64.5%) obscure-occult GI bleeding: 240/592 (40.5%) overt GI bleeding: 142/592 (24%)	Abdominal pain 27/592 (4.6%)	34/592 (5.7%)	31/592 (5.2%)	47/592 (7.9%)		Celiac disease: 50/592 (8.4%)		NR

Van Tuyl 2006	250 procedures Single centre experience The Netherlands Recruitment period not reported	177/250 (70%) (Occult:150, overt: 27)				57/250 (23%)			76%	70%
Yazici 2012	334 procedures Single centre experience USA March, 2003 to October, 2005	208/334 (62.3%) (overt: 47 occult:161)	Pain: 103/334 (30.8%)			91/334 (27.2%)	18/334 (5.4%)	Celiac disease: 4/334 (1.2%) Other: 9/334 (2.7%)	86%	NR
Zagorowicz 2013	150 procedures Single centre experience Poland March 2003 and July 2009	81/150 (54%) (Overt: 58, occult : 23)	Pain:7/150 (4.6%)	19/150 (12.6%)	4/150 (2.6%) (Peutz-Jeghers syndrome:2 Polyposis:2)	2/150 (1.3%)	Neuroendocrine tumors: 3/150 (2%)	Malabsorption: 18/150 (12%) Celiac disease: 5/15 (3.33%) Other: 9/150 (6%)	76.6%	54.6%
Zhang 2009	309 procedures Single centre experience China May 2003 to April 2008.	Overt: 309							81.8%	53.7%

Detection rate by appropriate indication (LG ESGE 2015)

Authors, year of publication	N procedures setting	Obscure bleeding	iron deficiency anemia	Suspected and established Crohn disease	Suspected small bowel tumors	Inherited polyposis syndromes
Calabrese 2013	481 procedures Single centre experience Italy May 2006 to May 2011	246/346(71.1%)				
Carey 2007	260 procedures Single centre experience USA 2001 to October 2003	Obscure-Overt 75 /126(60%) Obscure-Occult 62/134 (46%) Total:137/260 (52.7%)				
Carlo 2005	702 procedures Single centre experience USA January 2002 to September 2004	including anemia: 262/ 532 (49.2%)				
Cobrin 2006	562 procedures Single centre experience USA August 2001 to November 2003	43/443 (9.7%)		0/12 (0%)	Carcinoid primary: 5/23 (21.7%) Cancer surveillance: 1/11 (9.1%)	
Cuyle 2011	120 procedures Single centre experience Belgium	60/120 (50%)				

	July 2008- March 2010					
Enns 2004	226 procedures Single centre experience Canada December 2001-February 2004	(overt :n 88 and occult n:79) 85/167 (51%)	Anemia without any bleeding: 7/14 (50%)	4/12 (33%)		Polyposis syndrome Including familial adenomatous polyposis and Peutz–Jeghers syndrome 5/10 (50%)
Estevez 2006	100 procedures Single centre experience Spain February 2002 and December 2003	68/100 (68%)				
Fidder 2007	112 procedures Single centre experience Israel December 2001 and December 2005		3/76 (4%)			
Fireman 2004	160 procedures 4 centres experience Israel August 2001 and 30 November 2002	(overt :n 8 and occult n:70) 45/78(57.7%)		11/21 (52.4%)		familial adenomatous polyposis 1/2 (50%)
Goenka 2011	505 procedures Single centre experience India from August 2003 to December 2009	284/385 (73.8%)				
Holleran 2013	309 procedures Single centre experience Ireland December 2009 to August 2011		35/64 (54.7%)			
Kalantzis 2005	193 procedures Single centre experience Grece	84/108 (78%)		15/22 (64%)		9/14 (64%)

	June 2002 to December 2003					
Kalla 2013	315 procedures Single centre experience UK 2003 to 2009			78/315 (24.8%)		
Katsinelos 2010	101 procedures Single centre experience Greece May 2007 to February 2009	23/56 (41%)				
Kav 2009	125 procedures Single centre experience Turkey September 2003 to March 2009	54/70 (77%)		6/8 (75%)		
Khan 2013	122 procedures Single centre experience New Zealand December 2009 to December 2011	27/33(81.8%)	34/53(64.1%)			
Kim 2013	125 procedures Single centre experience Korea April 2007 to December 2009	62/125 (52%)				
Koulaouzidis 2012	221 procedures Single centre experience UK March 2005 and June 2011		68/221 (30.7)			
Liao 2010	2400 procedures 27 hospitals experience China	769/1232 (62.4%)				
Maieron 2004	195 procedures Three centres experience Austria November 2001 to May 2003	85/151(56.%)	85/151(56.%)	7 /25 (28%)		3/5 (60%)
Matas 2006	416 procedures	66.5%		44%		

	Single centre experience Spain November 2001 and January 2005					
Mehdizadeh 2010	146 procedures Single centre experience October 2001 and December 2005	Abdominal pain plus GIB: 9/15 (60%)	GIB/iron deficiency anemia: 11/19 (57.9%)			
Muhammad 2009	652 procedures Single centre experience USA 2002 to 2007		358/424 (84.4%)			
Mussetto 2012	118 procedures Single centre experience Italy March 2009 and March 2011	68/118 (57.6%)				
Pongprasobchai 2013	103 procedures Single centre experience Thailand 2005 to 2009	52/103(50.5%)				
Qvigstad 2006	195 (167 pz) procedures Single centre experience Norway January 2003 and 31 December 2004	Gastrointestinal bleeding: 17/ 50 (34%)	11/40 (27.5%)	12/20 (60%)		
Riccioni 2010	650 procedures Single centre experience Italy from 2002 to 2007		91/138 (65.9%)			
Sturniolo 2006	314 procedures Two centres experience Italy September 2001 to November 2004	112/193 (58%)		11/35 (31%)	2/13(15.4%)	14/18 (77.8%)
Tatar 2006	200 procedures	41/62 (65%)	81/135 (61%)			

	Single centre experience USA September 2003 and January 2005					
Tukey 2009	105 procedures Single centre experience Israel before May 2007			37%		
van Turenhout 2010	592 procedures Single centre experience The Netherlands February 2003 until June 2007	obscure-occult GI bleeding: 106/240 (44.2%) overt GI bleeding: 82/142 (57.8%)				
Van Tuyl 2006	250 procedures Single centre experience The Netherlands Recruitment period not reported	130/177 (73.4%)		36/57 (63.2%)		
Zhang 2009	309 procedures Single centre experience China May 2003 to April 2008.	166/309 (53.7%)				

Detection rate by other indications

Authors, year of publication	**N procedures setting**	**suspected celiac disease**	**Abdominal Pain**	**diarrhea**	**abdominal pain and diarrhea**	**Malabsorption**	**other**
Carlo 2005	702 procedures Single centre experience USA January 2002 to		Abdominal pain (including suspected	Diarrhea: 10/22 (45.4%)			history of GI malignancy, suspected fistula, malabsorption

	September 2004		Crohn's disease): 38/81 (46.9%)				syndromes, or other indications :50/ 67 74.6%)
Cobrin 2006	562 procedures Single centre experience USA August 2001 to November 2003		0/26 (0%)	0/6 (0%)			Abnormal imaging: 1/14 (7.1%) IBS: 0/ 7 (0%) Other: 0/20 (0%)
Enns 2004	226 procedures Single centre experience Canada December 2001-February 2004		Pain: 6/19 (32%)	4/16 (25%)		6/11 (54%)	
Fidder 2007	112 procedures Single centre experience Israel December 2001 and December 2005		0/13 (0%)	0/11 (0%)	4/12(33%)		
Fireman 2004	160 procedures 4 centres experience Israel August 2001 to 30 November 2002		1/24 (4.2%)			4/4 (100%)	Miscellaneous (e.g. unexplained diarrhea, ulcerative colitis, collagenous colitis) 3/31(9.7%)
Kalantzis 2005	193 procedures Single centre experience Grece June 2002 to December 2003	2/4 (50%)	5/16 (31%)	26/32 (81%)			
Katsinelos 2010	101 procedures Single centre experience Greece May 2007 to February 2009	5/5 (100%)	11/23 (47.8%)				Fever of unknown origin with increased ESR and CRP:0/1 (0%)
Kav 2009	125 procedures Single centre experience Turkey		5/9 (55%)	9/18 (50%)			14/20 (70%)

	September 2003 to March 2009						
Khan 2013	122 procedures Single centre experience New Zealand December 2009 to December 2011		2/10 (20%	12/18 (66.6%)			1/8 (12.5%)
Liao 2010	2400 procedures 27 hospitals experience China		253/642 (39.4%)	32/223 (14.3%)			
Maieron 2004	195 procedures Three centres experience Austria November 2001 to May 2003						
Matas 2006	416 procedures Single centre experience Spain November 2001 and January 2005		36.8%				
Mehdizadeh 2010	146 procedures Single centre experience October 2001 and December 2005		33/66 (50%) Weight loss±abdominal pain: 2/5 (4059	16/22 (72.7%)	5/13 (38.5%)		Combination: 5/6 (83.3%)
Qvigstad 2006	195 (167 pz) procedures Single centre experience Norway January 2003 and 31 December 2004		1/25 (4%)	1/21 (4.8%)			Other (lymphoma, familial adenomatous polyposis, coeliac disease, weight loss, carcinoid tumour, nausea, hypoalbuminaemia and cobalamine deficiency): 4/11 (36.4%)

Sturniolo 2006	314 procedures Two centres experience Italy September 2001 to November 2004						Intestinal lymphangectasia: 3/3 (100%) Vascular abnormalities: 2/3(66.6%)
Tatar 2006	200 procedures Single centre experience USA September 2003 and January 2005		7/41 (17%)	12/33 (36%)			6/17 (36%)

Conclusions

Indications

Eight studies included only patients with obscure bleeding (Calabrese 2013, Carey 2007, Cuyle 2011, Estevez 2006, Kim 2013, Mussetto 2012, Pongprasobchai 2013, Zhang 2009); one included only patients with Iron Deficiency Anemia (Koulaouzidis 2012) and two included only patients with established or suspected Crohn's disease (Kalla 2013, Tukey 2009) so they were not considered in the calculation of percent of indications.
In the remaining 28 studies, the indications are distribuited as explained below.
The most frequent indications listed in 24 studies were: *obscure gastrointestinal bleeding*, with a median value of 57.65% (range: 14.3% to 83.3%)
The second most frequent indication was *pain* listed in 22 studies with the median percentage of this indication of 9.85%, range: 3.8% to 45.2%
Diarrhea listed in 16 studies, the median percentage of this indication was 9.55%, range. 1.1% to 16.6%
Four studies counted together patients with *abdominal pain* and/or *diarrhea* and reported a percentage of this indication ranging from 4.6% to 22.8% respectively.
Anemia, which was listed among the indications in 15 studies; the median percentage of this indication was 23.9%, range 1.4% to 67.9%.
Polyposis, including Familial adenomatous polyposis and Peutz–Jeghers syndrome was listed among the indications only in 13 studies; the median percentage of this indications was 2.6%, range 0.4% to 13.8%.
Suspected IBD (including Crohn disease) was listed among the indications in 18 studies, the median percentage of this indication was 11.5%, ranging from 1.3% to 27.2%
Suspected *small bowel tumors* were listed among the indications only in 9 studies; the median percentage of this indication was 3.4%, ranging from 1% to 5.4%.
Celiac disease was listed among the indications in 8 studies; the median percentage of this indication was 3.45%, ranging from 0.8% to 8.4%
Malabsorption was listed among the indications only in 4 studies; the median percentage of this indication varied greatly ranging from 2.5 to 18%
Other indications were listed in 19 studies; the types of indications grouped under this category varied greatly between studies; moreover 9 studies did not specify which indications were considered. So the data related to the percentages of indications were not informative.

Cecum visualization

Percentages of complete examination were reported in 23 studies. The results were quite homogeneous, ranging from to 64% to 96%, with a median of 80%

Overall detection rate

Overall detection rate (diagnostic yield) was reported in 32 studies; the median was 51.55%, ranging from 6.2% to 83%

Detection rate by indication

<u>Adequate indications, according to ESGE 2015 guidelines</u>
Obscure bleeding: in the 25 studies that reported this result, the median detection rate was 57.7%, ranging from 9.7% to 81.8%

Anemia: in the 10 studies that reported this result the median detection rate was 55.35% ranging from 4% to 84.4%
Suspected or established Crohn disease: in the 12 studies that reported this result, the median detection rate was 40.5% ranging from 0% to 75%
Suspected small bowel tumors: only two studies reported this results which were 15.4% and 21.7%.
Inherited polyposis syndromes: the five studies that reported this result defined cases as " polyposis" without further specification: median detection rate was 60%, ranging from 50% to 77.4% .

Other indications:
Abdominal Pain: 14 studies reported this results, which varied greatly. Median detection rate was 31.5, ranging from 0% to 50%
D*iarrhea*: 11 studies reported this results, which varied greatly. Median detection rate was 36, ranging from 0% to 81%
Abdominal pain and/or diarrhea: 2 studies reported this results with the values of 33% and 38.5%.
Malabsorption: in the two studies that reported this outcome the detection rate was 100% and 54% but these percentages referred only to 4 and 11 cases respectively.
Suspected celiac disease: in the two studies that reported this outcome the detection rate was 100% and 50% but these percentages referred only to 5 and 4 cases respectively.

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Awaiting assessment

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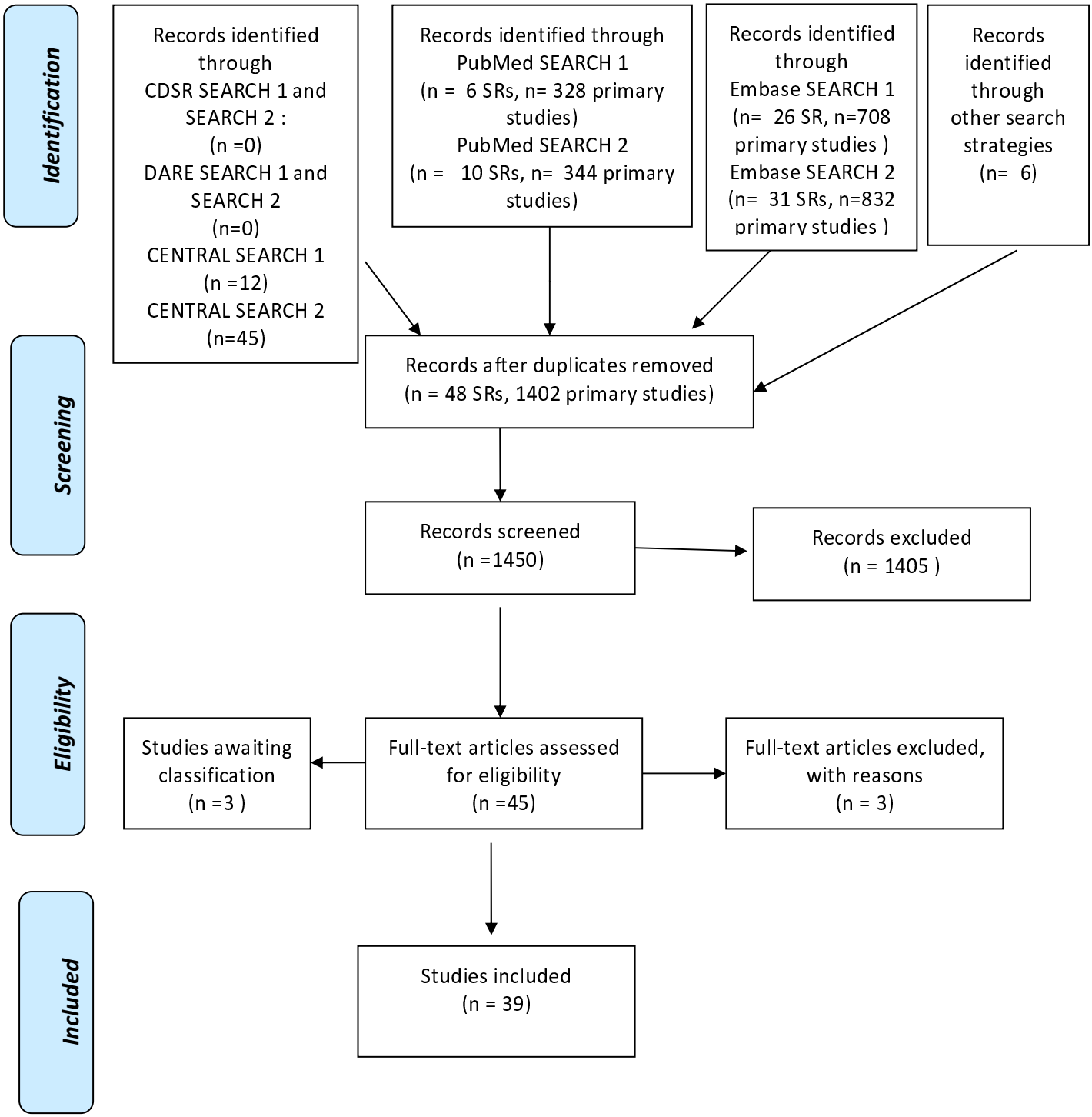
PRISMA 2009 Flow Diagram



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Capsule Excretion

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2.1 (St. 5.1) Capsule Excretion

P: Patients having CE
I: Ask the patient for CE excretion verification
C: no verification
O: morbidity/retention
Notes: should we verify capsule excretion? When and how? Always: 1) if CE is incomplete, to check-out retention and 2) if CE is complete, to avoid contamination/pollution. If the CE is incomplete and the patient did not recover the capsule, an x.ray should be done?. If the CE is complete and the patient did not recover the capsule, no problem, nothing to do (the risk of CE retention in the colon is very low).

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 15/2/2016 separately for systematic reviews and primary studies using the following two different search strategies:

Systematic reviews and meta-analysis

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** (retention[Title/Abstract] OR retained[Title/Abstract] OR "complications" [Subheading] OR "adverse effects" [Subheading] OR obstruct*[Title/Abstract] OR complication[Title/Abstract] OR complications[Title/Abstract]) **AND** (excret*[Title/Abstract] OR eliminat*[Title/Abstract] OR verificat*[Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** (obstruct*:ab,ti OR complications:ab,ti OR complication:ab,ti OR adverse:ab,ti OR retention:ab,ti OR retained:ab,ti) **AND** (excret*:ab,ti OR verificat*:ab,ti OR eliminat*:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

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

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Intestine, Small] explode all trees
#5 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
#7 Any MeSH descriptor with qualifier(s): [Adverse effects - AE, Complications - CO]
#8 complication or obstruction:ti,ab,kw (Word variations have been searched)
#9 retention:ti,ab,kw (Word variations have been searched)
#10 #8 or #7 or #9
#11 excretion verification:ti,ab,kw (Word variations have been searched)
#12 #3 and #6 and #10 and #11 Publication Year from 2000 to 2016

Primary studies

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** (retention[Title/Abstract] OR retained[Title/Abstract] OR "complications" [Subheading] OR "adverse effects" [Subheading] OR obstruct*[Title/Abstract] OR complication[Title/Abstract] OR complications[Title/Abstract]) **AND** (excret*[Title/Abstract] OR eliminat*[Title/Abstract] OR verificat*[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** (obstruct*:ab,ti OR complications:ab,ti OR complication:ab,ti OR adverse:ab,ti OR retention:ab,ti OR retained:ab,ti) **AND** (excret*:ab,ti OR verificat*:ab,ti OR eliminat*:ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Intestine, Small] explode all trees
#5 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
#7 Any MeSH descriptor with qualifier(s): [Adverse effects - AE, Complications - CO]
#8 complication or obstruction:ti,ab,kw (Word variations have been searched)
#9 retention:ti,ab,kw (Word variations have been searched)
#10 #8 or #7 or #9
#11 excretion verification:ti,ab,kw (Word variations have been searched)
#12 #3 and #6 and #10 and #11 Publication Year from 2000 to 2016

Results

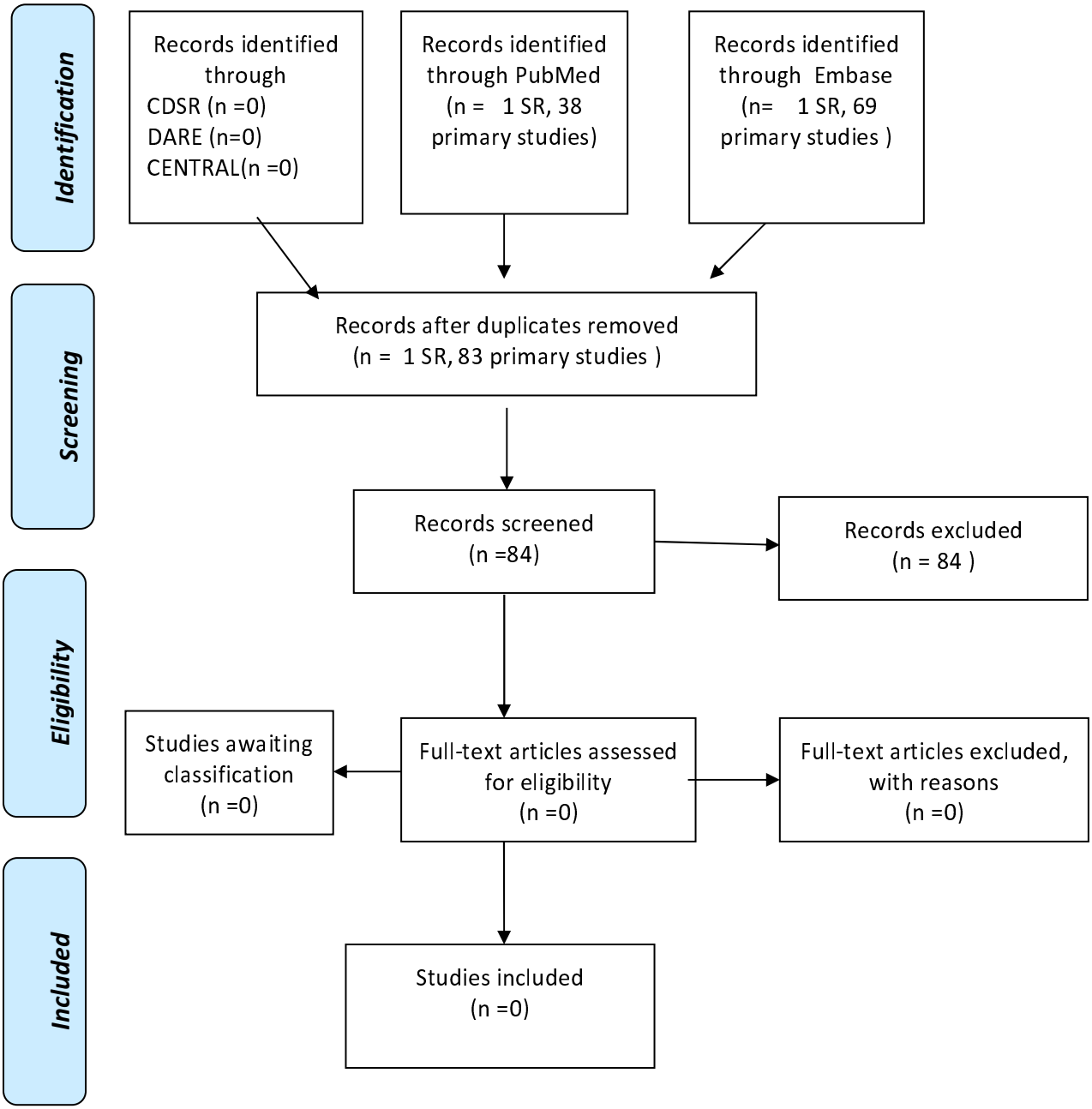
Results of the bibliographic searches

After removing duplicates, 84 articles (1 systematic review and 83 primary studies) were found. No relevant studies were found addressing this question.

Conclusions

No conclusion can be drawn because no evidence about the relationship between morbidity or retention and capsule excretion verification was found.

PRISMA 2009 Flow Diagram



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Capsule Retention Per Indications

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3.1 (St. 7.1) **Retention per indications**

P: subgroups of patients having CE (NSAID users/abdominal radiation/previous Small Bowell surgery/IBD (inflammatory bowel disease, Chron)/abdominal symptoms (pain , diarrhoea, sub occlusive symptoms)
I: CE
O: capsule retention, need for surgery /endoscopic removal
Notes: descriptive. Are there groups of patients with increased risk for capsule retention?

3.2 (St. 7.2) **Capsule retention per indications /Endoscopist (DMcN)**
P: endoscopist
I: capsule retention
C: published capsule retention rates per indication
O: Improved quality of capsule endoscopy performance, in particular patient selection, reduced risk of complications
Notes: Can capsule retention rates by indication per endoscopist reflect procedure quality?

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 15/2/2016 separately for systematic reviews and primary studies using the following two different search strategies:

Systematic reviews and meta-analysis

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** ("Device Removal"[Mesh] OR retention[Title/Abstract] OR retained[Title/Abstract] OR "complications" [Subheading] OR "adverse effects" [Subheading] OR obstruct*[Title/Abstract] OR complication[Title/Abstract] OR complications[Title/Abstract]) **AND** (indication[Title/Abstract] OR indications[Title/Abstract]) **AND** ("systematic review" [Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis [Title/Abstract])

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** ('device removal'/exp OR retention:ab,ti OR retained:ab,ti OR obstruct*:ab,ti OR complications:ab,ti OR complication:ab,ti OR adverse:ab,ti) **AND** (indications:ab,ti OR indication:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

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

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Intestine, Small] explode all trees
#5 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
#7 indication:ti,ab,kw (Word variations have been searched)
#8 MeSH descriptor: [Device Removal] explode all trees
#9 Any MeSH descriptor with qualifier(s): [Adverse effects - AE, Complications - CO]
#10 retention or complication or obstruction:ti,ab,kw (Word variations have been searched)
#11 #8 or #9 or #10
#12 #3 and #6 and #7 and #11 Publication Year from 2000 to 2016

Primary studies

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** ("Device Removal"[Mesh] OR retention[Title/Abstract] OR retained[Title/Abstract] OR "complications" [Subheading] OR "adverse effects" [Subheading] OR obstruct*[Title/Abstract] OR complication[Title/Abstract] OR complications[Title/Abstract]) **AND** (indication[Title/Abstract] OR indications[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** ('device removal'/exp OR retention:ab,ti OR retained:ab,ti OR obstruct*:ab,ti OR complications:ab,ti OR complication:ab,ti OR adverse:ab,ti) **AND** (indications:ab,ti OR indication:ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)

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Results

Results of the bibliographic searches

After removing duplicates, 402 articles (13 SRs, 389 primary studies) were found.
Only full publications reporting data of at least 50 procedures were considered for inclusion.
18 studies were considered potentially relevant and acquired in full text for more detailed evaluation. 2 further studies with useful data were found within results of search strategies performed for other questions.

Excluded studies

2 studies were excluded: one because less than 50 patients were included (Ang 2003), another because did nor reported enough data about indication and retention (Trifan 2010)

Included studies

15 studies with 37129 procedures analyzed were finally included. All were retrospective or prospective analyses of registries of single or multiple centres experiences.

Awaiting assessment

3 studies were classified as awaiting assessment: one systematic review because did not report the references of the included studies and we wrote to the author asking for data, but he didn't reply (Liao 2010); one because in Croatian language (Banic 2009); and one because in Chinese language (Nakamura 2007).

Authors, year of publi-cation	N procedures setting		Obscure bleeding	Abdominal pain or diarrhea	Anemia	Polyposis (Familial adenomatous polyposis, Peutz–Jeghers syndrome)	Suspected IBD (Crohn's disease)	Suspected small bowel tumors	Other	Overall Retention
Al-Bawardy 2015	5593 CE Single centre experience from January 2002 through January 2013	**Indications for capsule endoscopy**	NR	NR	NR	NR	NR	NR	NR	
		Retentions per indications	7/NR	Abdominal pain:2/NR			Crohn's disease:5/NR		Celiac disease:1/NR	15/5593 (0.30%)
Carey 2007	260 procedures Single centre experience USA 2001 to October 2003	**Indications for capsule endoscopy**	Obscure-Overt: 126/260 Obscure-Occult: 134/260							
		Retentions per indications	4/260 (1.5%)							4/260 (1.5%)
Carlo 2005	702 procedures Single centre experience USA January 2002 to September 2004	**Indications for capsule endoscopy**	532/702 (75.8%)	pain (including suspected Crohn's disease): 81/702 (11.3%) Diarrhea: 22/702 (3.1%)					history of GI malignancy, suspected fistula, malabsorption syndromes, or other indications 67/702 (9.5%)	
		Retentions	5/532	Abdomin						12/702(1.

		per indications	(0.94%)	al pain: 7/81 (8.64%)						7%)
Fry 2006	68 procedures in 64 patients Single centre experience USA between August 2001 and June 2004	**Indications for capsule endoscopy**		Abdominal pain: 35/64 (54.69%) Diarrhea: 14/64 (21.9%) Both: 15/64 (23.44%)						
		Retentions per indications		2/64 (3.1%)						2/64(3.1%)
Katsinelos 2010	101 procedures Single centre experience Greece May 2007 to February 2009	**Indications for capsule endoscopy**	(overt :n 20 and occult n:36) 56/101 (55.4%)	Pain with/without diarrhea:23/101 (22.8%)		14/101 (13.8%)		Prior resected neuroendocrine neoplasms:2/101 (2%) Fever of unknown origin, increased ESR and CRP:1/101 (1%)	Celiac disease: 5/101 (5%)	
		Retentions per indications		Pain with/without diarrhea: 1/23 (4.35%)						2/101 (1.98%)

Liao 2010	22840 procedures 27 hospitals experience China (SR)	**Indications for capsule endoscopy**	14623/22840 (64%)	2358/22840 (10.3%)			2295/22840 (10%)	786/22840 (3.4%)	Health examinatio: 174/22840 (0.7%) Other: 1555/228400 (6.8%)	
		Retentions per indications	1.2% (95%CI 0.9-1.6)				2.6 (95% CI1.6-3.9)	2.1 % (95%CI 0.7-4.3)		4% (95%CI 1.2-1.6)
Lim 2015	2914 procedures 24 hospitals experience Korea October 2002 to September 2012.	**Indications for capsule endoscopy**	(overt :n 1311 and occult n:418): 1729/2914 (59.3%)	Pain: 497/2914 (17%) Diarrhea 102/2914 (3%)			105 /2914 (3.7%)	86/2914 (2.9%)	Ulcerative colitis, Behcet's disease, ischemic Enteritis; 15/2914 (0.5%) Weight loss :15/2914 (0.5%) Cancer of unknown primary; 4/2914 (0.14%) Healthy volunteer 158/2914 (5.8%) Protein losing enteropathy :3/2914 (0.1%)	

									Others: 200/2914 (6.8%)	
		Retentions per indications	11/1729 (0.63%)	Abdominal pain: 1/497 (0.20%) Chronic diarrhea: 1/102 (0.98%)			Crohn's disease: 59/105 (56.19)	Small bowel tumor: 6/86 (6.98%)		90/2914 (3.09%)
Long 2011	124 procedures Single centre experience USA from July 2003 to Dec. 2009	**Indications for capsule endoscopy**					inflammatory bowel disease (IBD): 124/124 (100%)			
		Retentions per indications					7/124 (5.6%)			7/124(5.6%)
Musset to 2012	118 procedures Single centre experience Italy March 2009 & March 2011	**Indications for capsule endoscopy**	Occult obscure bleeding: 118							
		Retentions per indications	3/118(2.54%)							3/118 (2.54%)
Napierkowski 2005	72 procedures Single centre experience USA between August 2001	**Indications for capsule endoscopy**	(97.14%)	Abdominal pain: (8.7%)			Suspected Crohn's: (2.90%)			

	and June 2002									
		Retentions per indications								1/72(1.39 %)
Purdy 2011	555 procedures Single centre experience Finland between January 2002 & Dec. 2008	**Indications for capsule endoscopy**	NR	NR	NR	NR	NR	NR	NR	
		Retentions per indications			4/NR		3/ NR		Obstructive symptoms: 1/ Anemia + activity of crohn: 2/	10/555 (1.8%)
Rondo notti 2008	124 procedures 29centres experience procedures Europe recruitment period not specified	**Indications for capsule endoscopy**	108/124 (87.1%)	Pain: 9/124 (7.26%) diarrhea with malabsorption: 1/124(0.81%)				search for primary neoplasm: 6/124 (4.84%)		
		Retentions per indications	10/108 (9.2%)					2/6 (33.3%)		12/124 (9.68%)
Rondo notti 2010	2921 procedures 23 centres experience procedures Italy 2001 and 2008	**Indications for capsule endoscopy**	1268/2921 (43.3%)	Pain: 155 /2921 (5.3%) diarrhea:140/2921 (4.8%)	698 /2921 (23.9%)	90/2921 (3.1%)	336/2921 (11.5%) (Suspected 7.8%, Known 3.7%	101/2921 (3.4%)	Celiac disease: 94/2921 (3.2%) Other:39/2921 (1.4%)	
		Retentions per	15/1268	Pain:	1/698	1/90 (1.11%)	Suspected			61/2921(2

		indications	(1.18%)	2/155 (1.29%) Diarrhea: 2/140 (1.43%)	(0.14%)		IBD: 7/228 (3.07%) Known IBD: 1/108 (0.92%)			.09%)
Toy 208	145 procedures Single centre experience USA March 2003 to July 2005	**Indications for capsule endoscopy**	88/145 (60.6%) (overt 55, occult 32)	Pain 30/145 (20.7%)	4/145 (2.7%)		18/145 (12.4%)		4/145 (2.7%)	
		Retentions per indications		Abdominal pain: 3/30 (10%)	1/4 (25%)		Crohn's disease: 2/18 (11.1%)			6/145 (4.14%)
van Turenhout 2010	592 procedures Single centre experience The Netherlands February 2003 until June 2007	**Indications for capsule endoscopy**	382/592 (64.5%) obscure-occult : 240/592 (40.5%) overt: 142/592 (24%)	Abdominal pain 27/592 (4.6%)	34/592 (5.7%)	31/592 (5.2%)	47/592 (7.9%)		Celiac disease: 50/592 (8.4%)	
		Retentions per indications	3/382 (0.8%)				1/47 (2%)		2/50 (4%)	6/592 (1%)

Conclusions

The overall capsule retention ranged from 0.3% to 9.68%, median percentage of 2.09%.
Retention in patients with indications of obscure gastrointestinal bleeding was listed in 8 studies ranging from 0.63% to 9.2%; median value was 1.2%.
Only two studies reported retention for patients with indications of anemia: 0.14% and 25%.
Retention in patients with indications of pain was listed in 7 studies : with the median percentage of 4.35%, range 0.20% to 10%
Only two studies reported retention in patients who underwent capsule endoscopy for diarrhea respectively with a percentage of 0.98% and 1.43%.
Retention in patients with suspected small bowel tumors was reported in three studies with a percentage of 2.1%, 6.98% and 33.3% respectively.
Retention in patients with indications of Crohn's disease was reported in 6 studies; median percentage was 4.1%, range: 2% to 56.2%.

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Excluded studies

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Awaiting assessment

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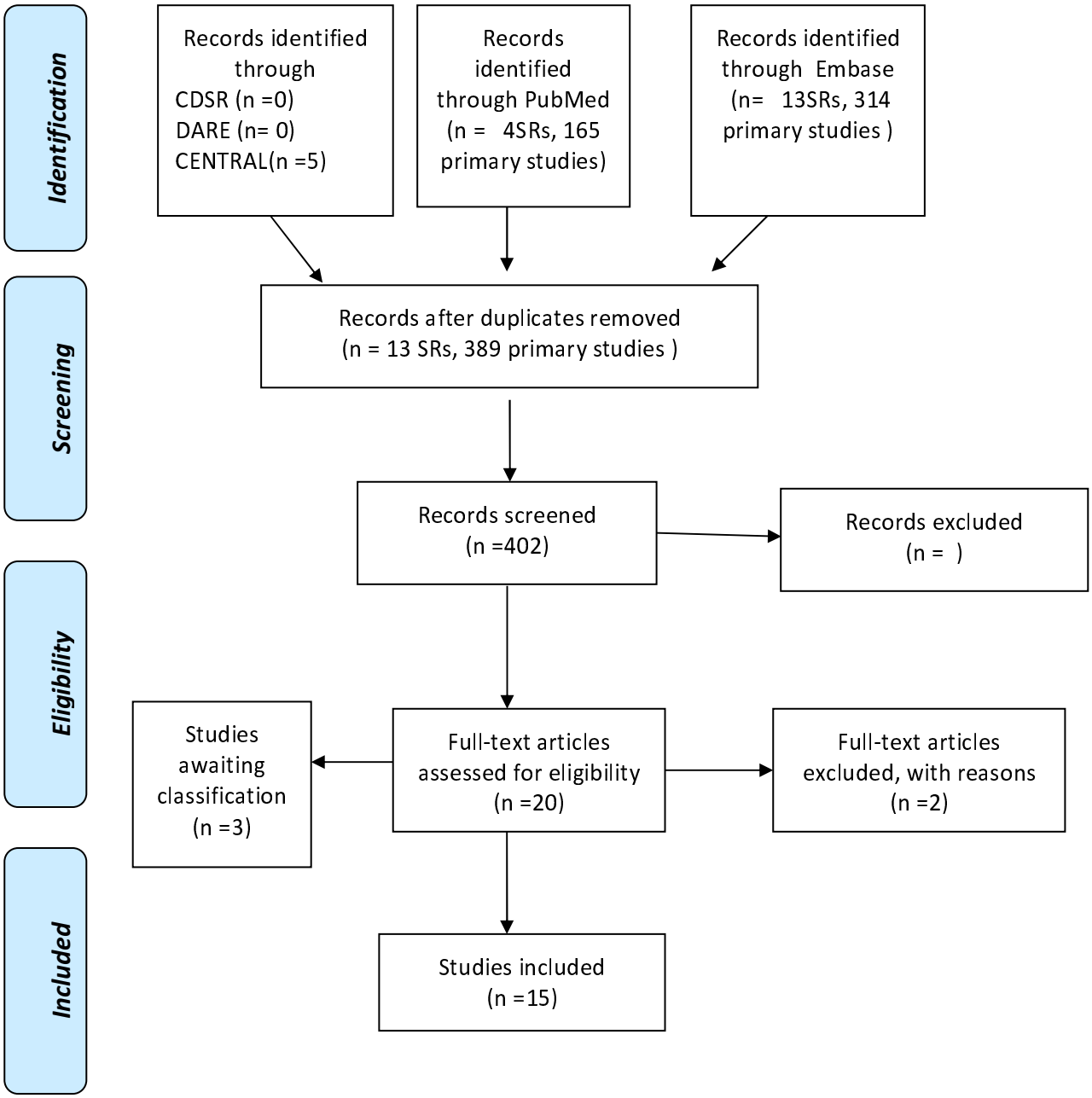
PRISMA 2009 Flow Diagram



AZIENDA OSPEDALIERO-UNIVERSITARIA
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Centro di Riferimento per l'Epidemiologia e la Prevenzione Oncologica in Piemonte

Capsule Retention

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

4.1 (St. 6.1-6.2) **Capsule rentention**

P: Asymptomatic patients with CE retention
I: endoscopic/surgical retrieval
C: wait and watch (no invasive approach)
O: Morbidity, mortality, rate of obstruction/perforation/progress of underlying disease
NOTES: Should a retained capsule in an asymptomatic patient be retrieved? Should we select the retrieval method depending on the retention ethiology; tumor (surgery), IBD (medical therapy/DBE), unknown (DBE)

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 15/2/2016 separately for systematic reviews and primary studies using the following two different search strategies:

Systematic reviews and meta-analysis

PubMed

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Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** ('device removal'/exp OR obstruct*:ab,ti OR complications:ab,ti OR complication:ab,ti OR adverse:ab,ti) **AND** (retention:ab,ti OR retained:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

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#12 #3 and #6 and #10 and #11 Publication Year from 2000 to 2016

Primary studies

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** ("Device Removal"[Mesh] OR "complications" [Subheading] OR "adverse effects" [Subheading] OR obstruct*[Title/Abstract] OR complication[Title/Abstract] OR complications[Title/Abstract]) **AND** (retention[Title/Abstract] OR retained[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** ('device removal'/exp OR obstruct*:ab,ti OR complications:ab,ti OR complication:ab,ti OR adverse:ab,ti) **AND** (retention:ab,ti OR retained:ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)

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Results

Results of the bibliographic searches
After removing duplicates, 248 (12 SRs and 235 RCTs) articles were found. 11 articles were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies

6 articles were excluded: 2 because no outcome of interest (Fernandez-Urien 2015, Li 2008); 3 because no comparison of interest (Purdy 2011, Sachdev 2007, Van Weyenberg 2010); 2 because no comparison and no outcome of interest (Makipour 2014, Mitsui 2016).

Included studies
4 uncontrolled case series were included (Al-Bawardy 2015, Cheon 2007, Rondonotti2010, Singeap 2011).

Study	N patients with CE retention	Intervention	Control	symptoms of obstruction
Al-Bawardy 2015	15	surgical intervention because symptoms of obstruction (n = 10) endoscopic retrieval (n =2)	passing of capsule after treatment of inflammation (n = 3), passage after conservative measures for SB obstruction (n =1) loss to follow-up (n = 1).	surgical intervention because symptoms of obstruction: 10/15 (66.6%)
Cheon 2007	32	<u>Intervention group:</u> early laparotomy (7 patients) or DBE (4 patients)	<u>Passage group:</u> Medical therapy (21 patients) and followed until they developed symptoms related to obstruction or passed the capsule spontaneously	<u>Among 21 patients with medical therapy</u> Laparotomy due to obstruction symptoms or medical treatment failure n=10/21 (47.6%) Of these: In 5 patients definite obstruction symptoms requiring emergency surgery, and in the other 5 failure of medical treatment
Rondonotti 2010	61	retained capsules required endoscopic or surgical interventions (n=29)	retained capsules excreted naturally without any therapy or intervention (n=32)	2/29 urgent surgical intervention was performed because of acute obstruction. Not specified reason of surgical intervention for the other patients
Singeap 2011	3	Surgical for capsule retention (n=3)		Obstruction symptoms within 2–7 days postingestion in all 3 patients

Only one (Cheon 2007) study stated that the objective of the study was to compare the two different approaches (early laparotomy vs wait and watch or medical therapy). The other three simply described the clinical course of patients; in these studies it seems that surgical intervention was done when symptoms of obstruction appeared, but it is not always clear or not for all patients. Length of follow up after which surgical treatments was done is not specified in all the studies.

Quality of evidence

Study limitations (risk of bias): yes (retrospective case series)
Inconsistency of results: no
Indirectness of evidence: no
Imprecision: yes (only four studies with 111 participants)
Publication bias: undetected
Factors that can higher quality
large magnitude of effect: no
opposing plausible residual bias or confounding: no
dose-response gradient: no

Overall quality of evidence: overall quality of evidence was judged as very low for study limitation and imprecision

CONCLUSIONS: The only conclusion that can be drawn on the base of the paucity of available data in that surgical intervention because of symptom of obstruction or failure of medical therapy occurs on about the 50% of the patients with capsule retention. (**VERY LOW QUALITY EVIDENCE**)

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2. Cheon, J. H.; Kim, Y.-S.; Lee, I.-S.; Chang, D. K.; Ryu, J.-K.; Lee, K. J.; Moon, J.-S.; Park, C. H.; Kim, J.-O.; Shim, K.-N.; Choi, C. H.; Cheung, D. Y.; Jang, B. I.; Seo, G.-S.; Chun, H.-J., and Choi, M.-G. Can we predict spontaneous capsule passage after retention? A nationwide study to evaluate the incidence and clinical outcomes of capsule retention. Endoscopy. 2007; 39(12):1046-1052
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4. Singeap, A. M.; Trifan, A.; Cojocariu, C.; Sfarti, C., and Stanciu, C. Outcomes after symptomatic capsule retention in suspected small bowel obstruction. Eur J Gastroenterol Hepatol. 2011 Oct; 23(10):886-90.

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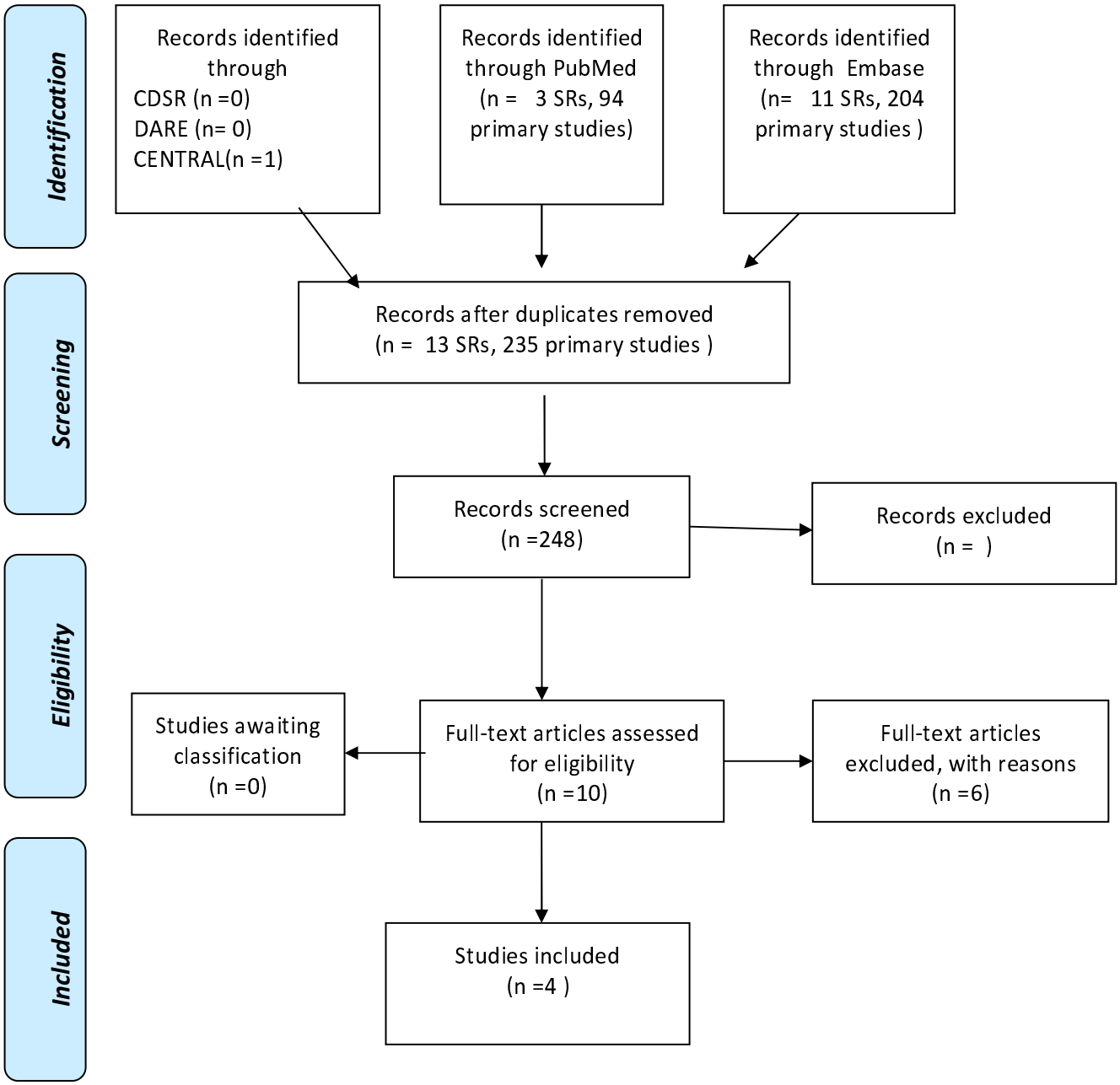
2. Li, F.; Gurudu, S. R.; De Petris, G.; Sharma, V. K.; Shiff, A. D.; Heigh, R. I.; Fleischer, D. E.; Post, J.; Erickson, P., and Leighton, J. A. Retention of the capsule endoscope: a single-center experience of 1000 capsule endoscopy procedures. Gastrointest Endosc. 2008 Jul; 68(1):174-80.
3. Makipour, K.; Modiri, A. N.; Ehrlich, A.; Friedenberg, F. K.; Maranki, J.; Enestvedt, B. K.; Heller, S.; Tokar, J., and Haluszka, O. Double balloon enteroscopy: effective and minimally invasive method for removal of retained video capsules. Dig Endosc. 2014 Sep; 26(5):646-9
4. Mitsui, K.; Fujimori, S.; Tanaka, S.; Ehara, A.; Omori, J.; Akimoto, N.; Maki, K.; Suzuki, M.; Kosugi, Y.; Ensaka, Y.; Matsuura, Y.; Kobayashi, T.; Yonezawa, M.; Tatsuguchi, A., and Sakamoto, C. Retrieval of retained capsule endoscopy at small bowel stricture by double-balloon endoscopy significantly decreases surgical treatment. J. Clin. Gastroenterol. 2016; 50(2):141-146
5. Purdy, M.; Heikkinen, M.; Juvonen, P.; Voutilainen, M., and Eskelinen, M. Characteristics of patients with a retained wireless capsule endoscope (WCE) necessitating laparotomy for removal of the capsule. In Vivo. 2011; 25(4):707-710 Sachdev, M. S.; Leighton, J. A.; Fleischer, D. E.; Heigh, R. I.; Hara, A. K.; Post, J. A.; Erickson, P. J., and Sharma, V. K. A prospective study of the utility of abdominal radiographs after capsule endoscopy for the diagnosis of capsule retention. Gastrointest. Endosc. 2007; 66(5):894-900
6. Van Weyenberg, S. J.; Van Turenhout, S. T.; Bouma, G.; Van Waesberghe, J. H.; Van der Peet, D. L.; Mulder, C. J., and Jacobs, M. A. Double-balloon endoscopy as the primary method for small-bowel video capsule endoscope retrieval. Gastrointest Endosc. 2010 Mar; 71(3):535-41.

PRISMA 2009 Flow Diagram



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Clear Instructions with regard to diet, fastening and restrictions

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

5.1 (St. 8.1) **Clear (and type of) instructions with regard to diet, fastening and restrictions (Iron …)**

P: Patients referred for CE
I: provision of information regarding fasting and diet
C:
O: compliance with provided indications
Notes: Modality of information (oral, written, doctor or nurse…). Is there any evidence that who provides the information and the type of information have an impact on compliance?

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 15/2/2016 separately for systematic reviews and randomized controlled trials using the following search strategies:

Systematic reviews and meta-analysis

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** (fasting[Text Word] OR "Diet"[Mesh] OR diet[Text Word] OR instruction[Title/Abstract] OR indication[Title/Abstract] OR information[Title/Abstract] OR instructions[Title/Abstract] OR indications[Title/Abstract] OR informations[Title/Abstract]) **AND** ("Patient Compliance"[Mesh] OR compliance [Title/Abstract] OR Adherence[Title/Abstract] OR attendance[Title/Abstract] OR compliant[Title/Abstract] OR compliants[Title/Abstract]) **AND** ("systematic review" [Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** (fasting:ab,ti OR diet:ab,ti OR 'diet restriction'/exp OR

instruction:ab,ti OR indication:ab,ti OR information:ab,ti OR instructions:ab,ti OR indications:ab,ti OR informations:ab,ti) **AND** ('patient compliance'/exp OR Adherence:ab,ti OR attendance:ab,ti OR compliants:ab,ti OR compliant:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

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

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Intestine, Small] explode all trees
#5 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
7 MeSH descriptor: [Diet] explode all trees
#8 fasting or diet:ti,ab,kw (Word variations have been searched)
#9 indication or instruction or information:ti,ab,kw (Word variations have been searched)
#10 #7 or #8 or #9
#11 MeSH descriptor: [Patient Compliance] explode all trees
#12 compliance or attendance or Adherence:ti,ab,kw (Word variations have been searched)
#13 #11or #12
#14 #3 and #6 and #10 and #13 Publication Year from 2000 to 2016

Primary studies

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** (fasting[Text Word] OR "Diet"[Mesh] OR diet[Text Word] OR instruction[Title/Abstract] OR indication[Title/Abstract] OR information[Title/Abstract] OR instructions[Title/Abstract] OR indications[Title/Abstract] OR informations[Title/Abstract]) **AND** ("Patient Compliance"[Mesh] OR compliance [Title/Abstract] OR Adherence[Title/Abstract] OR attendance[Title/Abstract] OR compliant[Title/Abstract] OR compliants[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** (fasting:ab,ti OR diet:ab,ti OR 'diet restriction'/exp OR instruction:ab,ti OR indication:ab,ti OR information:ab,ti OR instructions:ab,ti OR indications:ab,ti OR informations:ab,ti) **AND** ('patient compliance'/exp OR Adherence:ab,ti OR attendance:ab,ti OR compliants:ab,ti OR compliant:ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta

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

Cochrane Central Register of Controlled Trials (CENTRAL)

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Intestine, Small] explode all trees
#5 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
7 MeSH descriptor: [Diet] explode all trees
#8 fasting or diet:ti,ab,kw (Word variations have been searched)
#9 indication or instruction or information:ti,ab,kw (Word variations have been searched)
#10 #7 or #8 or #9
#11 MeSH descriptor: [Patient Compliance] explode all trees
#12 compliance or attendance or Adherence:ti,ab,kw (Word variations have been searched)
#13 #11or #12
#14 #3 and #6 and #10 and #13 Publication Year from 2000 to 2016

Results

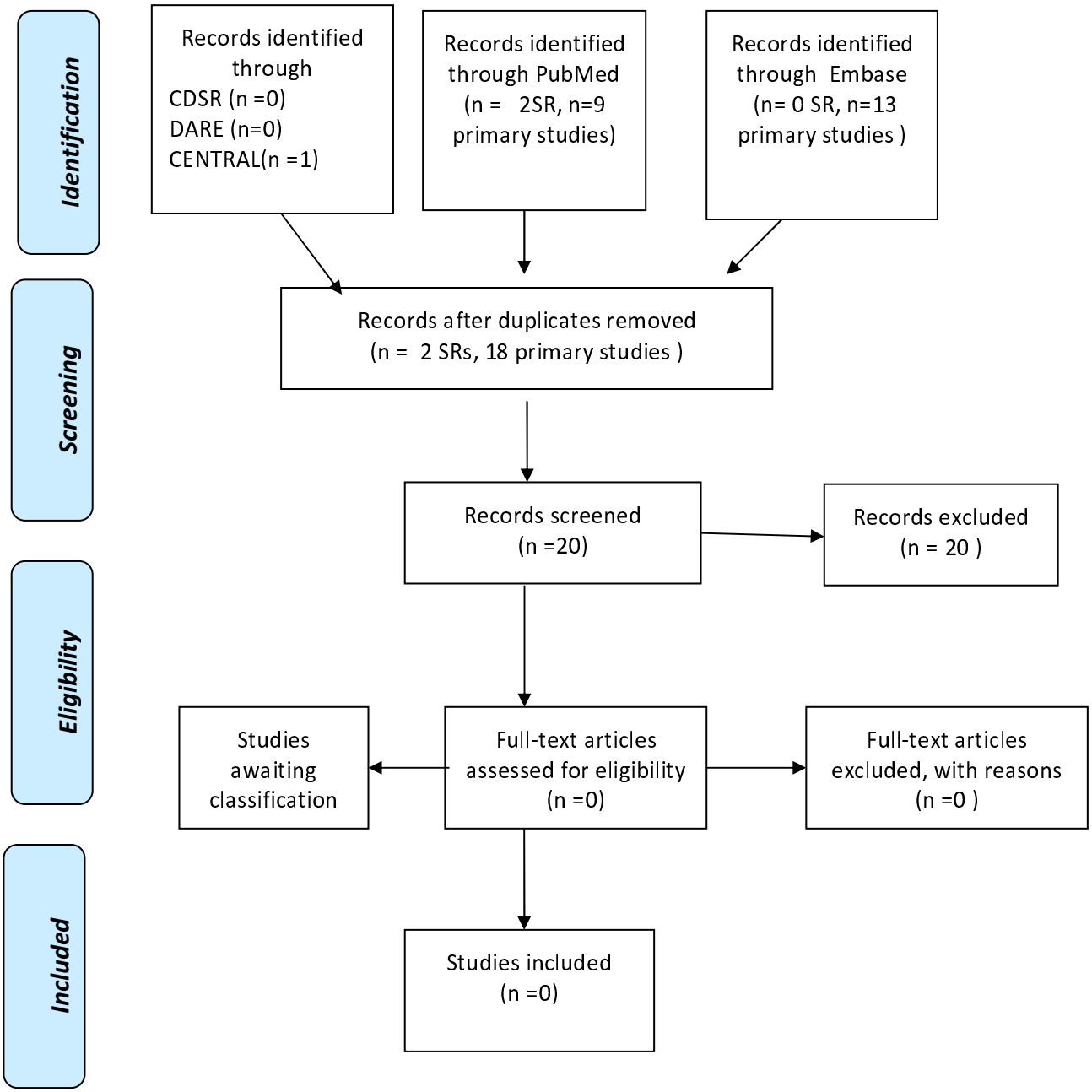
Results of the bibliographic searches

After removing duplicates, 20 articles (2 systematic reviews and 18 primary studies) were found. No relevant studies were found addressing this question.

Conclusions

No evidence about the relation between modality of information and compliance was found.

PRISMA 2009 Flow Diagram



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Completeness of Procedure

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6.1 (St. 9.1) **Completeness of procedure**

P: Patients having CE and risk factors for not completeness (Diabetes, neurological diseases, hospitalisation, immobilisation, previous abdominal surgery, IBD)
I: use of promotility agents, use of real time viewer
C: No promotility agents, no real time viewer
O: rate of complete bowel visualisation

Notes: Are there other factors influencing completenss of SB visualization (chewing gum, right lateral position after swallowing the capsule etc). The main factors influencing the completeness rate are those that you have included. Rate pf gastric retention should be defined. Does general use of real time viewer with endoscopic transport of the capsule to the duodenum or application of prokinetics in case of delayed gastric transport increase completeness of CE?

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 15/2/2016 separately for systematic reviews and primary studies using the following two different search strategies:

Systematic reviews and meta-analysis

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** (promotility[Title/Abstract] OR prokinetic[Title/Abstract] OR "T 1815" [Supplementary Concept] OR "AU 116" [Supplementary Concept] OR "AU 130" [Supplementary Concept] OR "Cisapride"[Mesh] OR "real time viewer"[Title/Abstract] OR "real time image"[Title/Abstract] OR mosapride[Title/Abstract] OR "Metoclopramide"[Mesh] OR "Gastrointestinal Motility"[Mesh] OR "Erythromycin"[Mesh] OR "Antiemetics"[Mesh] OR "Domperidone"[Mesh] OR "mosapride" [Supplementary Concept] OR Domperidone[Title/Abstract] OR Erythromycin[Title/Abstract] OR Antiemetic[Title/Abstract]) **AND** ("systematic review" [Title/Abstract] OR "systematic reviews"

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

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** (promotility:ab,ti OR prokinetic:ab,ti OR 'cisapride'/exp OR 'prokinetic agent'/exp OR 'real time viewer':ab,ti OR 'real time image':ab,ti OR 'mosapride'/exp OR mosapride:ab,ti OR 'metoclopramide'/exp OR 'gastrointestinal motility'/exp OR 'erythromycin'/exp OR 'antiemetic agent'/exp OR Domperidone:ab,ti OR Erythromycin:ab,ti OR Antiemetic:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

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

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#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Intestine, Small] explode all trees
#5 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
#7 MeSH descriptor: [Cisapride] explode all trees
#8 MeSH descriptor: [Metoclopramide] explode all trees
#9 MeSH descriptor: [Gastrointestinal Motility] explode all trees
#10 MeSH descriptor: [Erythromycin] explode all trees
#11 MeSH descriptor: [Antiemetics] explode all trees
#12 MeSH descriptor: [Domperidone] explode all trees
#13 promotility or prokinetic or real time viewer or real time image or mosapride or Domperidone or Erythromycin or Antiemetic:ti,ab,kw (Word variations have been searched)
#14 #7or #8 or #9 or #10 or #11 or #12 or #13
#15 #3and #5 and #14 Publication Year from 2000 to 2016

Primary studies

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** (promotility[Title/Abstract] OR prokinetic[Title/Abstract] OR "T 1815" [Supplementary Concept] OR "AU 116" [Supplementary Concept] OR "AU 130" [Supplementary Concept] OR "Cisapride"[Mesh] OR "real time viewer"[Title/Abstract] OR "real time image"[Title/Abstract] OR mosapride[Title/Abstract] OR "Metoclopramide"[Mesh] OR "Gastrointestinal Motility"[Mesh] OR "Erythromycin"[Mesh] OR "Antiemetics"[Mesh] OR "Domperidone"[Mesh] OR "mosapride" [Supplementary Concept] OR Domperidone[Title/Abstract] OR Erythromycin[Title/Abstract] OR Antiemetic[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews" [Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** (promotility:ab,ti OR prokinetic:ab,ti OR 'cisapride'/exp OR 'prokinetic agent'/exp OR 'real time viewer':ab,ti OR 'real time image':ab,ti OR 'mosapride'/exp OR mosapride:ab,ti OR 'metoclopramide'/exp OR 'gastrointestinal motility'/exp OR 'erythromycin'/exp OR 'antiemetic agent'/exp OR Domperidone:ab,ti OR Erythromycin:ab,ti OR Antiemetic:ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)

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#3 #1 or #2
#4 MeSH descriptor: [Intestine, Small] explode all trees
#5 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
#7 MeSH descriptor: [Cisapride] explode all trees
#8 MeSH descriptor: [Metoclopramide] explode all trees
#9 MeSH descriptor: [Gastrointestinal Motility] explode all trees
#10 MeSH descriptor: [Erythromycin] explode all trees
#11 MeSH descriptor: [Antiemetics] explode all trees
#12 MeSH descriptor: [Domperidone] explode all trees
#13 promotility or prokinetic or real time viewer or real time image or mosapride or Domperidone or Erythromycin or Antiemetic:ti,ab,kw (Word variations have been searched)
#14 #7or #8 or #9 or #10 or #11 or #12 or #13
#15 #3and #5 and #14 Publication Year from 2000 to 2016

Results

Results of the bibliographic searches

After removing duplicates, 387 (17 SRs and 370 primary studies) articles were found. 14 articles were considered potentially relevant and acquired in full text (See flow chart).

Awaiting classification

One review was classified as awaiting classification because it is written in Chinese (He 2013). One primary study (Chen 2012) was classified as awaiting classification because it is written in Chinese.

Excluded studies

One review was excluded because it was a narrative review (Pennazio 2010). Four primary studies were excluded: two because they were letters without useful data (Koulanzidis 2014, De Castro 2015) one because both groups received real time viewer (Ogata 2008) and one (Liao 2009) because the intervention was not in the inclusion criteria.

Included studies

Real time viewer: no systematic reviews were found assessing the efficacy of real time viewer; five primary studies were finally included (Cotter 2013, Gao 2010, Hosono 2011, Lai 2007, Shiotani 2011).
Promotility agents: two systematic reviews (Kotwal 2014, Koulaouzidis 2013) were found assessing the efficacy of promotility agents. There was a total overlapping of primary studies included by the two reviews, and Koulanzidis 2013 included many more studies (Table 1), so only the review by Koulanzidis 2013 was considered for data extraction. The bibliographic search of Koulanzidis 2013 was updated to November 2012, so primary studies were considered for inclusion only if published since December 2012. One primary study was finally included (Koulanzidis 2015).

Completion rate in all studies except one was defined as the capsule reaching the caecum; in Hosono 2011 small bowel examination was considered to be complete if the capsule had passed into the colon.

Table 1. Overlapping of primary studies included in the reviews

	Kotwal 2014	**Koulaouzidis 2013**
Almeida 2010	X	X
Apostolopoulos 2008		X
Caddy 2006	X	X
Hooks 2009		X
Hosono 2011		X
Ida 2012		X
Iwamoto 2010		X
Leung 2005		X
Nakaji 2011 Available at: http:// www.intechopen.com/books/new-techniques-in-gastrointestinal-endoscopy/effectiveness-of-daikenchuto-a-traditional-japanese-herbal-medicine-inaccelerating-capsule-endoscop [last accessed 21 May 2013		X
Niv 2008		X
Postgate 2009		X
Selby 2005		X
Shiotani 2011		X
Song 2010		X
Wei 2007	X	X
Xiong 2012		X
Zhang 2011	X	X

Table 2. Promotility agents

Study	**N Patients or examinations** **Type of risk factor**	**Intervention**	**Control**	**small bowel capsule endoscopy completion rate**
Koulaouzidis 2013	1904 in 17 studies (14 prospective, 3 retrospective) Type of risk factor not evaluated	876 who received a prokinetic (Metoclopramide, Erythromycin, mosaprid, lubiprostone, and the combined effect of daikenchuto metoclopramide)	1028 individuals who ingested the capsule with no prokinetic	Overall= OR (95% CI)=1.96 (1.38–2.78) According to type of prokinetics **erythromycin** 3 studies, I^2=37.6%, P=0.201; pooled OR (95% CI) =1.36 (0.61–3.03). **metoclopramide** 10 studies , I^2=38.3%, P=0.103); OR (95% CI) = 2.08 (1.35–3.21). **Other prokinetics** 4 studies, I2=58.7%, P=0.064; OR (95% CI) =1.89 (0.75–4.82).
Koulaouzidis 2015	635 SBCE Examinations: Type of risk factor not evaluated; 30.7% of patients had known/suspected Chron disease	437/635 (68.8%) ingested the capsule with liquid domperidone (5 mg)	198 (31.2%) ingested the capsule without any domperidone	Overall =565/635 (88.9%) domperidone vs without any domperidone 91.1% vs. 84.3%, P=0.012.

Table 3. Real time viewer

Study	**N Patients or examinations** **Type of risk factor**	**Intervention**	**Control**	**small bowel capsule endoscopy completion rate**
Gao 2010	534 consecutive outpatients with suspected small-bowel lesions referred for second-generation CE Type of risk factor not evaluated	Group B: CE with a real-time viewer . If the capsule did not reach the small bowel, the patient would receive propofol 1.2 mg/kg and fentanyl 1 μg/kg for analgesia and sedation and undergo endoscopic placement of the	Group A: conventional CE (n=273) CE performed before the introduction of real time in clinical practice	Group A= 213/273 (78%) Group B=228/261 (87.4%) P=0.004

		capsule in the duodenum with a polypectomy snare (n=261)		
Hosono 2011 (RCT)	80 adult subjects Exclusion criteria: history of gastric or intestinal surgery, clinical or suspected abnormalities in gastric emptying, pregnancy, and intake of medications during the previous week that could potentially affect the gastrointestinal motility.	'real-time group' pre-procedure preparation like conventional CE group, plus a real-time viewer was attached to the patients. At 60 min after swallowing the capsule, if the capsule had reached the small bowel, 500 ml of polyethylene glycol was administered (n=33); if the capsule was still located in the stomach, 10 mg of metoclopramide was given intramuscularly, followed by 500 ml of polyethylene glycol solution (n=7).	'conventional group': the patients instructed to fast for 12 h prior to the CE procedure, and swallow the capsule with water and 0.5 ml simethicone (n=40)	Conventional:29/40 (72.5%) Real time: 36/40 (90.0%) P=0.04
Lai 2007	45 consecutive patients Type of risk factor not evaluated	Real-time WCE . If the capsule had not reached the small bowel after the first 30 minutes, a liter of polyethylene glycol was given. If the capsule still failed to enter the small bowel after another 30 minutes, 250 mg of erythromycin was given orally. (n=18)	Conventional Wireless capsule endoscopy (WCE) (n=27) CE performed before the introduction of real time in clinical practice	Conventional= 19/27 (70.4%) Real-time=17/18 (94.4%) P=0.048
Shiotani 2011	200 patients Type of risk factor not evaluated	real time viewer group procedures. If the capsule did not pass through the esophagus, 200 mL of water was given. If the	control group Procedures excluded if CE preparation such as polyethylene glycol, sodium phosphate,	Control group= 66/100 (66%) Viewer group=86/100 (86%) p=0.002

		capsule did not pass through the stomach, 200 mL of water was given in the right lateral position . If the capsule remained in the stomach after 30 minutes , 10 mg of metoclopramide was administered intravenously. If after 30 min the capsule remained in the stomach, it was passed into the duodenum with endoscopic assistance. (n: 100)	prokinetics, etc. including metoclopramide were used. CE performed before the introduction of real time in clinical practice (n:100)	
Cotter 2013	389 patients	<u>RTV group: (n=82)</u> If the capsule remained in the stomach, 10 mg of domperidone were administered per os and the location of the capsule was rechecked after 30 min. If it still remained in the stomach, an additional dose of 10 mg of domperidone was administered orally and after another 30 min the location of the capsule was rechecked; then if still in the stomach the capsule was placed directly in the duodenum by upper endoscopy using a basket.	<u>standard procedure : (n=307)</u>	Incomplete examination Control group =48/307 (15.6%) RTV group=3/82 (3.7%) P=0.003

Quality of evidence

Rate of complete bowel visualisation

<u>Factors that can lower quality</u>

Study limitations (risk of bias): yes (none of the cohort studies adjusted for potential confounding)

Inconsistency of results: no

Indirectness of evidence: yes (subjects not selected for having risk factors for retention)

Imprecision: no (18 studies with 2539 participants for promotility agents, 5 studies with 1248 participants).
Publication bias: no
Factors that can higher quality
large magnitude of effect: no
opposing plausible residual bias or confounding: no
dose-response gradient: no

Overall quality of evidence: overall evidence was rated as *very low* because coming from observational studies (only one RCT for real time viewer, Hosono 2011) with study limitation and indirectness.

Conclusions

Bothe the use of prokinetics and of real-time viewer improves completion rate (**VERY LOW QUALITY OF EVIDENCE**).

References

Awaiting classification

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Included studies

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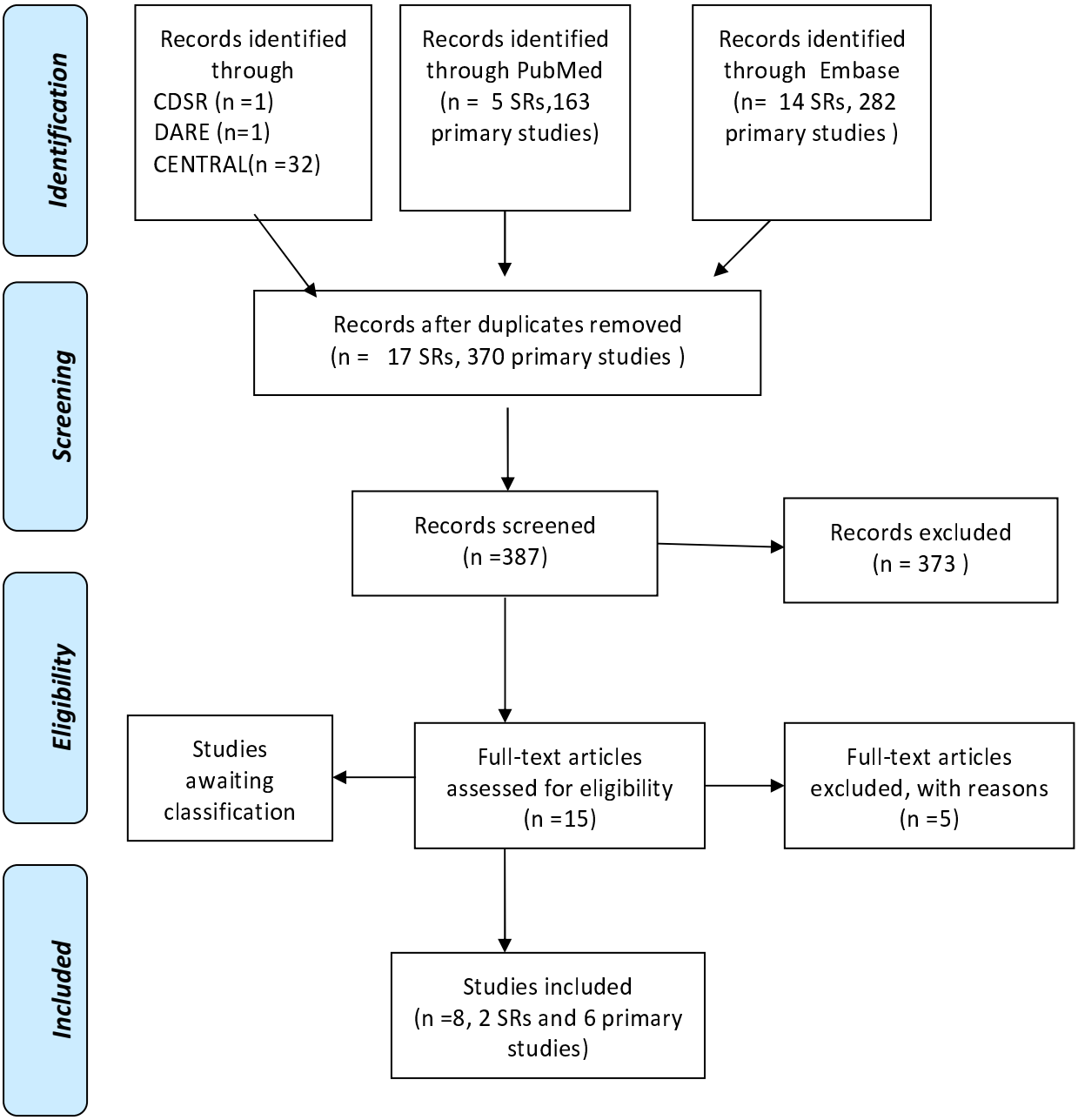
PRISMA 2009 Flow Diagram



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Enteroscopy Post CE

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

7.1 (St. 10.1) **Rate of post CE referral to enteroscopy (DAE), Angiography, Surgery, Chemo-therapy etc**

P: Patients having enteroscopy post CE
I: Triage with small bowel capsule
C: Enteroscopy without capsule triage
O: improved lesion detection rates /reduced missed rates when enteroscopy is performed after CE

Notes: Is CE able to select patients to improve the quality of enteroscopy? Is there a minimum concordance rate between CE and enteroscopy? Does a low diagnostic yield at enteroscopy (post CE) mean a low CE quality? in other terms, is enteroscopy directly influenced by the quality of the CE report (i.e: lesion location, size ...)?

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 15/2/2016 separately for systematic reviews and primary studies using the following two different search strategies:

Systematic reviews and meta-analysis

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** ("Double-Balloon Enteroscopy" [Text Word] OR DAE[Title/Abstract] OR Enteroscopy[Text Word] OR Enteroscopies[Title/Abstract])**AND** ("Diagnostic yield"[Title/Abstract] OR "Intestinal Diseases/diagnosis"[Mesh] OR findings[Title/Abstract] OR finding[Title/Abstract] OR missed[Title/Abstract] OR missing[Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** (DAE:ab,ti OR Enteroscopies:ab,ti OR Enteroscopy:ab,ti OR 'double balloon enteroscopy'/exp) **AND** ('diagnostic yield':ti,ab OR 'small intestine disease'/exp/dm_di OR findings:ab,ti OR finding:ab,ti OR missed:ab,ti OR missing:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

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

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Intestine, Small] explode all trees
#5 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
#7 MeSH descriptor: [Double-Balloon Enteroscopy] explode all trees
#8 Enteroscopy or DAE:ti,ab,kw (Word variations have been searched)
#9 #7or #8
#10 MeSH descriptor: [Intestinal Diseases] explode all trees and with qualifier(s): [Diagnosis - DI]
#11 diagnostic yield or finding or missed rates:ti,ab,kw (Word variations have been searched)
#12 #10 or #11
#108 #3 and #6 and #9 and #12 Publication Year from 2000 to 2016

Primary studies

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** ("Double-Balloon Enteroscopy" [Text Word] OR DAE[Title/Abstract] OR Enteroscopy[Text Word] OR Enteroscopies[Title/Abstract]) **AND** (detect*[Title/Abstract] OR prevalence[Text Word] OR presence[Text Word] OR rate[Text Word] OR rates[Text Word] OR diagnos*[Title/Abstract] OR predict*[Title/Abstract] OR missed[Title/Abstract] OR missing[Title/Abstract] OR "diagnostic yield"[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** (DAE:ab,ti OR Enteroscopies:ab,ti OR Enteroscopy:ab,ti OR 'double balloon enteroscopy'/exp) **AND** (detection:ab,ti OR detected:ab,ti OR prevalence:ab,ti OR presence:ab,ti OR rate:ab,ti OR rates:ab,ti OR diagnos*:ab,ti OR predict*:ab,ti OR missed:ab,ti OR missing:ab,ti OR 'diagnostic yield':ab,ti) **NOT** (cochrane OR

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

Cochrane Central Register of Controlled Trials (CENTRAL)

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Intestine, Small] explode all trees
#5 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
#7 MeSH descriptor: [Double-Balloon Enteroscopy] explode all trees
#8 Enteroscopy or DAE:ti,ab,kw (Word variations have been searched)
#9 #7or #8
#10 MeSH descriptor: [Intestinal Diseases] explode all trees and with qualifier(s): [Diagnosis - DI]
#11 diagnostic yield or finding or missed rates:ti,ab,kw (Word variations have been searched)
#12 #10 or #11
#108 #3 and #6 and #9 and #12 Publication Year from 2000 to 2016

Results

Results of the bibliographic searches

After removing duplicates, 1026 (37 SRs and 989 primary studies) articles were found. 20 articles were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies

15 primary studies were excluded: eleven because no comparison of interest (Balmadrid 2013, Chen 2013, Chu 2016, Huang 2015, Li 2007, Li 2010, Maeda 2015, Matsumura 2013, Nakamura 2006, Rey 2009, Shiani 2016); two because no outcome of interest (Gomez 2013, Ross 2008); one because a letter (Manes 2009); one because abstract of already included study (Sethi 2013).

Included studies

5 cross sectional studies were included; for two studies data were available in conference abstracts form . Overall 781 patients were included.

Study	Patient and setting	Intervention	Control	Diagnostic yield
Brahmbhatt 2015 (conference abstract)	243 patients evaluated for over OGIB; single tertiary center; between 2/2009 and 9/2013	VCE (video capsule endoscopy) prior to double-balloon enteroscopy (DBE) (n=126)	Only DBE (n=117)	VCE cohort=67% no-VCE cohort=69% no significant difference
Fry 2009 (conference abstract)	51 consecutive patients evaluated for OGIB; single tertiary center; Germany	second period, 2007 (DBE after CE) 24 patients underwent 27 DBEs for OGIB	first period, 2006 (DBE alone) 27 patients underwent 33 DBEs for OGIB	DBE after CE: 62.9% DBE alone: 39.9% (p< 0.002).
Holleran 2015	233 patients for any indication; two centres;	small bowel capsule endoscopy (SBCE) prior to DBE (n = 46)	DBE only (n=187)	SBCE prior: 28 (61%) without SBCE prior: 87 (43 %) P<0.0001.
Sethi 2014	150 patients for any indication; single tertiary center;	Single balloon enteroscopy (SBE) with prior CE (n = 113)	SBE alone (n= 37)	SBE with prior CE:68.2 % SBE alone:43.8% P= 0.002
Sidhu 2008	104 patients for any indication , excluding celiac disease. Single tertiary center	Push enteroscopy (PE) with prior CE (n = NR)	PE alone (n:NR)	CE followed by PE: 47% only PE :41%, (P:NS).

Quality of evidence

Diagnostic yield

Factors that can lower quality

Study limitations (risk of bias): yes (cross sectional studies not adjusting for potential confounders)
Inconsistency of results: no (only one conference abstract has a better diagnostic yield for control group but with no significant difference)
Indirectness of evidence: no
Imprecision: no
Publication bias: not evaluated

Factors that can higher quality

large magnitude of effect: yes
opposing plausible residual bias or confounding: no
dose-response gradient: no

Overall quality of evidence: overall evidence was rated as *low* because coming from observational studies with study limitation (risk of bias) and imprecision but with a large magnitude of effect.

Conclusions

The use of SBCE with DBE improved the diagnostic yield. Prior capsule endoscopy is associated with an increased diagnostic and therapeutic yield during single-balloon enteroscopy (**LOW QUALITY OF EVIDENCE**).

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1. Balmadrid, B. L.; Seven, G.; Kozarek, R. A.; Ross, A. S.; Irani, S.; Gluck, M.; Schembre, D. B.; Koch, J., and Gan, S. I. Video capsule endoscopy and double balloon enteroscopy in the evaluation of obscure gastrointestinal bleeding. Gastrointest. Endosc. 2013; 77(5):AB277
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14. Sethi, S.; Thaker, A.; Cohen, J.; Garud, S.; Sawhney, M.; Chuttani, R.; Pleskow, D.; Falchuk, K., and Berzin, T. Prior capsule endoscopy improves the diagnostic and therapeutic yield of single-balloon enteroscopy. Am. J. Gastroenterol. 2013; 108S101
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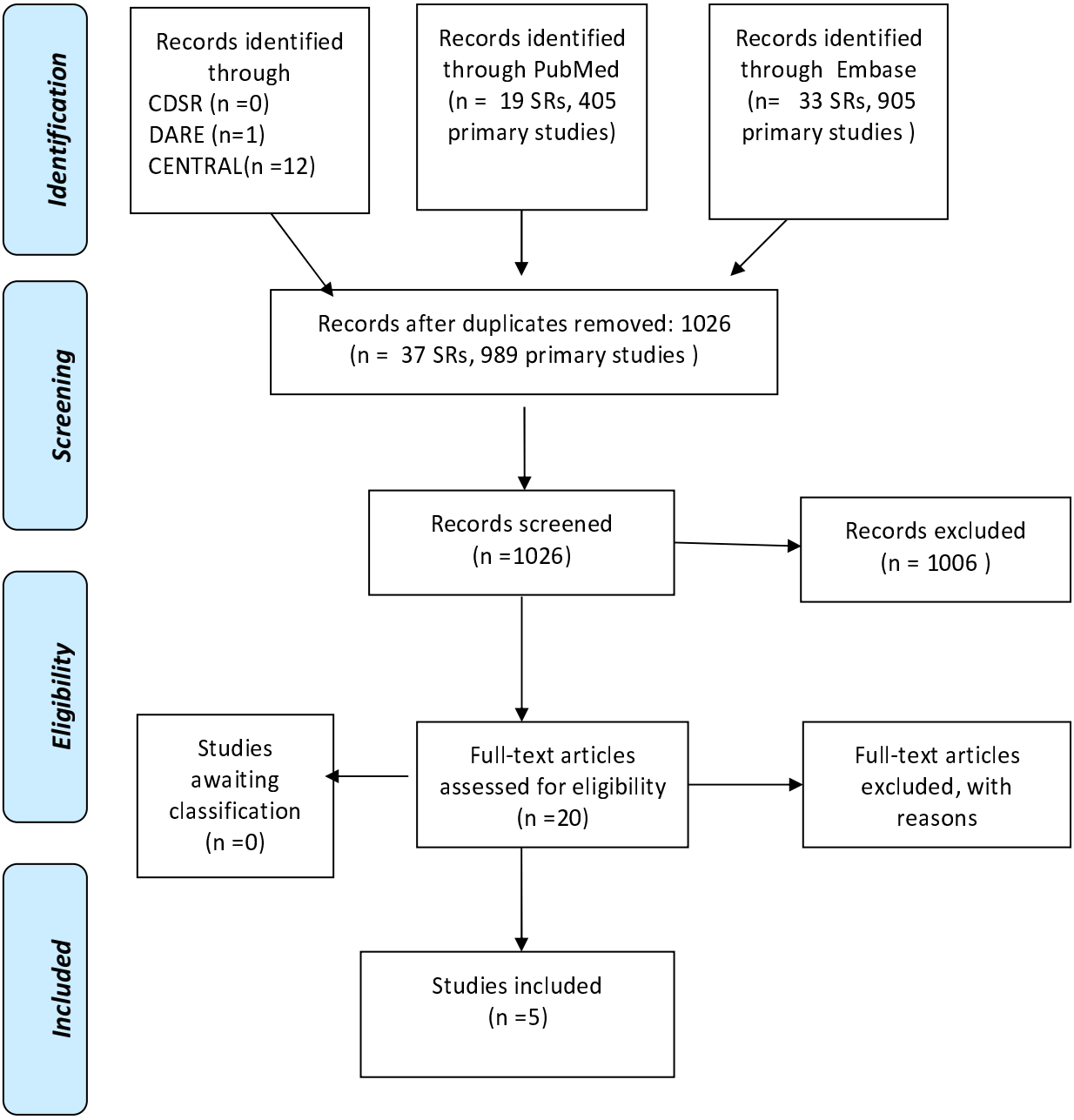
PRISMA 2009 Flow Diagram



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Patency Capsule

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8.1 (St. 11.1) **Capsule retention**

P: Patients having CE
I: Patency capsule
C: no Patency capsule
O: lower incidence of capsule retention
Notes: Can the use of Patency capsule reduce the incidence of capsule retention in high risk patients?

8.2. (St. 11.2) **Patency capsule Usage / Rates per Indication**

P: Patients having CE small bowel
I: Utilisation in selected patients only (Crohn)
C: routine utilisation / no utilisation
O: risk avoidance: retention
Notes: Should patency capsule be indicated only in a selected group of patients or routinely in every patient indicated to CE?

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 15/2/2016 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** "Patency capsule"[Title/Abstract] **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** 'Patency capsule':ab,ti **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

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

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Intestine, Small] explode all trees
#5 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
#7 patency capsule:ti,ab,kw (Word variations have been searched)
#8 #3 and #6 and #7 Publication Year from 2000 to 2016

Primary studies

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** "Patency capsule"[Title/Abstract] **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** 'Patency capsule':ab,ti **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 MeSH descriptor: [Intestine, Small] explode all trees

#5 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#6 #4 or #5
#7 patency capsule:ti,ab,kw (Word variations have been searched)
#8 #3 and #6 and #7 Publication Year from 2000 to 2016

Results

Results of the bibliographic searches
After removing duplicates, 151 (16 SRs and 135 RCTs) articles were found. 11 articles were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies

8 articles were excluded: one because letter without useful data (Spada 2008); two because conference abstracts of already included study (Nemeth Gastrointest. Endosc. 2015, Nemeth J Crohn's Colitis 2015); 5 because no comparison of interest (Albuquerque 2016, Herrerias 2008, Nakamura 2015, Signorelli 2006, Spada 2007).

Included studies
Three studies were finally included. One (Fernández-Urién 2015) was a multicentre retrospective cohort study on 5,428 consecutive CE-procedures (212 esophagus, 5013 small bowell, 203 colon) conducted on all patients, 22.7% of which with IBD. The study compared the incidence of capsule retention in centres were patency capsule was never used, in centres where patency was introduced only at a definite time point before and after the it introduction (pre patency era and post patency era).
One (Nemeth 2016) was a retrospective multicentre study assessing the impact of patency capsule on capsule retention in 343 patients with established Crohn's disease.
One (Handa 2013) was a conference abstract of a pilot randomised trials on 24 patients with Crohn's disease who were randomised to receive or not patency capsule. Only the results for the no patency groups were reported.

Clinical question 1: Patency vs no patency

Study	**Population**	**Intervention vs control**	**Capsule retention**
Fernández-Urién 2015	5,428 CE-procedures (212 esophagus, 5013 small bowell, 203 colon) 1232 patients had IBD	patency capsule: 2036 no patency: 1705	**AEs (Capsule retention)** =102/5428 (1.9%) Pre-Patency era= 14/ 824 (1.7%) Post-Patency era= 25/ 2,036 (1.2%) No Patency era =16/ 881 (1.8 %) P:ns
Nemeth 2016	406 patients who performed VCE with established Crohn's disease	Patency capsule before VCE(n= 274) VCE performed in 211 patients	**Capsule retention** Patency capsule=6/211 (2.8%) no patency capsule=3/132 (2.3%) in patency group

		vs VCE performed without patency capsule (n=132)	positive patency capsule test= 2/18 (11.1%) Negative patency capsule test= 4/193 (2.1%)
Handa 2013 (pilot RCT, conference abstract)	24 patients with Crohn's disease (CD) at remission stage (CDAI<150)	Group A: no patency capsule, abdominal CT + VCE (n=12) Group B: abdominal CT + VCE + patency capsule before VCE(n=12)	no patency: 5/12 (41.7%)

Clinical question 2: Utilisation in selected patients only (Crohn) vs routine utilisation / no utilisation

Study	**Population**	**Intervention vs control**	**Capsule retention**
Nemeth 2016	342 patients who performed VCE with established Crohn's disease	non- selective strategy (all patents with Chron disease received patency) (162) vs selected strategy (patency capsule administered only to patients with obstructive symptoms, history of obstruction or previous abdominal surgery) (n:180)	non selective strategy: patency capsule performed in all patients, VCE performed in 127/162 (78.4%) selective strategy: patency performed in 73/180 (40.5%) patients, VCE performed in 155/180 (86.1%) **Capsule retention** non selective strategy:2/162 (1.6%) selective strategy:2/180 (1.3%) p:ns

Quality of evidence

Clinical question 1: patency vs no patency
Study limitations (risk of bias): yes (observational studies)
Inconsistency of results: no
Indirectness of evidence: yes (in one study only the 26.7% of participants were at high risk of capsule retention)
Imprecision: no

Publication bias: undetected
Overall quality of evidence: overall quality of evidence was judged as very low for study limitation and indirectness

Clinical question 2: Utilisation in selected patients only (Crohn) vs routine utilisation / no utilisation

Study limitations (risk of bias): yes (observational study)
Inconsistency of results: no
Indirectness of evidence: yes (only patients with Chron disease included; routine vs selected utilisation assessed within Chron disease patients)
Imprecision: yes (only one study with 343 participants
Publication bias: undetected
Overall quality of evidence: overall quality of evidence was judged as very low for study limitation, indirectness and imprecsion

Conclusions
No significant difference has been found between the non selective and selective strategy use of patency capsule in patients with Chron disease in capsule retention (**VERY LOW QUALITY EVIDENCE**).

References

Included studies

1. Fernández-Urién I, Carretero C, González B, Pons V, Caunedo Á, Valle J, Redondo-Cerezo E, López-Higueras A, Valdés M, Menchen P,Fernández P, Muñoz-Navas M, Jiménez J, Herrerías JM. Incidence, clinical outcomes, and therapeutic approaches of capsule endoscopy-related adverse events in a large study population. Rev. Esp. Enferm. Dig. 2015; 107(12):745-752
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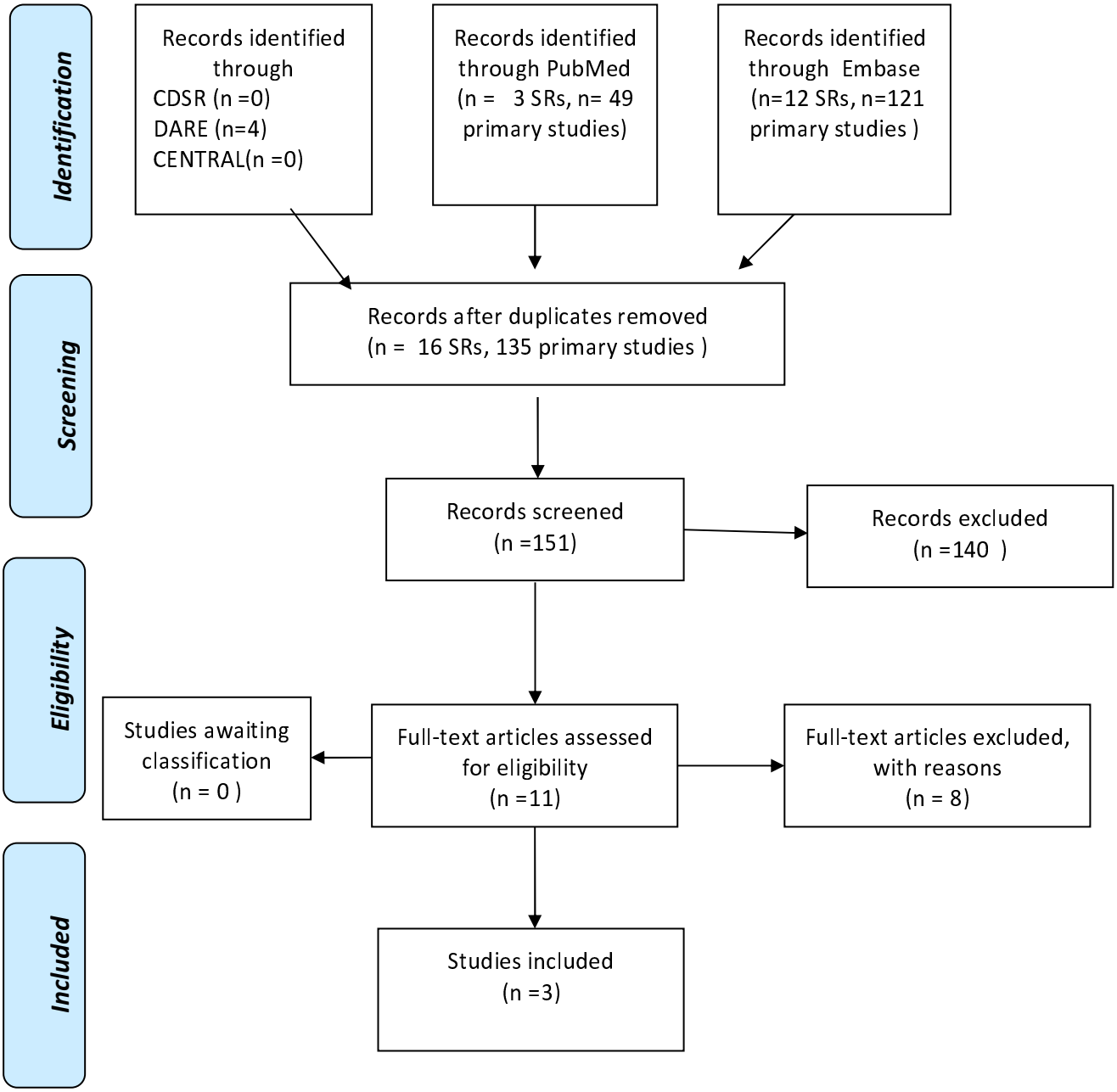
3. Nemeth, A.; Kopylov, U.; Koulaouzidis, A.; Wurm Johansson, G.; Thorlacius, H.; Amre, D.; Eliakim, R.; Seidman, E. G., and Toth, E. Use of patency capsule in patients with established Crohn's disease. Endoscopy. 2016 Apr; 48(4):373-9.

Excluded studies

1. Albuquerque, A.; Cardoso, H.; Marques, M.; Rodrigues, S.; Vilas-Boas, F.; Lopes, S.; Dias, C. C., and Macedo, G. Predictive factors of small bowel patency in Crohn's disease patients. Rev Esp Enferm Dig. 2016 Feb; 108(2):65-70
2. Herrerias, J. M.; Leighton, J. A.; Costamagna, G.; Infantolino, A.; Eliakim, R.; Fischer, D.; Rubin, D. T.; Manten, H. D.; Scapa, E.; Morgan, D. R.; Bergwerk, A. J.; Koslowsky, B., and Adler, S. N. Agile patency system eliminates risk of capsule retention in patients with known intestinal strictures who undergo capsule endoscopy. Gastrointest Endosc. 2008 May; 67(6):902-9

3. Nakamura, M.; Hirooka, Y.; Yamamura, T.; Miyahara, R.; Watanabe, O.; Ando, T.; Ohmiya, N., and Goto, H. Clinical usefulness of novel tag-less Agile patency capsule prior to capsule endoscopy for patients with suspected small bowel stenosis. Dig. Endosc. 2015; 27(1):61-66;
4. Nemeth, A.; Kopylov, U.; Koulaouzidis, A.; Johansson, G. W.; Eliakim, R.; Thorlacius, H.; Amre, D.; Eliakim, R.; Seidman, E. G., and Toth, E. Patency capsule in patients with established Crohn's disease undergoing videocapsule endoscopy of the small bowel. J. Crohn's Colitis. 2015; 9S165;
5. Nemeth, A.; Kopylov, U.; Koulaouzidis, A.; Johansson, G. W.; Thorlacius, H.; Amre, D. K.; Eliakim, A. R.; Seidman, E. G., and Toth, E. Patency capsule in patients with established Crohn's disease undergoing videocapsule endoscopy of the small bowel. Gastrointest. Endosc. 2015; 81(5):AB137-AB138
6. Signorelli, C.; Rondonotti, E.; Villa, F.; Abbiati, C.; Beccari, G.; Avesani, E. C.; Vecchi, M., and de Franchis, R. Use of the Given-« Patency System for the screening of patients at high risk for capsule retention. Dig. Liver Dis. 2006; 38(5):326-330
7. Spada, C.; Riccioni, M. E., and Costamagna, G. The new, dissolving patency capsule: A safe and effective tool to avoid the complication of retained video capsules. J. Clin. Gastroenterol. 2008; 42(6):761-762
8. Spada, C.; Shah, S. K.; Riccioni, M. E.; Spera, G.; Marchese, M.; Iacopini, F.; Familiari, P., and Costamagna, G. Video capsule endoscopy in patients with known or suspected small bowel stricture previously tested with the dissolving Patency capsule. J. Clin. Gastroenterol. 2007; 41(6):576-582;

PRISMA 2009 Flow Diagram



AZIENDA OSPEDALIERO - UNIVERSITARIA
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Centro di Riferimento per l'Epidemiologia e la Prevenzione Oncologica in Piemonte

Patient Experience

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

9.1 (St.12.1) **Patience Satisfaction**

P: patients having CE
I: preparation
C: fasting alone
O: patients satisfaction, willingness to repeat the procedure, complaints
Notes: Does the use of laxatives reduce patients´satisfaction during CE?

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 15/2/2016 separately for systematic reviews and randomized controlled trials using the following search strategies:

Systematic reviews and meta-analysis

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** (Preparation[Text Word] OR cleansing[Text Word] OR regimen[Text Word] OR preparations[Title/Abstract] OR regiments[Title/Abstract] OR "Cathartics"[Mesh] OR fasting[Text Word] OR "Laxatives"[Mesh] OR Laxatives[Title/Abstract] OR Laxative [Title/Abstract]) **AND** ("Patient Satisfaction"[Mesh] OR satisfaction[Title/Abstract] OR complaints[Title/Abstract] OR complaint[Title/Abstract] OR "Patient Acceptance of Health Care"[Mesh] OR acceptability[Text Word] OR acceptance[Text Word] OR "Patient experience" [Text Word] OR worry[Title/Abstract] OR worries [Title/Abstract] OR distress[Title/Abstract] OR discomfort[Title/Abstract] OR comfort[Title/Abstract] OR willingness [Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** ('intestine preparation'/exp OR preparation:ab,ti OR

preparations:ab,ti OR 'cleaning'/exp OR cleansing:ab,ti OR regimen:ab,ti OR cleansings:ab,ti OR regimens:ab,ti OR fasting:ab,ti OR 'laxative'/exp OR laxative:ab,ti OR laxatives:ab,ti) **AND** (worry:ab,ti OR worries:ab,ti OR distress:ab,ti OR 'patient preference'/exp OR 'patient preference':ab,ti OR 'patient satisfaction'/exp OR 'patient satisfaction':ab,ti OR acceptability:ab,ti OR discomfort:ab,ti OR comfort:ab,ti OR acceptance:ab,ti OR complaint:ab,ti OR complaints:ab,ti OR distress:ab,ti OR willingness:ab,ti OR 'patient attitude'/exp) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

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

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 MeSH descriptor: [Cathartics] explode all trees
#4 MeSH descriptor: [Laxatives] explode all trees
#5 preparation or cleansing or regimen or laxative or fasting or Cathartics:ti,ab,kw (Word variations have been searched)
#6 MeSH descriptor: [Patient Acceptance of Health Care] explode all trees
#7 MeSH descriptor: [Patient Satisfaction] explode all trees
#8 complaints or acceptability or acceptance or Patient experience or worry or distress or discomfort or comfort or willingness or satisfaction:ti,ab,kw (Word variations have been searched)
#9 #1 or #2
#10 #3 or #4 or #5
#11 #6 or #7 or #8
#12 MeSH descriptor: [Intestine, Small] explode all trees
#13 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#14 #12 or #13
#15 #10 and #11 and #9 and #14 Publication Year from 2000 to 2016

Randomized controlled trials

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** (Preparation[Text Word] OR cleansing[Text Word] OR regimen[Text Word] OR preparations[Title/Abstract] OR regiments[Title/Abstract] OR "Cathartics"[Mesh] OR fasting[Text Word] OR "Laxatives"[Mesh] OR Laxatives[Title/Abstract] OR Laxative [Title/Abstract]) **AND** ("Patient Satisfaction"[Mesh] OR satisfaction[Title/Abstract] OR complaints[Title/Abstract] OR complaint[Title/Abstract] OR "Patient Acceptance of Health Care"[Mesh] OR acceptability[Text Word] OR acceptance[Text Word] OR "Patient experience" [Text Word] OR worry[Title/Abstract] OR worries [Title/Abstract] OR distress[Title/Abstract] OR discomfort[Title/Abstract] OR comfort[Title/Abstract] OR willingness [Title/Abstract]) **AND** ((Randomized Controlled Trial[ptyp] OR Controlled Clinical Trial[ptyp] OR randomized[Title/Abstract] OR placebo[Title/Abstract] OR "drug therapy" [Subheading] OR randomly [Title/Abstract] OR trial[Title/Abstract] OR group[Title/Abstract]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]))

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** ('intestine preparation'/exp OR preparation:ab,ti OR preparations:ab,ti OR 'cleaning'/exp OR cleansing:ab,ti OR regimen:ab,ti OR cleansings:ab,ti OR regimens:ab,ti OR fasting:ab,ti OR 'laxative'/exp OR laxative:ab,ti OR laxatives:ab,ti) **AND** (worry:ab,ti OR worries:ab,ti OR distress:ab,ti OR 'patient preference'/exp OR 'patient preference':ab,ti OR 'patient satisfaction'/exp OR 'patient satisfaction':ab,ti OR acceptability:ab,ti OR discomfort:ab,ti OR comfort:ab,ti OR acceptaance:ab,ti OR complaint:ab,ti OR complaints:ab,ti OR distress:ab,ti OR willingness:ab,ti OR 'patient attitude'/exp) **AND** ('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR 'controlled clinical trial'/exp OR 'clinical trial'/exp OR placebo:ab,ti OR 'double blind':ab,ti OR 'single blind':ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*:ab,ti OR random*:ab,ti OR factorial*:ab,ti OR crossover:ab,ti OR (cross:ab,ti AND over:ab,ti))

Cochrane Central Register of Controlled Trials (CENTRAL)

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 MeSH descriptor: [Cathartics] explode all trees
#4 MeSH descriptor: [Laxatives] explode all trees
#5 preparation or cleansing or regimen or laxative or fasting or Cathartics:ti,ab,kw (Word variations have been searched)
#6 MeSH descriptor: [Patient Acceptance of Health Care] explode all trees
#7 MeSH descriptor: [Patient Satisfaction] explode all trees
#8 complaints or acceptability or acceptance or Patient experience or worry or distress or discomfort or comfort or willingness or satisfaction:ti,ab,kw (Word variations have been searched)
#9 #1 or #2
#10 #3 or #4 or #5
#11 #6 or #7 or #8
#12 MeSH descriptor: [Intestine, Small] explode all trees
#13 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#14 #12 or #13
#15 #10 and #11 and #9 and #14 Publication Year from 2000 to 2016

Results

Results of the bibliographic searches

After removing duplicates, 26 (3 SRs and 23 RCTs) articles were found. 3 articles were considered potentially relevant and acquired in full text (See flow chart).

Included studies

3 RCTs were included (Hansel 2014, Postagate 2009, Van Tuyl 2007). In these studies patients referred for capsule endoscopy (CE) randomised to experimental group received different type of preparations: MoviPrep or 1 or 2 Litres of polyethylene glycol (PEG) or Citramag + senna bowel-purgative regimen the evening before CE or Citramag + senna + 10 mg metoclopramide before the procedure. The control groups in all RCTs were advised to ingest only clear fluids on the afternoon and evening before the procedure.

Study	Patients	Intervention	Control	patients satisfaction	willingness to repeat the procedure
Hansel 2014 (conference abstract)	46 outpatient undergoing CE	Bowel preparation intervention: 2L of MoviPrep starting at 7 p.m. the evening prior to CE. The day of the procedure, they ingested simethicone 5-mL p.o. and metoclopramide 5 mg p.o. 20-minutes prior to CE	Control: no solid foods after 7 p.m. evening prior and clear liquids up until 4 hours prior to CE.	Discomfort Prep patients did report more discomfort (pZ0.01).	
Postagate 2009	148 patients referred for CE	Group CS= Citramag and senna bowel purgatives taken on the afternoon and evening before the procedure. 2 The capsule was then was ingested, at 8:00 AM, with water and 0.5 mL simethicone (n= 39; mean age=44.9 ± 19.0) Group CSM= Citramag and senna bowel purgatives (as above) plus 10 mg oral metoclopramide	Group S= Standard preparation consisted of restriction to clear fluids on the afternoon and evening before the procedure and nothing by mouth after 10:00 PM. The capsule was ingested, at 8:00 AM, with water and 0.5 mL simethicone (n= 37; mean age=54.1±17.6).	**Preparation comfort visual analog scale questionnaires 0-100** S=median 96 (IQR 87-100) M=median 98 (IQR82-100) p value vs S group=0.78 CS=median 81 (IQR 45-94) p value vs S group<0.001 CSM=median57 (IQR41-98) p value vs S group<0.001 All groups vs S group P <0.001 **Preparation convenience visual analog scale questionnaires 0-100** S=median 92 (IQR 81-99) M=median 97 (IQR 69-100) p value vs S group=0.75 CS=median 50 (IQR 36-95) p value vs S group=0.001 CSM=median 54 (IQR 45-99) All groups	**Same preparation visual analog scale questionnaires0-100** S=median 97 (IQR 85-100) M=median 99 (IQR 94-100) p value vs S group=0.16 CS=median 84 (IQR 51-99) p value vs S group=0.03 CSM=median 82 (IQR 50-100) All groups vs S group=P : 0.003

		taken 10 minutes before capsule ingestion .The capsule was then ingested, at 8:00 AM, with water and 0.5 mL simethicone(n= 37; mean age=52.8 ± 19.0) Group M= Standard preparation plus 10 mg of oral metoclopramide taken 10 minutes before capsule ingestion (n= 37; mean age=49.7 ±17.9)		vs S group p <0.001	
Van Tuyl 2007	90 patients referred for CE	Group B 1 L of PEG solution before VCE Group C2 L of PEG solution before VCE	Group A underwent VCE after clear liquid diet and overnight fast	**Overall convenience and tolerability .numerical scale between 0 (no burden at all) and 10(intolerable procedure)** Group A =7.6±1.2 Group B=8.3±1.5 Group C=7.5±1.7 P=0.24 **Preparation regiment score** Group A =7.8±2.1 Group B=7.8±1.8 Group C=6.0±3.0 P=0.03	94% of patients were willing to undergo the procedure in the future, irrespective of preparation regimen

Quality of evidence:
Study limitations (risk of bias): no (blinding of participants not possible, but not relevant for type of outcome)
Inconsistency of results: no
Indirectness of evidence: no
Imprecision: yes (only three studies with 284 participants)
Publication bias: undetected
Overall quality of evidence: overall quality of evidence was judged as moderate for imprecision

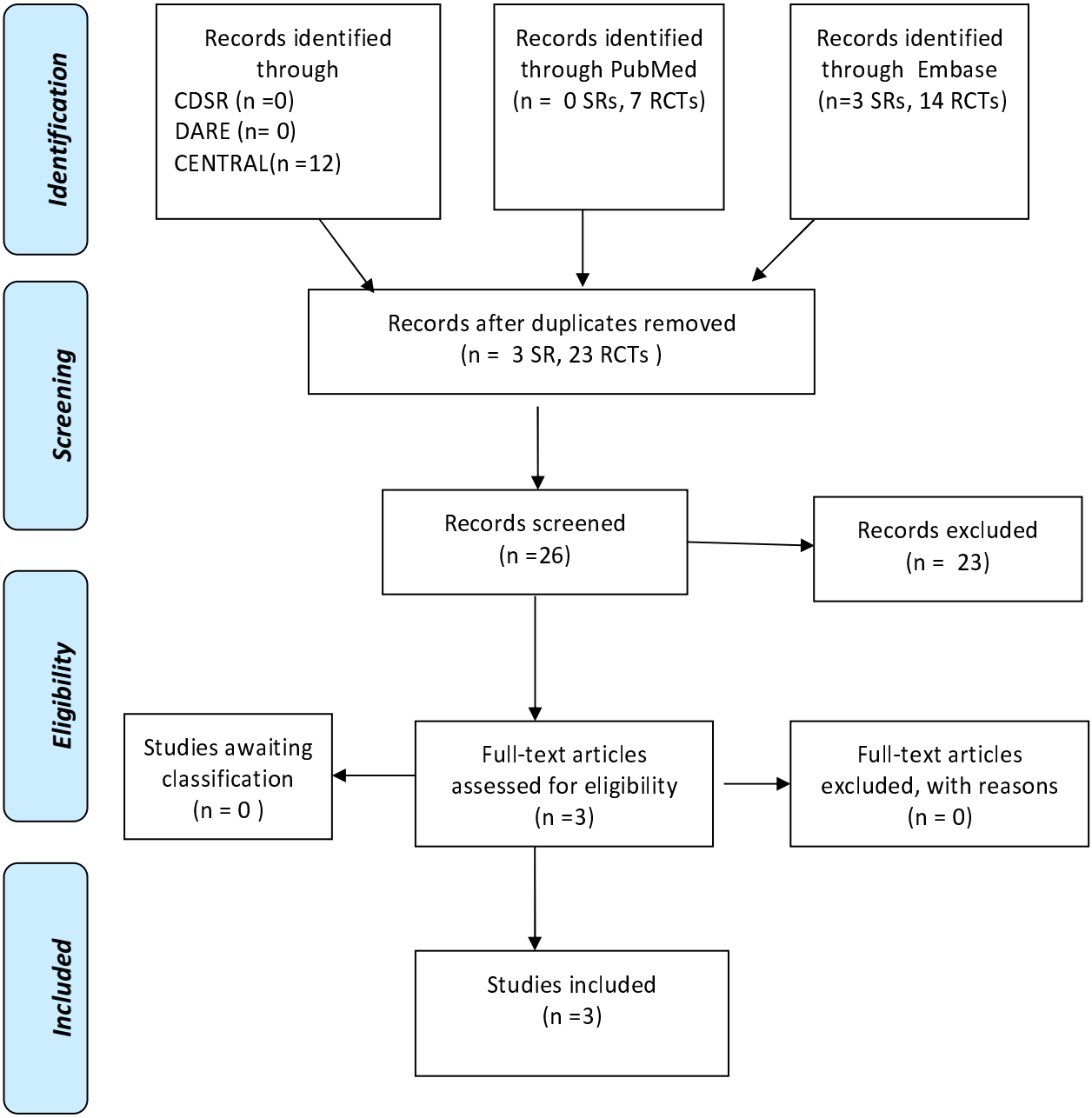
Conclusions
Patients reported more discomfort and less willingness to repeat the procedure with the use of preparations compared to fasting alone

References

Included studies

1. Hansel, S. L.; Gostout, C. J.; Murray, J. A.; Alexander, J. A.; Bruining, D. H.; Larson, M. V.; Mangan, T. F.; Dierkhising, R. A.; Almazar, A. E., and Rajan, E. Assessment of combined bowel preparation for capsule endoscopy: A prospective randomized controlled study. Gastrointest. Endosc. 2014; 79(5):AB209;
2. Postgate, A.; Tekkis, P.; Patterson, N.; Fitzpatrick, A.; Bassett, P., and Fraser, C. Are bowel purgatives and prokinetics useful for small-bowel capsule endoscopy? A prospective randomized controlled study. Gastrointest. Endosc. 2009; 69(6):1120-1128;
3. van Tuyl, S. A.; den Ouden, H.; Stolk, M. F., and Kuipers, E. J. Optimal preparation for video capsule endoscopy: a prospective, randomized, single-blind study. Endoscopy. 2007 Dec; 39(12):1037-40

PRISMA 2009 Flow Diagram



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Procedure numbers and training

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

10.1 (St. 13.1) **detection rates and training**

P: endoscopists
I: Mandatory formal training course/training period
C: no formal training
O: Detection Rate
Notes: Do formal capsule endoscopy training standards improve quality of capsule endoscopy reading and reporting?

10.2 (St. 13.2) **CE procedures per year**

QUALITY MEASURES:

P: endoscopists/unit
I: minimum capsule
C:none
O: Improved quality of capsule endoscopy in particular lesion detection
Notes: Is there a minimum number of capsule endoscopy procedures that should be performed regularly to maintain reading proficiency?

10.3 (St. 13.3) **Prior endoscopy experience**

P: endoscopists
I: prior endoscopy experience
C: none
O: Improved quality of capsule endoscopy in particular lesion detection and interpretation
Notes: Is prior endoscopy experience required to ensure competency as a capsule endoscopist?

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 15/2/2016 separately for systematic reviews and primary studies using the following search strategies:
Systematic reviews and meta-analysis

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** ("Diagnostic yield"[Title/Abstract] OR "Intestinal Diseases/diagnosis"[Mesh] OR findings[Title/Abstract] OR finding[Title/Abstract] OR "detection rate"[Title/Abstract] OR "detection rates"[Title/Abstract]) **AND** ("education"[Subheading] OR "Education, Medical"[Mesh] OR "Quality of Health Care"[Mesh] OR training[Title/Abstract] OR "Clinical Competence"[Mesh] OR competency[Title/Abstract] OR competence[Title/Abstract] OR experience[Title/Abstract] OR proficiency[Title/Abstract] OR "minimum number"[Title/Abstract] OR performance[Title/Abstract] OR volume[Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** ('diagnostic yield':ti,ab OR 'small intestine disease'/exp/dm_di OR findings:ab,ti OR finding:ab,ti OR 'detection rate':ab,ti OR 'detection rates':ab,ti) **AND** ('clinical competence'/exp OR 'medical education'/exp OR training:ab,ti OR 'health care quality'/exp OR competence:ab,ti OR volume:ab,ti OR 'detection rate':ab,ti OR training:ab,ti OR competency:ab,ti OR competence:ab,ti OR experience:ab,ti OR proficiency:ab,ti OR performance:ab,ti OR 'minimum number':ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

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

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#8 diagnostic yield:ti,ab,kw (Word variations have been searched)
#9 MeSH descriptor: [Intestinal Diseases] explode all trees and with qualifier(s): [Diagnosis - DI]
#10 finding:ti,ab,kw (Word variations have been searched)
#11 detection rate:ti,ab,kw (Word variations have been searched)
#12 #1 or #2
#13 #8 or #9 or #10 or #11
#14 Any MeSH descriptor with qualifier(s): [Education - ED]
#15 MeSH descriptor: [Education, Medical] explode all trees
#16 MeSH descriptor: [Quality of Health Care] explode all trees
#17 MeSH descriptor: [Clinical Competence] explode all trees
#18 training or competence or experience or proficiency or "minimum number" or performance or volume:ti,ab,kw (Word variations have been searched)
#19 #14 or #15 or #16 or #17or #18
#20 MeSH descriptor: [Intestine, Small] explode all trees
#21 small bowel or small intestine:ti,ab,kw (Word variations have been searched)

#22 #20 or #21
#23 #22 and #19 and #12 and #13 Publication Year from 2000 to 2016

Primary studies

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** ("Diagnostic yield"[Title/Abstract] OR "Intestinal Diseases/diagnosis"[Mesh] OR findings[Title/Abstract] OR finding[Title/Abstract] OR "detection rate"[Title/Abstract] OR "detection rates"[Title/Abstract]) **AND** ("education"[Subheading] OR "Education, Medical"[Mesh] OR "Quality of Health Care"[Mesh] OR training[Title/Abstract] OR "Clinical Competence"[Mesh] OR competency[Title/Abstract] OR competence[Title/Abstract] OR experience[Title/Abstract] OR proficiency[Title/Abstract] OR "minimum number"[Title/Abstract] OR performance[Title/Abstract] OR volume[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** ('diagnostic yield':ti,ab OR 'small intestine disease'/exp/dm_di OR findings:ab,ti OR finding:ab,ti OR 'detection rate':ab,ti OR 'detection rates':ab,ti) **AND** ('clinical competence'/exp OR 'medical education'/exp OR training:ab,ti OR 'health care quality'/exp OR competence:ab,ti OR volume:ab,ti OR 'detection rate':ab,ti OR training:ab,ti OR competency:ab,ti OR competence:ab,ti OR experience:ab,ti OR proficiency:ab,ti OR performance:ab,ti OR 'minimum number':ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#8 diagnostic yield:ti,ab,kw (Word variations have been searched)
#9 MeSH descriptor: [Intestinal Diseases] explode all trees and with qualifier(s): [Diagnosis - DI]
#10 finding:ti,ab,kw (Word variations have been searched)
#11 detection rate:ti,ab,kw (Word variations have been searched)
#12 #1 or #2
#13 #8 or #9 or #10 or #11
#14 Any MeSH descriptor with qualifier(s): [Education - ED]
#15 MeSH descriptor: [Education, Medical] explode all trees
#16 MeSH descriptor: [Quality of Health Care] explode all trees
#17 MeSH descriptor: [Clinical Competence] explode all trees

#18 training or competence or experience or proficiency or "minimum number" or performance or volume:ti,ab,kw (Word variations have been searched)
#19 #14 or #15 or #16 or #17or #18
#20 MeSH descriptor: [Intestine, Small] explode all trees
#21 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#22 #20 or #21
#23 #22 and #19 and #12 and #13 Publication Year from 2000 to 2016

Results

Results of the bibliographic searches

After removing duplicates, 1164 articles (47 reviews and 1117 primary studies) were found. 1 systematic review and 8 primary studies were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies
One article was excluded because narrative review (Perez-Cuadrado 2007).

Included studies
We included (8 articles) 7 studies (Alakkari 2013, Albert 2015, Chen 2006, Rajan 2013, Lee 2010, Philpott 2010, Rondonotti 2011 the last three available only as conference abstracts).

Clinical questions 1: Training

Three studies (Alakkari 2013, Albert 2015, Rondonotti 2011) answered to clinical question 1 evaluating how a training course improve the correct diagnosis of small bowel capsule endoscopy (SBCE) videos.
Alakkari 2013 compared detection rates of VCE reports by trained gastrointestinal physiologists (TP) to a consultant gastroenterologist (CG).
Albert 2015 compared the median score for correct diagnosis before and after the training (achievable total score 0 to 10). The findings of the consultant gastroenterologist were considered gold standard.
Rondonotti 2011 verified whether a training session-TS combining hands-on practice and experts' tutorial, is effective in improving both detection rate and interobserver agreement.

In table below we reported: positive findings and correlation of findings between the TP and CG for Alakkari 2013; median scores for correct diagnosis before and after training course for the Albert 2015;; number of SB findings before and after training and agreement with reference standard for Rondonotti 2011.

Study	Patients/ SBCE videos	N participants	Intervention	Control	Detection rates	Other measures to assess quality of lesion detection and interpretation
Alakkari 2013	60 patients underwent small bowel examination	Not reported	Training for gastrointestinal physiologists (TP) experienced in other GI procedures: ✓ completed an approved basic VCE training course in which performing the procedure and analysed software; ✓ encouraged to review the available image library ✓ reviewed at least 20 CG reports with a gastroenterology consultant prior to beginning the study.	No training for a consultant gastroenterologist (CG) but experience of over 8 years experience and 250 studies per annum	**Positive findings, n(%)** TP=33 (55%) CG= 23 (38%)	**correlation coefficient κ for positive VCE findings** κ= 0.54 first 30 VCEs κ = 0.39 second 30 VCEs κ = 0.66
Albert 2015	10 short SBCE videos	294 delegates: ✓ 233 physicians ✓ 48 endoscopy nurses ✓ 13 other professions (such as physiology lab assistants or technicians)	Training course which provided a combination of didactic lectures and practical computer based training, using a wide range of clinical cases.	Baseline experience		**Median Scores for correct diagnosis, maximum 10 Overall** Baseline=4 (IQR 3) After the course=7 (IQR 3) P<0.001 **For different baseline experience in CE** <u>0 SBCEs</u> Baseline=3 (IQR 3) After the course= 6 (IQR 4) P<0.001

		Evaluation forms from 268 course participants: From 0 to >100 Small bowel capsule endoscopy as experience (n=268)				<u>1–10 SBCEs</u> Baseline=4 (IQR 3) After the course= 7 (IQR 1) P<0.001 <u>11–25 SBCEs</u> Baseline=6 (IQR 4) After the course= 8 (IQR 3) P<0.001 <u>26–50 SBCEs</u> Baseline= 4 (IQR 4) After the course= 6 (IQR 4) P<0.001 <u>51–100 SBCEs</u> Baseline=5 (IQR 4) After the course= 8 (IQR 3) P<0.003 <u>>100 SBCEs</u> Baseline=6 (IQR 1) After the course= 7.5 (IQR 3) P=0.155 **Median Scores for Correct Classification of Relevance of Lesion, maximum 10** **Overall** Baseline=5 (IQR 3) After the course=7 (IQR 3) P<0.001 **For different baseline experience in CE** <u>0 SBCEs</u> Baseline=5 (IQR 3) After the course= 6 (IQR 3) P<0.001 <u>1–10 SBCEs</u>

						Baseline=6(IQR 2) After the course= 7 (IQR 3) P<0.001 <u>11–25 SBCEs</u> Baseline=6 (IQR 4) After the course= 7 (IQR 3) P<0.091 <u>26–50 SBCEs</u> Baseline= 6 (IQR 3) After the course= 7 (IQR 3) P=0.172 <u>51–100 SBCEs</u> Baseline=6(IQR 2) After the course= 7 (IQR 5) P=0.446 <u>>100 SBCEs</u> Baseline=6 (IQR 3) After the course= 7.5 (IQR 5) P=0.438
Ronodonotti 2011 (conference abstracts Gastrointest. Endosc. 2011:AB124, Dig. Liver Dis: 43S118-S119)	30CE videos evaluated before training session and 15 CE videos reviewed again after training seccion	17 readers 3 experts: Reference standard (RS)	training session-TS: during an 8 hour meeting, the SBF identified by the readers in the first set of 15 videos were collectively discussed and compared with those identified by the RS	Before training session	**Number of SB findings, Mean± SD** Before training=74± 45 After training=85 ±47 Reference standard=89	**mean number of SBF matching those identified by the RS, Mean± SD** Before training=35 ±11 After training=38 ±12 **overall agreement with the RS in describing SBF, k** Before training=0.14; CI 95%: 0.12-0.16 After training=0.15; CI 95%: 0.12-0.17

Quality of evidence

Detection rate

Factors that can lower quality

Study limitations (risk of bias): no (stratification in Albert 2015 and Rajan 2013 according to the number of CE interpretations completed at the time of assessment)

Inconsistency of results: no

Indirectness of evidence: yes(no direct comparison of formal courses versus informal /unstructured way to achieve experience and competence found) *Imprecision:* yes (2 studies with 311 readers)

Publication bias: undetected

Factors that can higher quality

large magnitude of effect: no

opposing plausible residual bias or confounding: no

dose-response gradient: no

Overall quality of evidence: overall evidence was rated as *very low* because risk of indirectness and imprecision

Conclusions

Participation in formal training course increase competence. Studies do not answers the question whether competence could be achieved in the same way also without participating in formal training courses (**VERY LOW QUALITY OF EVIDENCE**).

Clinical questions 2: Experience, CE procedures per year

Four studies (Alakkari 2013, Albert 2015, Lee 2010, Rajan 2013) answered to clinical question 2 assessing whether the number of CE performed improved quality of lesion detection and interpretation.

Three studies compared the preexisting CE experience in terms of number readings done (Albert 2015, Rajan 2013) and one in terms of years of capsule experience (Lee 2010).

In the table below we reported detection rates and mean scores for correct diagnosis for different level of experience.

Study	Patients/cases	Intervention	Control	Detection rate	Other measures to assess quality of lesion detection and interpretation
Alakkari 2013	60 patients underwent small bowel examination	second 30 VCEs lectures of trained gastrointestinal physiologists (TP) experienced in other GI procedures compared with gastroenterologist (CG) with over 8 years of experience and 250 studies per annum number of physiologists nor reported	first 30 VCEs lectures of trained gastrointestinal physiologists (TP) experienced in other GI procedures compared with gastroenterologist (CG) with over 8 years of experience and 250 studies per annum	**Positive findings, n(%)** TP=33 (55%) CG= 23 (38%)	**correlation coefficient κ for positive VCE findings** κ= 0.54 first 30 VCEs κ = 0.39 second 30 VCEs κ = 0.66
Albert 2015	10 short SBCE videos	Preexisting Experience of Delegates in Small bowel capsule endoscopy (SBCE): 1–10 SBCEs (n= 91) 11–25 SBCEs (n= 24) 26–50 SBCEs(n=21) 51–100 SBCEs (n=13) >100 SBCEs (n=8)	Preexisting Experience of Delegates in Small bowel capsule endoscopy (SBCE): 0 SBCEs (n= 111)		**Median ET-CET Scores for correct diagnosis, maximum 10** 0 SBCEs =3 (IQR 3) 1–10 SBCEs =4 (IQR 3) 11–25 SBCEs =6 (IQR 4) 26–50 SBCEs = 4 (IQR 4) 51–100 SBCEs =5 (IQR 4) >100 SBCEs=6 (IQR 1) **Median ET-CET Scores for Correct Classification of Relevance of Lesion** 0 SBCEs =5 (IQR 3) 1–10 SBCEs =6(IQR 2) 11–25 SBCEs =6 (IQR 4) 26–50 SBCEs = 6 (IQR 3) 51–100 SBCEs =6(IQR 2) >100 SBCEs=6 (IQR 3)
Lee 2010 (conference abstract)	425 SBCEs in 415 patients	Second period (more experience): 2006-2009: 183 CE	First period (less experience): 2003-2005 242 CE	Second period= 43.9% First period= 23.8%	

Rajan 2013	Not reported	Staff capsule endoscopists with more than 3 years of experience in CE interpretation (n:8)	39 gastroenterology fellows grouped according to the number of CE interpretations completed at the time of assessment: ✓10 or fewer cases (n =13), ✓11 to 20 cases(n = 19), ✓ 21 to 35 cases (n = 7).		**CapCT scores mean, range (%)** Staff= 91 (86-100) Fellows,<10 CE interpretations = 79 (69-88) P<0.001 compared with staff. Fellows, 11-20 CE interpretations= 79 (66-91) P<0.001 compared with staff. Fellows, >20 CE Interpretations= 85 (77-91) no significant difference in the scores between staff and fellows interpreting more than 20 cases (P = 0.26). **Number of fellows in each group who actually achieved competency** (definite as a CapCT score of 90% or higher of the mean staff score) Fellows,<10 CE interpretations= 31% (4/13) Fellows, 11-20 CE interpretations= 26% (5/19) Fellows, >20 CE Interpretations= 71% (5/7)

Quality of evidence

Detection rate
Factors that can lower quality
Study limitations (risk of bias): no
Inconsistency of results: no
Indirectness of evidence: no
Imprecision: yes (4 studies with 204 participants (only two studies reported number of readers) .
Publication bias: undetected
Factors that can higher quality
large magnitude of effect: no
opposing plausible residual bias or confounding: no
dose-response gradient: no

Overall quality of evidence: overall evidence was rated as *very low* because coming from observational studies with imprecision

Conclusions

Competence increases with number of readings performed. It seems that the minimum number of readings to achieve competence could be 20 -25 (**VERY LOW QUALITY OF EVIDENCE**).

Clinical questions 3: Prior endoscopy experience

Two studies answered to clinical question 3 comparing readers with no previous CE experience but other endoscopy (VE) experience. One was a conference abstract of a pilot study including only three readers with no CE experience but having performed between 200–700 gastroscopies and 50–600 colonoscopies; their interpretation was compared with the one of one gastroenterology consultant with more than 500 CE videos. The other is a diagnostic accuracy study including 10 readers with minimal endoscopic background.

Study	**Patients/cases**	**Intervention**	**Control**	**reference standard**	**Other measures to assess quality of lesion detection**
Philpott 2010 (conference abstract of pilot study)	10 CE video	3 gastroenterology registrars with no previous CE experience but with varying video endoscopy (VE) experience -between 200–700 gastroscopies -and 50–600 colonoscopies		gastroenterology consultant with experience of reporting more than 500 CE videos	**False negatives:** A small bowel polyp was missed by all three registrars **false positives:** The two more junior registrars recorded 'false positives' in two studies. All registrars accurately identified key anatomical landmarks and identified two incomplete studies.
Chen 2006	10 cases with significant lesions	10 readers (4 years medical students and minimal endoscopic	na	2 gastroenterologists (over 150 capsule	**overall sensitivity among the 10 readers=** 80% (range: 60%-100%)

	within the small intestine	background)		endoscopy cases each)	

Quality of evidence

Detection rate

Factors that can lower quality

Study limitations (risk of bias): yes (one was a conference abstract with few information) ; both studies did not directly compare readers with and without prior endoscopy experience

Inconsistency of results: yes

Indirectness of evidence: no

Imprecision: yes (two studies with 13 participants)

Publication bias: undetected

Factors that can higher quality

large magnitude of effect: no

opposing plausible residual bias or confounding: no

dose-response gradient: no

Overall quality of evidence: overall evidence was rated as *very low* because only two studies including 13 readers was found

Conclusions

no conclusion can be drawn because only two studies with 13 participants were found (**VERY LOW QUALITY OF EVIDENCE**).

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8. Ronodonotti, E.; Soncini, M.; Girelli, C. M.; Russo, A. G.; Conte, D.; Masci, E., and De Franchis, R. A training strategy to improve detection rate and interobserver agreement in capsule endoscopy (CE) for readers with different experience: Results of a multicentre study. Gastrointest. Endosc. 2011; 73(4):AB124;

Excluded

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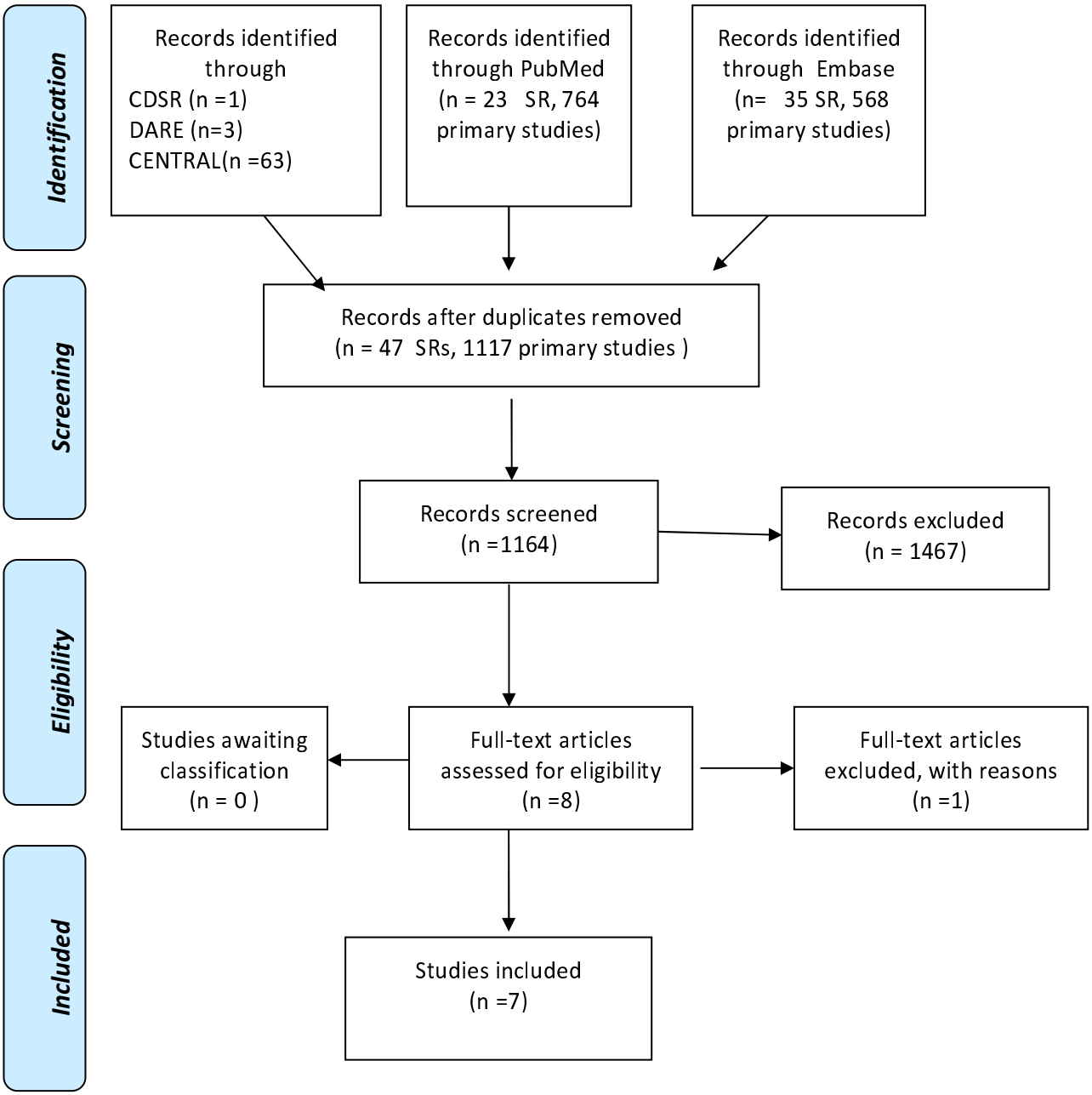
PRISMA 2009 Flow Diagram



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Reading Procedure

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11.1 (St. 14.1-14.3) **Reading**

P: reading
I: software mode/speed
C: standard reading
O: Improved reading time and reliable quality (diagnostic yield) of CE in particular lesion detection
Notes: Does the use of software mode (Quick view / express select / overview) reduce reading times, allowing a reliable sensitivity? Does a standardised reading speed improve interpretation?

11.2 (St. 14.4-14.5) **Detection rates by reading procedure**

P: Patients/Endoscopists
I: reading according to selection modes (FICE, blue mode)
C: standard reading
O: Improved diagnostic yield / reduction in unnecessary intervention
Notes: Does speed and the use of colour selection modes (FICE / blue mode / NBI) for detection of lesions at CE reading influence diagnostic accuracy (sensitivity and specificity) and or reading times?

11.3 (St. 14.6) Detection rates by reading speed

P: endoscopists
I: High Reeding speed
C: Low reading speed
O: Improved quality of CE in particular lesion detection
Notes: Is there a safe or optimal capsule reading speed to enhance lesion detection?

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 15/2/2016 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** ("Image Processing, Computer-Assisted"[Mesh] OR "Software"[Mesh] OR Software[Title/Abstract] OR mode[Title/Abstract] OR speed[Title/Abstract] OR "Quick view"[Title/Abstract] OR Quickview[Title/Abstract] OR FICE[Title/Abstract] OR "Blue mode"[Title/Abstract] OR NBI[Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** ('image processing'/exp OR software:ab,ti OR 'computer program'/exp OR mode:ab,ti OR speed:ab,ti OR 'Quick view':ab,ti OR Quickview:ab,ti OR FICE:ab,ti OR 'Blue mode':ab,ti OR NBI:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

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

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 MeSH descriptor: [Image Processing, Computer-Assisted] explode all trees
#4 MeSH descriptor: [Software] explode all trees
#5 Software or mode or speed or Quick view or FICE or "Blue mode" or NBI:ti,ab,kw (Word variations have been searched)
#6 #1 or #2
#7 #3 or #4 or #5
#8 MeSH descriptor: [Intestine, Small] explode all trees
#9 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#10 #8 or #9
#11 #6 and #7 and #10 Publication Year from 2000 to 2016

Primary studies

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** ("Image Processing, Computer-Assisted"[Mesh] OR "Software"[Mesh] OR Software[Title/Abstract] OR mode[Title/Abstract] OR speed[Title/Abstract] OR "Quick view"[Title/Abstract] OR Quickview[Title/Abstract] OR FICE[Title/Abstract] OR "Blue mode"[Title/Abstract] OR NBI[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** ('image processing'/exp OR software:ab,ti OR 'computer program'/exp OR mode:ab,ti OR speed:ab,ti OR 'Quick view':ab,ti OR Quickview:ab,ti OR FICE:ab,ti OR 'Blue mode':ab,ti OR NBI:ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 MeSH descriptor: [Image Processing, Computer-Assisted] explode all trees
#4 MeSH descriptor: [Software] explode all trees
#5 Software or mode or speed or Quick view or FICE or "Blue mode" or NBI:ti,ab,kw (Word variations have been searched)
#6 #1 or #2
#7 #3 or #4 or #5
#8 MeSH descriptor: [Intestine, Small] explode all trees
#9 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#10 #8 or #9
#11 #6 and #7 and #10 Publication Year from 2000 to 2016

Results

Results of the bibliographic searches

After removing duplicates, 348 (15 SRs and 333 primary studies) articles were found. 61 articles were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies

38 articles were excluded: five because no comparison of interest (Iakovidis 2014, Nakamura 2015, Rondonotti 2015, Shiotani 2012, Zheng 2012); one because commentary (Spada 2011); one because a narrative review (Pohl 2010), thirty-one because conference abstract of an excluded study (Abdelaal 2010, Aggarwal 2010, Delvaux 2011, Eckardt 2013, Murino 2011, Hotayt 2013, Jackson 2015, Jeen 2012, Jeen 2013, Klein J. Gastroenterol. Hepatol 2015, Klein Gastrointest. Endosc. 2015, Kobayashi 2011, Kobayashi 2013, Maeda 2012, Magalhães Gastroenterology 2013, Magalhães Inflammatory Bowel Dis. 2013, Murino 2012, Murino Dig. Liver Dis. 2011, Murino Gut. 2011, Nakamura Gut 2012, Nakamura Gastrointest. Endosc 2012, Oka 2011, Omori 2015, Rey 2009, Sagawa 2012, Sakai 2012, Sato 2012, Saurin 2009, Shibuya 2012, Shiotani 2015, Smirnidis 2012).

Included studies

23 diagnostic accuracy studies were included (Abdelaal 2015, Boal Carvalho 2016, Dias De Castro 2015, Duque 2012, Gunther 2012, Gupta 2011, Halling 2014, Imagawa 2011, Imagawa 2011Scandinavian Journal of Gastroenterology, Kobayashi 2012, Koulaouzidis 2012, Krystallis 2011, Matsumura 2012, Nogales Rincon 2013, Rimbas 2015, Sakai 2012, Sato 2014, Shiotani 2011, Saurin 2012, Stein 204, Subramanian 2012, Westerhof 2009, Xu 2014).

Clinical question 1

7 diagnostic accuracy studies answered to this clinical question. The reference standard was standard reading or consensus diagnosis made by experts.

4 studies (Halling 2014, Koulaouzidis 2012, Saurin 2012, Stein 2014) used “Quickview” (QV) system as software for reading. The “Quickview” (QV) system is a program that reduces the image quantity by analyzing specific patterns and colors to provide a shorter composite video. One articles used an additional algorithm contained in Rapid Reader 6.0, the suspected blood indicator (SBI), analyzes pixels to look for a red color that may be consistent with active or potential bleeding.

3 studies (Subramanian 2012, Westerhof 2009, Xu 2014) used a picture elimination mode which can eliminates images with no significant changes.

In the table below, we reported the results of the comparison between these software and standard reading in term of diagnostic yield and reading time.

Study	Participants	Intervention	Control	Reading time	Miss rate/ lesion detected compared with standard view	Accuracy
Halling 2014	40 patients with suspected Crohn's disease Denmark	quick view (qv) CE	Ileocolonoscopy with biopsies and CE served as gold standard for the presence and location of CD			**Accuracy of Qv-CE** Sensitivity=94% (CI 70–100) Positive predictive value: 100% (CI 78–100) Specificity: 100% (CI 86–100); Negative predictive value: 96% (CI80–100)
Koulaouzidis 2012	200 patients with OGIB, known or suspected Crohn's disease ,polyposis syndromes, Coeliac disease, Possible SB lesion or mass UK	QuickView with white light (QVWL) reading QuickView with Blue Mode (QVBM) reading	standard mode video sequence review	**mean evaluation time** (including reading and time to mark thumbnails) QVWL=475 (±270) s QVBM= 450 (±156) s (P=0.363).	**All findings, n(%)** QVWL =129 (49.6%), QVBM = 135 (51.9%) Standard view = 260 (P<0.0001) SBCE performed for Obscure gastrointestinal bleeding(n=106) **Angioectasias, n(%)** QVWL=54 (55.1%) QVBM= 63 (64.3%) Standard view= 98 (P=0.0506). SBCE performed for Suspected/known Crohn's disease (n=81) **Mucosal ulcers, n(%)** QVWL= 71 (45.8%) QVBM=68 (43.9%) Standard view= 155 P=0.0003. SBCE performed for polyposis syndromes or Possible SB	**OGIB** QVWL, as compared with reference reporting) sensitivity for P1+P2 lesions,:92.3% specificity, for P1+P2 lesions: 96.3% PPV for P1+P2 lesions: 96% NPV for P1+P2 lesions: 92.8% QVBM, , as compared with reference reporting) sensitivity for P1+P2 lesions,: 91% specificity, for P1+P2 lesions: 96% PPV for P1+P2 lesions: 96.2% NPV for P1+P2 lesions90.6% Chron disease QVWL, as compared with reference reporting) sensitivity for ulcer size (i.e. <1/2, 1/4–1/2 and >1/2 luminal circumference:42% PPV for ulcer size (i.e. <1/2,

					lesion or mass (n=10) **Polypoid lesions, n** QVWL= 4 QVBM=4 Standard view= 7	1/4–1/2 and >1/2 luminal circumference: 97% QVBM, , as compared with reference reporting) sensitivity for ulcer size (i.e. <1/2, 1/4–1/2 and >1/2 luminal circumference,: 52% PPV ulcer size (i.e. <1/2, 1/4–1/2 and >1/2 luminal circumference: 91%
Saurin 2012	106 patients (indications not reported) from 10 gastroenterology centres France	QV mode (using the Rapid 5 software version) standard reading	standard reading (IR) reference standard: standard reading + Review of discordant result only by 3 experts			<u>Per patient analysis</u> **Sensitivity** standard reading: 85.1% (95%CI 74.9–95.3) Quick-view reading: 85.1% (95%CI 74.9–95.3) **Specificity** standard reading: 81.3 (95%CI 70.1–94.5) Quick-view reading: 84.7 (95%CI 74.5–94.9) <u>Per lesion analysis</u> **Sensitivity** standard reading: 89.2 (95%CI 81.7–96.7) Quick-view reading: 89.2 (95%CI 81.7–96.7) **Specificity** standard reading: 76.1 (95%CI 65.8–86.4) Quick-view reading: 84.7 (95%CI 76.1–93.3)
Stein 2014	98 patients with obscure GI bleed, melena of unknown origin, and	Quickview'' (QV)+ suspected blood indicator (SBI)	Standard view (SV)			**Accuracy for active small bowel bleeding of QV+ SBI,** **Sensitivity (%)**

	hematochezia of unknown origin. USA					reader 1= 100 reader 2= 100 **Specificity (%)** reader 1= 94.3 reader 2= 93.2 **PPV (%)** reader 1= 84.8 reader 2= 82.4 **NPV (%)** reader 1= 100 reader 2= 100
Subramanian 2012	70 patients with Crohn's disease, iron deficiency anaemia ,obscure GI bleed and other indications UK	express viewing software eliminates images with no significant changes (compared with the previous frames in the video) in the CE video. auto-speed-adjusted modes The software automatically speeds up the rate to a maximum of 25 fps when it detects that repetitive images are being displayed and reduces the frame rate to the	reference standard: standard reading	auto-speed-adjusted mode = 34 ± 10 min express-selected mode=19 ± 5 min conventiona mode=45 ± 15 min. (p = 0.001)	**significant lesions detected** standard reading: 40 auto-speed-adjusted mode =39/40 (97.5%) express-selected mode=39/40 (97.5%)	

		minimum defined by the user when it detects that nonrepetitive images are being displayed.				
Westerhof 2009	study A:100 consecutive CE procedures study B: second 100 consecutive CE procedures Indications: Obscure-occult GI bleeding , Suspected inflammatory bowel disease , Obscure-overt GI bleeding , Polyposis syndromes ,Other indications The Netherlands	Study A removing every second image : the multiviewing mode displayed 4 images simultaneously, at a speed of 36 frames per second (fps). By neglecting 2 of every 4 images, the endoscopist actually views only 2 frames, at an effective speed of 18 fps, being frames 1 and 3, 5 and 7) study B: Quickview	Both studies : conventional viewing which consisted of simultaneously displaying 2 images at a speed of 18 fps	**median** removing every second image: 10.2 minutes [IQR 4.3] conventional viewing :17.3 minutes [IQR 6.88], P< 0.001 Quickview =4.4 minutes [IQR 3.0] conventional viewing = 17.8 minutes [IQR 8.88] P< 0.001	**crude diagnostic miss rate** removing every second image =4%(4/100) Quickview = 13%(13/100	
Xu 2014	148 patients indications : Suspected or confirmed Crohn's disease , Obscure	3 levels of OMOM similar picture elimination mode (As the	conventional mode Reference standard=	conventional mode: 32.25 (± 12.40) min, level I: 24.90 (± 10.02) min	**Number of lesions detected** Reference standard:282 conventional mode: 272 (96.5%) level I: 268 (95.3%)	**Sensitivity** conventional mode: 93.8% (85.6—97.7) level I: 87.7% (78.0—93.6) level II: 77.8% (66.9—86.0)

	gastrointestinal bleeding ,Anemia , Chronic abdominal pain, Chronic diarrhea , Familial polyposis , Health examination , Others	levels increase, it can eliminate more similar images) Level I Level II Level III	consensus diagnosis	level II: 20.54 (± 8.35) min level III: 14.96 (± 6.93) min. $P < 0.001$in all cases	level II: 253 (89.7%) level III: 245 (86.9%) **number of missed lesions** conventional mode: 10/282 (3.5%) level I: 14/282 (4.7%) level II: 29/282 (10.3%) level III: 37/282 (13.1%)	level III: 70% (58.6—79.5) **Specificity** conventional mode: 100% (93.2—100) level I: 98.5% (90.7—99.9) level II: 98.5% (90.7—99.9) level III: 98.5% (91.0—99.9)

Quality of evidence

Reading time
Factors that can lower quality
Study limitations (risk of bias): no
Inconsistency of results: no
Indirectness of evidence: no
Imprecision: no (3 studies with 418 participants)
Publication bias: undetected
Factors that can higher quality
large magnitude of effect: yes
opposing plausible residual bias or confounding: no
dose-response gradient: no

Overall quality of evidence: overall evidence was rated as moderate because coming from observational studies and upgraded because of large magnitude of the effect.

Accuracy
Factors that can lower quality
Study limitations (risk of bias): yes (no valid reference standard was used)
Inconsistency of results: no
Indirectness of evidence: no
Imprecision: no
Publication bias: undetected

Overall quality of evidence: overall evidence was rated as low because of study limitations

Conclusions

Reading time was significantly shorter with software which eliminates images than conventional viewing (**MODERATE QUALITY OF EVIDENCE**).
Diagnostic yield: none of the studies measured diagnostic yield, defined as number of lesions detected per patient, but all compared the lesions detected by quick view with the lesions detected by the standard view .
Accuracy: Miss rate of lesions ranged from 2.5% to 13%. Sensitivity ranged from 70% to 100%; specificity ranged from 84.7% to 100%. However it should be noted that none of the studies used a valid reference standard: some studies used the standard view as a reference standard, while other used a consensus diagnosis made by expert (**LOW QUALITY OF EVIDENCE**).

Clinical question 2

10 studies (Abdelaal 2015, Boal Carvalho 2016, Dias De Castro 2015, Duque 2012, Imagawa 2011, Imagawa 2011 Scandinavian Journal of Gastroenterology, Koulaouzidis 2012, Krystallis 2011, Matsumura 2012, Nogales Rincon 2013) that did not define any reference standard but simply compared white light with FICE or Blue mode, and 5 diagnostic accuracy studies (Gupta 2011, Kobayashi 2012, Rimbas 2015, Sakai 2012, Sato 2012) answered to this clinical question evaluating the improvement in the diagnostic yield with virtual chromoendoscopy techniques as Blue mode (BM) OR FICE. The five diagnostic accuracy studies used as reference standard the senior consultant diagnosis (Gupta 2011, Kobayaski 2012, Sakai 2012) final diagnoses, made by several modalities including CE, balloon enteroscopy, surgery and periodical observation (Sato 2014), designation at initial selection (Rimbas 2015).

Blue mode is a colour coefficient shift of light in the short wavelength range (490–430 nm) superimposed into a white light [red, blue, green (RGB)] image.
FICE, the flexible spectral imaging colour enhancement has been developed with the objective of enhancing surface patterns or mucosal lesions through the narrowing of white light bandwidth and reconstituting virtual images for different wavelengths of red, green and blue. In FICE, different wave length settings correspond to one of three different modes: FICE1 (wavelength red 595 nm, green 540 nm, blue 535 nm), FICE2(wavelength red 420 nm, green 520 nm, blue 530 nm), or FICE3(wavelength red 595 nm, green 570 nm, blue 415 nm).

In the table below, we reported the results of the comparison between chromoendoscopy techniques and standard reading in term of diagnostic yield, reading time and accuracy.

Study	Participants	Intervention	Control	Reading time	Lesion detection/diagnostic yield	Accuracy
Abdelaal 2015	70 CE procedures indications: OGIB a clinical trial that studied the portal hypertensive enteropathy in 30 pts with liver cirrhosis suspected CD, anemia, and follow up after GI bleeding Egypt	-Blue Mode at 10 fps (Ab), Or -Blue Mode at 20 fps (Bb) White light at 20 fps (Bw) All CE procedures were reviewed in four different ways using two different imaging modes (white light and BM) and at two different viewing speeds (10 and 20 frames per second (fps) using QV) of SingleView.	white light at 10 fps (Aw)		**Small-bowel lesions detection**, n (mean±SD) <u>White light 10 fps vs Blue mode 10fps</u> **Vascular** White light (Aw) =73 (1±1.17) Blue mode (Ab)= 140 (2±1.5) p <0.001 **Inflammatory** White light (Aw) =51 (0.7±1.0) Blue mode (Ab)= 94 (1.3±1.1) P= 0.005 **Others** White light (Aw) =26 (0.4±0.7) Blue mode (Ab)= 28 (0.4±0.8) P=1.000 <u>White light 10 fps vs blue mode 20 fps</u> **Vascular** White light 10 fps (Aw)= 73 (1±1.17) Blue mode 20 fps (Bw)= 116 (1.7±1.4) P= 0.035 **Inflammatory** White light 10 fps (Aw)= 51 (0.7±1.0) Blue mode 20 fps (Bw)= 75 (1.1±1.0)	

					P= 0.217 **Others** White light 10 fps (Aw)= 26 (0.4±0.7) Blue mode 20 fps (Bw)= 27 (0.4±0.8) P= 1.000	
Boal Carvalho 2016	60 patients with obscure gastrointestinal bleeding Portugal	Virtual chromoendoscopy techniques FICE1 (wavelength red 595 nm, green 540 nm, blue 535 nm)	white light (WL)		**Diagnostic yield** FICE1= 55% WL= 42%, p = 0.021 **total number of P2 lesions** (lesions with high bleeding potential) FICE1=74 WL = 44, p = 0.003 8 patients previously considered to have a normal exam or P1 lesions during WL visualization were diagnosed with P2 lesions with FICE1, corresponding to a 13%increase of the SBCE diagnostic yield.	
Dias De Castro 2015	42 patients with obscure gastrointestinal bleeding (OGIB) and with a negative examination under white light. Portugal	FICE1	white light		**nondiagnostic SBCE** White light=42 FICE 1= 14/42 (33%) **overall diagnostic yield wit FICE1** P2 lesions (mainly angioectasias) = 9/42 (21%) P1 lesions (erosions)= 26/42(62%) both P1 and P2 lesions = 7/42	

					patients (17%)	
Duque 2012	20 patients with obscure gastrointestinal bleeding (OGIB). Portugal	FICE set 2 (wavelengths red 420 nm, green 520 nm, blue 530 nm); frame rate of 10 per second	conventional reading		**Small bowel endoscopic findings** Erosions Conventional mode=24 FICE2=41 Angiodysplasia Conventional mode=32 FICE2=35 Polyps Conventional mode=3 FICE2=3 Sub-epithelial lesions Conventional mode=2 FICE2=2 Ulcerated stenosis Conventional mode=1 FICE2=1 Other findings: lymphanglectasias and mucosal atrophy areas. Conventional mode=13 FICE2=13 Overall findings: Conventional mode=75 FICE2=95	
Gupta 2011	60 patients with OGIB Belgium	FICE	white light senior consultant by white light: reference standard	FICE=75min White light=55min	**lesions diagnosed** FICE=153 White light=118 $P = 0.15$ reference standard: 131	for P2 lesions **sensitivity** FICE=94% (0.87-1.02) white light =97% (0.92-1.02) **specificity** FICE=95% (0.87-1.03) white light =96% (0.86-1.04)
Imagawa 2011	145 lesions obtained from	FICE settings 1: red 595	conventional CE		visibility compared to conventional CE **Angioectasia**	

	122 patients for obscure GI bleeding , extent of tumor spread , abdominal pain , chronic diarrhea , inflammatory bowel disease , suspected tumor Japan	nm, green 540 nm, blue 535 nm; setting 2: red 420 nm, green 520 nm, blue 530 nm; setting 3: red 595 nm, green 570 nm, blue 415 nm)			FICE 1: improved 20 (87.0%)P <0 .01 no change:3(13%) worsened:0 FICE 2: improved 87.0%)P <0 .01 no change:2 (8.7%) worsened:1 (4.3%) FICE 3: improved 1 (4.3% P <0.01 no change : 22 (95.7%) worsened: 0 **Erosion/ulceration** FICE 1: improved 26 (55.3%) P <0 .01 no change: 19 (40.4%) worsened: 2 (4.3%) FICE 2: improved 12 (25.5%) P <0 .01 no change: 32 (68.1%) worsened: 3 (6.4%) FICE 3: improved 0 P <0.01 no change: 34 (72.3%) worsened: 13 (27.7%) **Tumor** FICE 1: improved 19 (25.3 %) P <0 .01 no change: 54 (72.0%) worsened: 2 (2.7%) FICE 2: improved 15 (20.0%) P <0 .01	

					no change: 58 (77.3%) worsened: 2 (2.7%) FICE 3: improved 1 (1.3 %) P <0.01 no change: 44 (58.7%) worsened: 30 (40%)	
Imagawa 2011, Scandinavian Journal of Gastroenterology	50 patients examined for for obscure GI bleeding , extent of tumor spread , abdominal pain , chronic diarrhea , inflammatory bowel disease , suspected tumor Japan	FICE settings 1: red 595 nm, green 540 nm, blue 535 nm; setting 2: red 420 nm, green 520 nm, blue 530 nm; setting 3: red 595 nm, green 570 nm, blue 415 nm)	conventional CE	Conventional: 36 ± 6.9 min FICE 1: 36 ± 6.4 min FICE 2: 38 ± 5.8 FICE 3: 35 ± 6.7 min Differences did not differ statistically	**lesions detected** **Angioectasia** Conventional: 17 FICE 1: 48 p = 0.0003 vs. conventional CE FICE 2: 45 p = 0.001 vs. conventional CE FICE 3: 24 **Erosion** Conventional: 20 FICE 1: 27 FICE 2: 33 FICE 3: 31 **Ulceration** Conventional: 12 FICE 1: 13 FICE 2: 21 FICE 3: 20 **Lymphangioma** Conventional: 40 FICE 1: 45 FICE 2: 44 FICE 3: 40 **Adenomatous polyp** Conventional: 1 FICE 1: 1 FICE 2: 1 FICE 3: 1 **Peutz-Jeghers polyp**	

					Conventional:7 FICE 1: 7 FICE 2: 7 FICE 3: 7 **GIST** Conventional: 5 FICE 1: 6 FICE 2: 4 FICE 3: 4 **Hemangioma** Conventional: 2 FICE 1: 2 FICE 2: 1 FICE 3: 1	
Kobayashi 2012	24 patients: 6 patients without significant lesions and 18 patients with following diseases: four tumors, five angioectasias, seven ulcerative diseases, one ulcerative lesion and tumor and one ulcerative lesion and angioectasia Japan	FICE settings 1: red 595 nm, green 540 nm, blue 535 nm; setting 2: red 420 nm, green 520 nm, blue 530 nm; setting 3: red 595 nm, green 570 nm, blue 415 nm)	Standard mode <u>final diagnosis</u> by a consensus of three independent reviewers when each CE was performed, and was confirmed by balloon enteroscopy, surgery or periodical observation		**lesion detected** **Polyps** (M,SD) S mode 10.0 ±1.0; F1: 4.3 ± 0.6;p:0.003 F2: 4.3 ± 4.1;p:0.11 F3, 6.3 ± 2.5p:0.05 **angioectasias** S mode: 21.0 ± 2.6; F1: 25.7 ± 3.2; P = 0.005 F2: 22.0 ± 3.0; P = 0.48 F3; 22.7 ± 2.1. P = 0.34. **ulcerative lesions** S mode: 14.0 ± 0.0; F1, 19.3 ± 2.3;p:ns F2: 15.3 ± 1.2; p:ns F3, 11.3 ± 4.0. p:ns	<u>Per patients analysis</u> **Sensitivity (%) of any significant lesion** Standard mode= 94.4±0.0 FICE1 = 90.7±3.7 FICE 2=87.0 ± 4.9 FICE 3=87.0 ± 3.7 **Specificity (%) of any significant lesion** Standard mode=66.7±9.6 FICE1 =55.6± 14.7 FICE 2=77.8±14.7 FICE 3=66.7 ±9.6 no significant difference in the sensitivity e specificity between the S mode and each FICE mode
Koulaouzidis 2012	200 patients with	QuickView with white light	standard mode video	**mean evaluation**	**All findings, n(%)** QVWL =129 (49.6%),	

	OGIB, known or suspected Crohn's disease ,polyposis syndromes, Coeliac disease, Possible SB lesion or mass UK	(QVWL) reading QuickView with Blue Mode (QVBM) reading	sequence review	**time** (including reading and time to mark thumbnails) QVWL=475 (±270) s QVBM= 450 (±156) s (P=0.363).	QVBM = 135 (51.9%) Standard view = 260 (P<0.0001) SBCE performed for Obscure gastrointestinal bleeding(n=106) **Angioectasias, n(%)** QVWL=54 (55.1%) QVBM= 63 (64.3%) Standard view= 98 (P=0.0506). SBCE performed for Suspected/known Crohn's disease (n=81) **Mucosal ulcers, n(%)** QVWL= 71 (45.8%) QVBM=68 (43.9%) Standard view= 155 P=0.0003. SBCE performed for polyposis syndromes or Possible SB lesion or mass (n=10) **Polypoid lesions, n** QVWL= 4 QVBM=4 Standard view= 7	
Krystallis 2011	167 small bowel images/lesions, from 52 patients with a variety of indications as	FICE settings 1: red 595 nm, green 540 nm, blue 535 nm; setting 2: red 420 nm,	White light		**FICE 1 vs white light** Image improved: 34% no changed: 8.9% worse:55.9% **FICE 2 vs white light**	

	part of their regular diagnostic work-up UK	green 520 nm, blue 530 nm; setting 3: red 595 nm, green 570 nm, blue 415 nm) Blue filter			Image improved: 8.6% no changed:13% worse:77.5% **FICE 3 vs white light** **Image improved** Overall= 7.7% no changed:12% worse:79.9% **Blue filter vs white light** Image improved: 83% no changed: 12% worse:3%	
Matsumura 2012	81 patients with OGIB Japan	FICE Set 1: red 595 nm, green 540 nm, blue 535 nm(n=27) FICE Set 2: red 420 nm, green 520 nm, blue 530 nm; (n=27) FICE Set 3: red 595 nm, green 570 nm, blue 415 nm(n=27)	conventional CE (n=81)		**overall diagnostic yields** FICE sets 1=51.9% FICE sets 2=40.7%, FICE sets 3=51.9% conventional CE= 48.1% FICE1 vs conventional imaging, $P = 0.5$ FICE2 vs conventional imaging, p=0.23 FICE3 vs conventional imaging, p= 0.5	
Nogales Rincon 2013	50 lesions in 41 patients, indications not reported	FICE settings 1: red 595 nm, green 540 nm, blue 535 nm; setting 2: red 420 nm, green 520 nm, blue 530 nm;	standard visualization		**Lesion detected** **by standard visualization** vascular lesions and angiodysplasias =18 erosions and ulcers=18 polyps and tumors=14 Tot=50 **vascular lesions** FICE 1 better visualization=16/18 (88.9%)	

		setting 3: red 595 nm, green 570 nm, blue 415 nm)			no change :1/18(5.5%) worse : 1/18(5.5%) FICE 2 better visualization=16/18 (88.9%) no change :2/18(11.1%) worse : 0 FICE 3 better visualization=5/18 (27.7%) no change :91/ (5%) worse:4/18 (22.2%) **erosions/ulcers** FICE 1. better visualization= 14/18 (77.8%) no change 4/18 (22.2%) worse:0 FICE 2 better visualization = 10/18(55.5%) no change :6/18(33.3%) worse :2/18 (11.1%) FICE 3 better visualization=1/18 (5.5%) no change : 9/18 (50%) worse: 8/18 (44.4%) **polyps/tumors** FICE 1 better visualization= 2/14 (14.2%), no change :8/14(57.1%) worse:4/14 (28.6%) FICE 2 better visualization= 3/13 (21.4%) no change :7/14 (50%)	

					worse: 4/14(28.6%) FICE 3 better visualization=4/14 (28.5%) no change :9/14 (64.2%) worse:1/14 (7.1%)	
Rimbas 2015	250 difficult-to-interpret small-bowel ulcerative and 50 artifact lesions from 64 video capsule endoscopy Romania	Chromoendoscy (FICE 1, 2, and 3 and Blue mode)	conventional white light endoscopic imaging (WLI) The gold standard ,although subjective, was the designation at initial selection (i. e., true ulcerative or not).			**Overall image evaluation** Accuracy with WLI =53.7% Accuracy with chromoendoscopy = 70.2 % Improvement in accuracy,=16.5% [95%CI13.6, 19.4] p< 0.001* **True ulcerative image evaluation** Accuracy with WLI = 49.4% Accuracy with chromoendoscopy= 71.4% Improvement in accuracy, 22% [95%CI18.9, 25.1] p< 0.001 **False ulcerative image evaluation** Accuracy withWLI = 75% Accuracy with chromoendoscopy = 64 Improvement in accuracy, : 11% [95%ci 4.1, 17.7]

						P= 0.003
Sakai 2012	12 patients, indication not reported Japan	FICE setting 1 (red 595 nm, green 540 nm, blue 535 nm), FICE setting 2 (red 420 nm, green 520 nm, blue 530 nm) FICE setting 3 (red 595 nm, green 570 nm, blue 415 nm)	conventional visualization method findings of the CE experts': gold standard			**Angioectasia** Lesions detected by the CE experts =60 **Sensitivity** Conventional =26/60 (43.3%) Setting 1=40/60 (66.7%), vs conventional p = 0.0017 Setting 2 =38/60 (63.3%), vs conventional P = 0.014, Setting 3=31 (51.7%) vs conventional: p: NS **Erosion/ulceration** Lesions detected by the CE experts =82 **Sensitivity** Conventional =38/82 (46.3%) Setting 1=62/82 (75.6%), vs conventional p =0.0012 Setting 2 =60/82 (73.2%), vs conventional p =0.0094 Setting 3=20/82 (24.4%) vs conventional p: P = 0.015
Sato 2014	50 patients, indications: OGIB , extent of tumor spread , chronic abdominal pain or	FICE 1 FICE2 FICE3 blue mode (BM)	White light reference standard: final diagnoses, made by			**sensitivity of Vascular** WL=83.3(50.8 –97.0) FICE 1=100(69.8 –100) FICE2=100(69.8 –100) FICE3=75.0(42.8 –93.3) BM=83.3 (50.8 -97.0)

	diarrhea and miscellaneous Japan		several modalities including CE, balloon enteroscopy, surgery and periodical observation			**sensitivity of Erosion/Ulceration** WL=84.6 (53.6 –97.2) FICE 1=92.3 (62.0 –99.5) FICE2=100 (71.6 –100) FICE3=76.9 (45.9 –93.8) BM=84.6(53.6 –97.2 **sensitivity of Tumor** WL=90.9(57.1 –99.5) FICE 1=81.8 (47.7 –96.7) FICE2=81.8 (47.7 –96.7) FICE3=72.7 (39.3 –92.6) BM=81.8 (47.7 –96.7) **specificity of Vascular** WL=92.1 (77.5 –97.9) FICE 1=100 (88.5 –100) FICE 2=97.3 (84.5 –99.8) FICE3=94.7 (80.9 –99.0) BM=92.1 (77.5 –97.9) **specificity of Erosion/Ulceration** WL=89.2 (73.6 –96.4) FICE 1=94.6 (80.4 –99.0) FICE2=97.2 (84.1 –99.8) FICE3=91.9 (76.9 –97.8) BM=89.2 (73.6 –96.4) **specificity of Tumor** WL=87.1 (71.7 –95.1) FICE 1=84.6 (68.7 –93.5) FICE2=84.6 (68.7 –93.5) FICE3=84.6 (68.7 –93.5) BM=84.6 (68.7 –93.5)

Quality of evidence

Reading time
Factors that can lower quality
Study limitations (risk of bias): no
Inconsistency of results: yes
Indirectness of evidence: no (but for one study considered evaluation time that including reading and time to mark thumbnails)
Imprecision: yes (3 studies including 310 patients)
Publication bias: undetected
Factors that can higher quality
large magnitude of effect: no
opposing plausible residual bias or confounding: no
dose-response gradient: no

Overall quality of evidence: overall evidence was rated as very low because coming from observational studies with imprecision.

Diagnostic yield
Factors that can lower quality
Study limitations (risk of bias): no
Inconsistency of results: no for FICE, yes for blue mode
Indirectness of evidence: no
Imprecision: no (11 studies with more than 800 participants)
Publication bias: undetected
Factors that can higher quality
large magnitude of effect: no
opposing plausible residual bias or confounding: yes
dose-response gradient: no

Overall quality of evidence: overall evidence was rated as low because coming from observational studies.

Accuracy
Factors that can lower quality
Study limitations (risk of bias): yes (reference standard unlikey to correctly classify the target condition: reading by expert gastroenterologist of CE by White light)
Inconsistency of results: not possible to ascertain because the studies used different ways to measure accuracy
Indirectness of evidence: no
Imprecision: yes (5 studies including 310 patients)
Publication bias: undetected

Overall quality of evidence: overall evidence was rated as very low because of study limitation and imprecision.

Conclusions

Reading time: Two studies found no difference in reading time between with light and FICE or blue mode, whereas the third found that reading with FICE took 20 minutes more than with white light (**VERY LOW QUALITY OF EVIDENCE**).
Diagnostic yield: 5 studies found that FICE had a higher diagnostic yield than white light; two found higher diagnostic yield only for angioectasia detection: one study found higher diagnostic yield for blue mode while the other did not. Three studies compared visibility of lesions between white light and FICE measuring the percentages of images with improved, no change or worsened visibility. One study found that FICE improves visibility of small-bowel angioectasia, erosion/ulceration, and tumor, another found better visualization for FICE setting 1 and 2 but not for setting 3 and only for vascular lesions and erosions/ulcers but not for polyps or tumors The third study found beter visualization only with FICE setting 1 and Blue mode, but not for FICE setting 2 and 3 (**LOW QUALITY OF EVIDENCE**).
Accuracy: the five studies that compared white light and FICE or blue mode with a reference standard used different measures for accuracy. One study assessed overall accuracy for every lesion and found an accuracy of 53.7% for white light compared to an accuracy of 70.2 % for chromoendoscopy, with an improvement in accuracy with chromoendoscopy of 16.5% [95%CI13.6, 19.4] . Another study measured sensitivity and specificity for detecting any lesion and did not found significant difference in the sensitivity e specificity between the S mode and each FICE mode. A third study measured sensitivity and specificity for detecting P2 lesions and found a small difference in favour of white light (FICE: sensitivity 94%, specificity 95%, white light sensitivity 97%, specificity 96%). The last two studies measured sensitivity and specificity for detecting specific lesions. Both found higher sensitivity for detecting angioectasia and erosion/ulceration and one for detecting tumor for FICE setting 1 and 2 but not for setting 3 when compared to white light. Specificity was measured by one study and was slightly higher for FICE for vascular and erosion/ulceration lesions but not for tumors. Blue mode had equal or worse values of sensitivity and specificity when compared to white light(**VERY LOW QUALITY OF EVIDENCE**).

Clinical question 3

3 studies (Abdelaal 2015, Gunther 2012, Shiotani 201) answered to this clinical question evaluating different reading speed measured as number of images seen simultaneously and frames per second (fps).

In table below, we reported the results of the comparison between high reading speed and low reading speed in term of diagnostic yield.

Study	Participants	Intervention	Control	Reading time	Lesion detection
Abdelaal 2015	70 CE procedures indications: OGIB a clinical trial that studied the portal hypertensive enteropathy in 30 pts with liver cirrhosis suspected CD, anemia, and follow up after GI bleeding Egypt	white light at 20 fps (Bw)	white light at 10 fps (Aw)		White light 10 fps (Aw) vs 20 fps (Bw), n (mean±SD) **Vascular** 10 fps (Aw) =73 (1±1.17) 20 fps (Bw)= 46 (0.7±0.9) P=0.175 **Inflammatory** 10 fps (Aw) = 51 (0.7±1.0) 20 fps (Bw)= 35 (0.5±0.7) P= 0.146 **Others** 10 fps (Aw) = 26 (0.4±0.7) 20 fps (Bw)= 22 (0.3±0.6) P= 0.107
Gunther 2012	70 CE videos 45 cases retrospectively chosen with OGIB, suspected or established Crohn's disease and suspected or complicated celiac disease, and 25 CEs prospectively performed for obscure bleeding Germany	quadview (four images simultaneously) mode at 20 fps	single view at 10 fps	**Mean evaluation time** single view at 10 fps =22 min (SD±9.1 min) quadview mode at 20 fps =11.9 min (SD±4.8 min)	**for Obscure bleeding patients** Angiodysplasias single view at 10 fps =87 quadview mode at 20 fps =72 p<0.05 Erosions single view at 10 fps =22 quadview mode at 20 fps =13 p<0.05 Ulcerations , Fresh blood , Duodenal varices ,Lymphangiectasias , Lipomas , Small polyps . Tumorous lesions: no significant difference **for Suspected or established Crohn's disease patients** Angiodysplasias , Erosions ,Ulcerations

					Inflamed mucosa segments , Fresh blood , Lymphangiectasias , Lipomas , Small polyps Pseudopolyps: no significant differences **for Suspected or complicated celiac disease patients** Angiodysplasias , Erosions ,Ulcerations Inflamed mucosa segments , Fresh blood , Lymphangiectasias , Lipomas , Small polyps Pseudopolyps: no significant differences
Shiotani 2011	30 patients	Quadview: manual mode and simultaneously displaying four images at a speed of 35 fps; Quickview: manual mode and a single image at a speed of 6 fps	Single view: auto mode and displaying a single image at a speed of 12 fps	**Reading time** Single view =32.9 min(SD15.6) Quadview =20.0 min(SD9.2) Quickview= 17.9min (9.1SD)	

Quality of evidence

Diagnostic yield
Factors that can lower quality
Study limitations (risk of bias): no
Inconsistency of results: yes (for vascular lesions)
Indirectness of evidence: no
Imprecision: yes (two studies with less than 150 participants)
Publication bias: undetected
Factors that can higher quality
large magnitude of effect: no
opposing plausible residual bias or confounding: no
dose-response gradient: no

Overall quality of evidence: overall evidence was rated as very low for inconsistency and imprecision.

Conclusions

Diagnostic yield: one study did not find signficant difference in detection rate of vascular, inflammatory and other lesions between White light 10 fps and 20 fps . The second study found higher detection rate with single view at 10 fps compared with quadview mode at 20 fps only for Angiodysplasias and Erosions for patients with OGIB; no significant diference were found for other lesions in patients with OGB and for any kind of lesion in patients with Crohn disease and celiac disease **(VERY LOW QUALITY OF EVIDENCE**).
Accuracy: no studies assessed this outcome.

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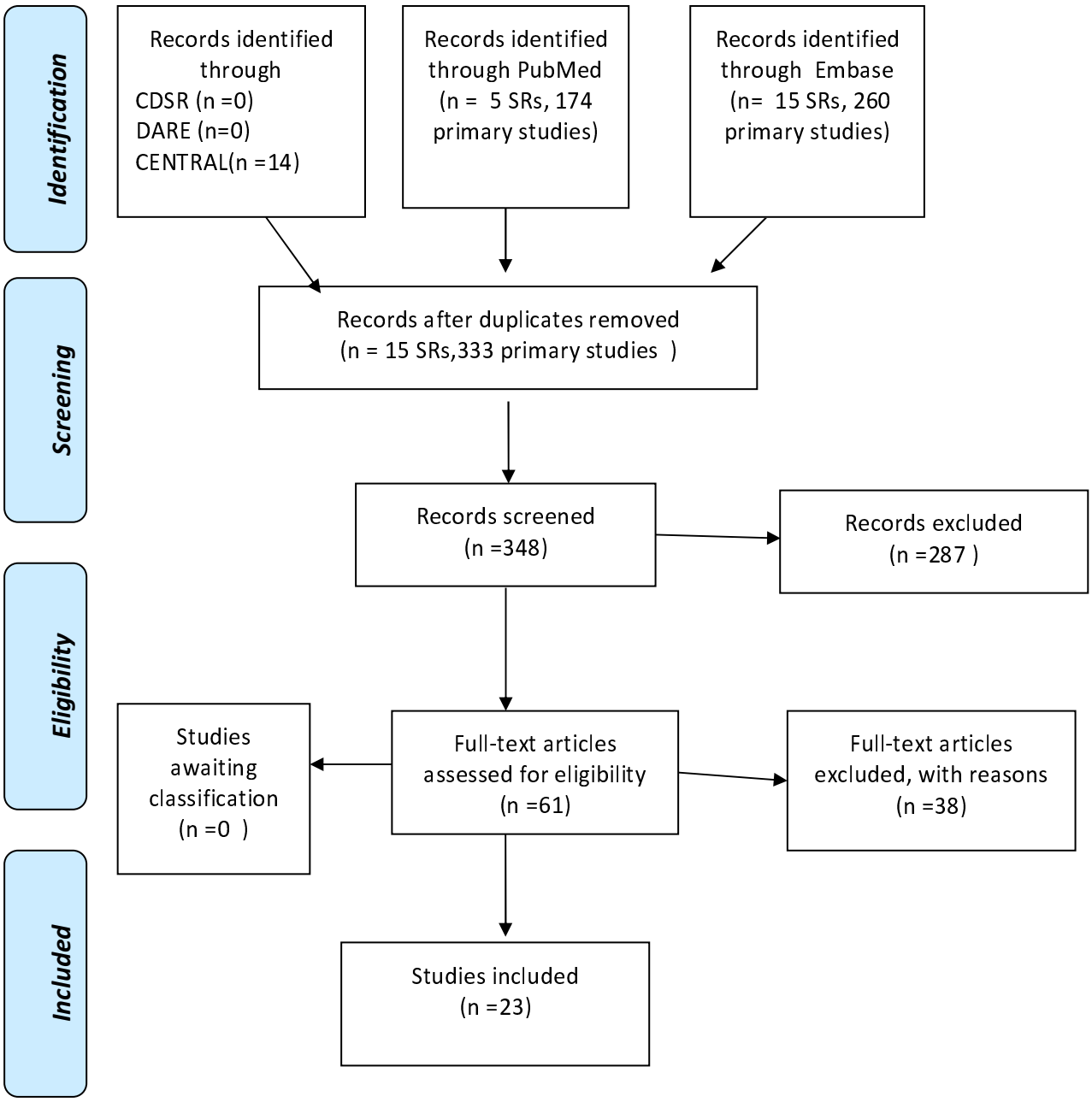
PRISMA 2009 Flow Diagram



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

Standardised report of procedure and findings

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

12.1 (St. 15.1) Standardised report of procedure and findings including indication, reader, speed, preparation quality, landmarks, (completeness), all relevant findings including image and time notes, recommendations (see below for details); management.

P: patients undergoing CE
I: standardised reporting
C. none
O: yield of pathology
Notes: Does inclusion of a standardised reporting in small bowel capsule endoscopy improve interpretation?

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 15/2/2016 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** ("Diagnostic yield"[Title/Abstract] OR "Intestinal Diseases/diagnosis"[Mesh] OR findings[Title/Abstract] OR finding[Title/Abstract]) **AND** (report*[Title/Abstract] OR reporting[Text Word] OR standardi*[Title/Abstract] OR "Video Recording"[Mesh] OR video[Title/Abstract] OR picture[Title/Abstract] OR pictures[Title/Abstract] OR documentation[Title/Abstract] OR photo[Title/Abstract] OR imaging[Text Word] OR "Anatomic Landmarks"[Text Word] OR speed[Title/Abstract] OR time[Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** ('diagnostic yield':ti,ab OR 'small intestine disease'/exp/dm_di OR findings:ab,ti OR finding:ab,ti) **AND** ('anatomic landmark'/exp OR 'videorecording'/exp OR video:ab,ti OR picture:ab,ti OR pictures:ab,ti OR documentation:ab,ti OR reporting:ab,ti OR standardi*:ab,ti OR report:ab,ti OR photo:ab,ti OR imaging:ab,ti OR speed:ab,ti OR time:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

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

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 diagnostic yield:ti,ab,kw (Word variations have been searched)
#5 MeSH descriptor: [Intestinal Diseases] explode all trees and with qualifier(s): [Diagnosis - DI]
#6 finding:ti,ab,kw (Word variations have been searched)
#7 #4or #5or #6
#8 MeSH descriptor: [Intestine, Small] explode all trees
#9 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#10 #8 or #9
#11 MeSH descriptor: [Anatomic Landmarks] explode all trees
#12 MeSH descriptor: [Video Recording] explode all trees
#13 Report or video or picture or documentation or photo or imaging or "Anatomic Landmarks" or speed or time or standardized:ti,ab,kw (Word variations have been searched)
#14 #11 or #12 or #13
#15 #3 and #7 and #10 and #14 Publication Year from 2000 to 2016

Primary studies

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** ("Diagnostic yield"[Title/Abstract] OR "Intestinal Diseases/diagnosis"[Mesh] OR findings[Title/Abstract] OR finding[Title/Abstract]) **AND** (report*[Title/Abstract] OR reporting[Text Word] OR standardi*[Title/Abstract] OR "Video Recording"[Mesh] OR video[Title/Abstract] OR picture[Title/Abstract] OR pictures[Title/Abstract] OR documentation[Title/Abstract] OR photo[Title/Abstract] OR imaging[Text Word] OR "Anatomic Landmarks"[Text Word] OR speed[Title/Abstract] OR time[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) NOT Case Reports[ptyp]

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** ('diagnostic yield':ti,ab OR 'small intestine disease'/exp/dm_di OR findings:ab,ti OR finding:ab,ti) **AND** ('anatomic landmark'/exp OR 'videorecording'/exp OR video:ab,ti OR picture:ab,ti OR pictures:ab,ti OR documentation:ab,ti OR reporting:ab,ti OR standardi*:ab,ti OR report:ab,ti OR photo:ab,ti OR imaging:ab,ti OR speed:ab,ti OR time:ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 #1 or #2
#4 diagnostic yield:ti,ab,kw (Word variations have been searched)
#5 MeSH descriptor: [Intestinal Diseases] explode all trees and with qualifier(s): [Diagnosis - DI]
#6 finding:ti,ab,kw (Word variations have been searched)
#7 #4or #5or #6
#8 MeSH descriptor: [Intestine, Small] explode all trees
#9 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#10 #8 or #9
#11 MeSH descriptor: [Anatomic Landmarks] explode all trees
#12 MeSH descriptor: [Video Recording] explode all trees
#13 Report or video or picture or documentation or photo or imaging or "Anatomic Landmarks" or speed or time or standardized:ti,ab,kw (Word variations have been searched)
#14 #11 or #12 or #13
#15 #3 and #7 and #10 and #14 Publication Year from 2000 to 2016

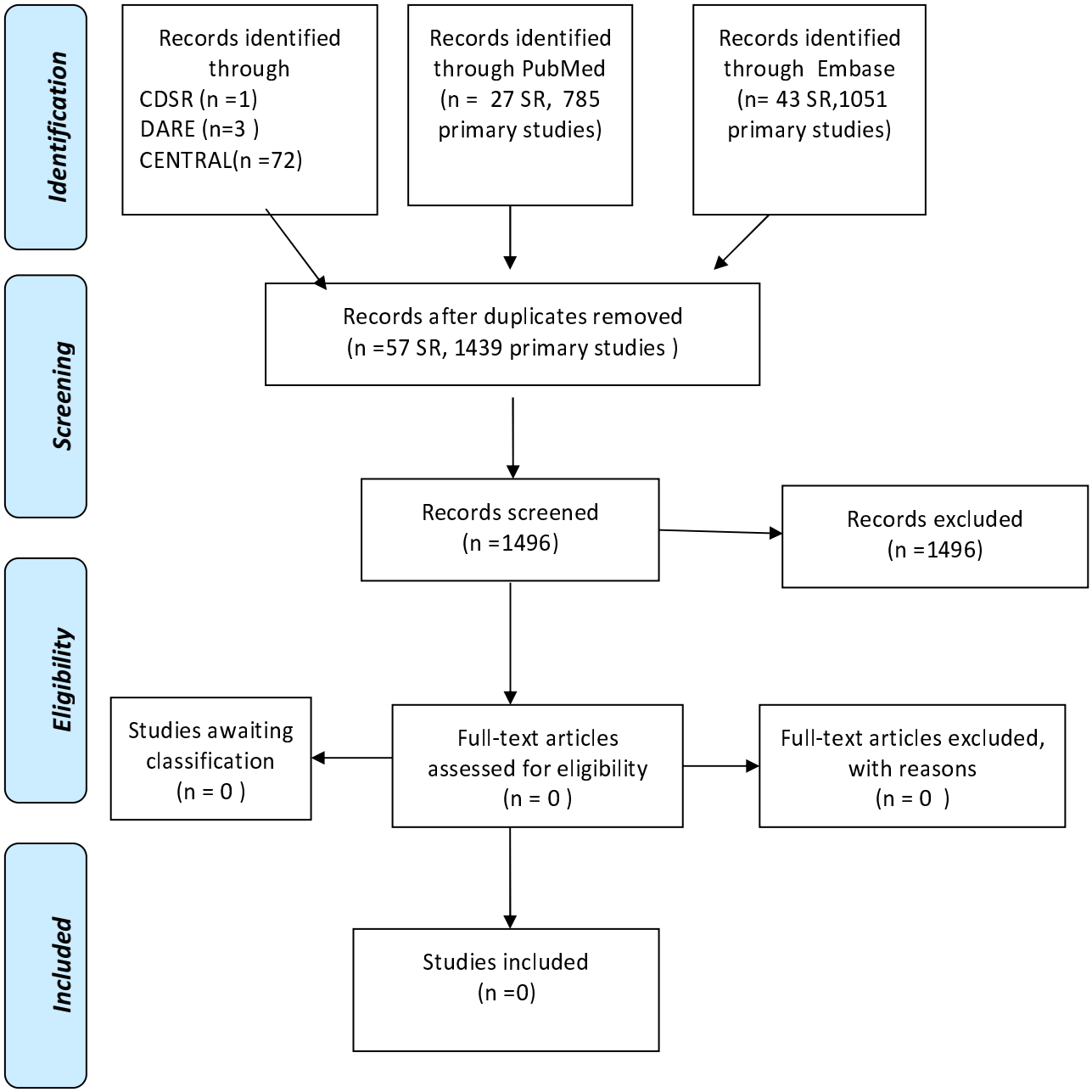
Results

Results of the bibliographic searches
After removing duplicates, 1496 articles (57 reviews and 1439 primary studies) were found. No relevant studies were found addressing this question.

Conclusions

No evidence about the relation between standardised report of procedure and all relevant findings of pathology was found.

PRISMA 2009 Flow Diagram



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Capsule Timing

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13.1 (St. 16.1) **Delay to capsule endoscopy procedure and effect on detection rates- Capsule timing**

P: Patients having CE
I: Early CE (<15 days)
C: delayed CE (>15 days)
O: improved lesion detection rates of bleeding lesions
Notes: bleeding

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 15/2/2016 separately for systematic reviews and primary studies using the following search strategies:

Systematic reviews and meta-analysis

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Diagnostic yield" [Title/Abstract] OR "Intestinal Diseases/diagnosis"[Mesh] OR findings[Title/Abstract] OR finding[Title/Abstract]) **AND** ("Gastrointestinal Hemorrhage"[Mesh] OR bleeding[Title/Abstract] OR Hemorrhage[Title/Abstract]) **AND** (timing[Title/Abstract] OR delay[Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('diagnostic yield':ti,ab OR 'small intestine disease'/exp/dm_di OR findings:ab,ti OR finding:ab,ti) **AND** ('gastrointestinal hemorrhage'/exp OR bleeding:ab,ti OR Hemorrhage:ab,ti) **AND** (timing:ab,ti OR delay:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

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

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 #1or #2
#4 MeSH descriptor: [Gastrointestinal Hemorrhage] explode all trees
#5 Hemorrhage or bleeding:ti,ab,kw (Word variations have been searched)
#6 timing or delay:ti,ab,kw (Word variations have been searched)
#7 #4 or #5
#8 diagnostic yield:ti,ab,kw (Word variations have been searched)
#9 MeSH descriptor: [Intestinal Diseases] explode all trees and with qualifier(s): [Diagnosis - DI]
#10 finding:ti,ab,kw (Word variations have been searched)
#11 #8 or #9or #10
#12 #3 and #7 and #6 and #11 Publication Year from 2000 to 2016

Primary studies

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Diagnostic yield" [Title/Abstract] OR "Intestinal Diseases/diagnosis"[Mesh] OR findings[Title/Abstract] OR finding[Title/Abstract]) **AND** ("Gastrointestinal Hemorrhage"[Mesh] OR bleeding[Title/Abstract] OR Hemorrhage[Title/Abstract]) **AND** (timing[Title/Abstract] OR delay[Title/Abstract]) **NOT** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract]) **NOT** ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]) **NOT** Case Reports[ptyp]

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('diagnostic yield':ti,ab OR 'small intestine disease'/exp/dm_di OR findings:ab,ti OR finding:ab,ti) **AND** ('gastrointestinal hemorrhage'/exp OR bleeding:ab,ti OR Hemorrhage:ab,ti) **AND** (timing:ab,ti OR delay:ab,ti) **NOT** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR 'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim OR [animals]/lim OR 'case report'/exp OR 'case report' OR 'report of case')

Cochrane Central Register of Controlled Trials (CENTRAL)

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 #1or #2
#4 MeSH descriptor: [Gastrointestinal Hemorrhage] explode all trees

#5 Hemorrhage or bleeding:ti,ab,kw (Word variations have been searched)
#6 timing or delay:ti,ab,kw (Word variations have been searched)
#7 #4 or #5
#8 diagnostic yield:ti,ab,kw (Word variations have been searched)
#9 MeSH descriptor: [Intestinal Diseases] explode all trees and with qualifier(s): [Diagnosis - DI]
#10 finding:ti,ab,kw (Word variations have been searched)
#11 #8 or #9or #10
#12 #3 and #7 and #6 and #11 Publication Year from 2000 to 2016

Results

Results of the bibliographic searches

After removing duplicates, 81 (2 SRs and 79 primary studies) articles were found. 13 articles were considered potentially relevant and acquired in full text (See flow chart).

Excluded studies

5 articles were excluded: one because editorial (Nakamura 2005); one because conference abstract without useful data (Juliao 2012); two because conference abstracts of already included study (Goenka 2010, Singh 2011); one because no comparison of interest (Calabrese 2013).

Included studies

8 studies were finally included which assessed timing of CE after the diagnosis of bleeding in relation of diagnostic yield. Timing of CE was dichotomised differently in the studies: only one study (Bresci 2015) used the cut-off of 15 days; two studies used the cut-off of 24 hours (Parikh 2012, Handa 2012); five studies used the cut-off of two days (Parikh 2012, Goenka 2011, Kim 2015, Lee 2014, Yamada 2012); one study used the cut off of three days (Sungh 2013). All but two studies (Bresci 2005, Parikh 2012) specified that patients had overt bleeding.

Study	Patients	Intervention	Control	Eligibility for VCE	Diagnostic yield
Bresci 2005	64 patients	within 15 days from OGIB diagnosis	at least 15 days after OGIB diagnosis.	Obscure gastrointestinal with negative upper endoscopy, colonoscopy, and small bowel series without discovery of sources of bleeding.	**Any significant lesion** <15 days: 29/32 (91%) >15 days: 11/32(34%) *P* < 0.001
Parikh 2012	410 patients	within 24, 48 or 72 hours or 1 week	more than 24 hours, 48 or 72 or after 1 week	obscure gastrointestinal bleeding	**Any significant lesion** within 24 hours=69%, P = 0.08, OR 2.9 [CI 95% (0.92-11.1)]. within 48 hours=65%, P = 0.04, OR= 3.2 [CI 95% (1.1-10.4)] within 72 hours=60%, P = 0.05, OR= 2.3 [CI 95% (1.0-5.5)] within 1 week=66%, P = 0.001, OR 3.7 [CI 95% (1.9-7.6)] **Angioectasias** Within 24 hours=46% more than 24 hours= 17% P = 0.02, OR= 4.1 [CI 95% (1.3-13.0)]. **SB masses** within 24 hours=23% more than 24 hours= 1.5%, P = 0.001, OR= 29 [CI 95% (4.9-167.6)].
Goenka 2011	289 Patients	Category I: overt bleeding documented within 48 h at the time of CE; n: 157	Category II:. last episode of overt bleeding > 48 h prior to the CE; n. 132	Obscure overt bleeding and a negative upper GI endoscopy and full length colonoscopy	**Any significant lesion** Category I:123/157 (48.3%) Category II: 64/132 (48.5%) OR:3.84 (95%CI 2.31-6.41)
Handa 2012	59 patients	within 24hr after final overt OGIB	>24hr after final overt OGIB	recurrent ongoing- or previous- overt OGIB negative findings by upper and lower	**Any significant lesion** within 24hr=87.5% >24hr=33.3%

				endoscopy within 1year before CE examination.	
Kim 2015	94 patients	VCE <48h	VCE >48h	overt OGIB VCE after a negative findings on bidirectional endoscopy	**active bleeding and/or angiodysplasia** 24 h=57.1 48 h=26.1 72h=11.1 96h =11.1 <48h =20 (66.7%) >48h =26 (40.6%) P=0.019
Lee 2014	81 Patients	CE within 2 days of last overt GI bleeding	CE after 2 days of last overt GI bleeding	obscure overt GI and negative result of initial upper endoscopy and colonoscopy	**Any significant lesion** ≤2-day= 75% >2-day =45% (p=0.022).
Singh 2013	144 patients	VCEs within 3 days of admission	VCEs after 3 days of admission	overt obscure GI bleeding and normal bidirectional endoscopy	**active bleed and/or an angioectasia** <3-day= (40 /90) 44.4% >3-day cohort= 27.8% (15/54) (*P* =0.046)
Yamada 2012	90 patients	0-2 days	3-10days 11-29 days ≥30 days	with overt OGIB without further specification	**Any significant lesion** 0-2 days =73% 3-10days=48%, 11-29 days=50% ≥30 =35% 0-2 days vs other groups: p=0.08 **OR (95%CI)** 0-2 days =4.8 (1.2-2.1), p=0.025 3-10 days=1.7 (0.50-5.9), p=0.40 11-29 days=1.9 (0.57-6.4), p=0.30 ≥30 days =reference

Quality of evidence

Diagnostic yield

Factors that can lower quality

Study limitations (risk of bias): yes (no adjustment for possible confounding in all but one study)
Inconsistency of results: no
Indirectness of evidence: no
Imprecision: no (8 studies with 1201 participants)
Publication bias: undetected

Factors that can higher quality

large magnitude of effect: yes (OR greater than 2)
opposing plausible residual bias or confounding: no
dose-response gradient: yes

Overall quality of evidence: overall evidence was rated as moderate because coming from observational data downgraded because at high risk of bias and upgraded because of large magnitude of the effect and dose –response gradient

Conclusions: Cut-off for timing varied among studies, however all studies found that earlier timing of CE achieved a higher diagnostic yield for patients with overt OGIB (**MODERATE QUALITY OF EVIDENCE**).

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Excluded studies

1. Calabrese, C.; Liguori, G.; Gionchetti, P.; Rizzello, F.; Laureti, S.; Di Simone, M. P.; Poggioli, G., and Campieri, M. Obscure gastrointestinal bleeding: single centre experience of capsule endoscopy. Intern Emerg Med. 2013; 8(8):681-687
2. Goenka, M. K.; Majumder, S.; Kumar, S.; Sethy, P. K., and Goenka, U. Single center experience of capsule endoscopy in 385 consecutive patients with obscure gastrointestinal bleeding: Impact of timing. Indian J. Gastroenterol. 2010; 29(1):A110-A111
3. Juliao, F.; Ortiz, E. M., and Yepes, C. The diagnostic yield of capsule endoscopy and findings in patients with obscure gastrointestinal bleeding in a single center in latin America. Gastrointest. Endosc. 2012; 75(4):AB247
4. Nakamura, T. When is the optimal timing for performing video capsule endoscopy for obscure gastrointestinal bleeding? J. Gastroenterol. 2005; 40(3):322-323
5. Singh, A.; Chaudhury, B.; Marshall, C. A.; Okoli, C. I.; Foley, A.; Bhattacharya, K., and Cave, D. R. Does timing of video capsule endoscopy relative to obscure overt gastrointestinal bleed alter diagnostic yield? Gastrointest. Endosc. 2011; 73(4):AB123-AB124

Included studies

1. Bresci, G.; Parisi, G.; Bertoni, M.; Tumino, E., and Capria, A. The role of video capsule endoscopy for evaluating obscure gastrointestinal bleeding: Usefulness of early use. J. Gastroenterol. 2005; 40(3):256-259

2. Parikh, D. A.; Mittal, M.; Mann, S. K., and Ekanayake, P. S. Improved diagnostic yield with early video capsule endoscopy after diagnosis of obscure gastrointestinal bleeding. Gastroenterology. 2012; 142(5):S53;
3. Goenka, M. K.; Majumder, S.; Kumar, S.; Sethy, P. K., and Goenka, U. Single center experience of capsule endoscopy in patients with obscure gastrointestinal bleeding. World J. Gastroenterol. 2011; 17(6):774-778
4. Handa, O.; Yagi, N.; Fukuda, W.; Horie, H.; Yoshida, N.; Katada, K.; Kamada, K.; Uchiyama, K.; Takagi, T.; Konishi, H., and Naito, Y. Urgent capsule endoscopy raises diagnostic yield for overt obscure gastrointestinal bleeding. Gastrointest. Endosc. 2012; 75(4):AB262
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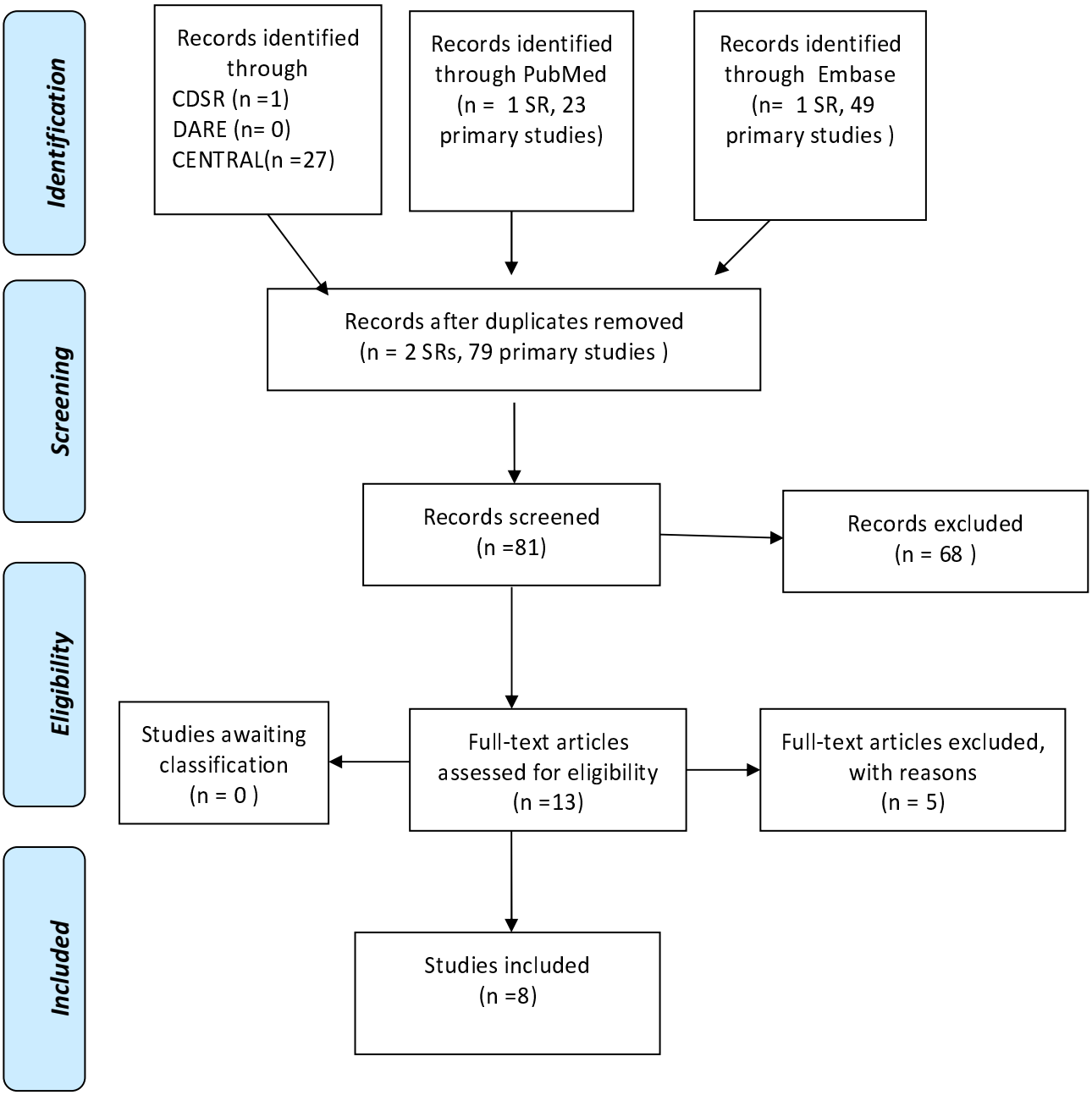
6. Lee, J. S.; Keum, B.; Kim, S. H.; Lee, J. M.; Choi, H. S.; Kim, E. S.; Jeen, Y. T.; Lee, H.; Chun, H. J.; Kim, C. D., and Nam, S. J. What is the optimal timing of capsule endoscopy in obscure GI bleeding patients? Gastrointest. Endosc. 2014; 79(5):AB377
7. Singh, A.; Marshall, C.; Chaudhuri, B.; Okoli, C.; Foley, A.; Person, S. D.; Bhattacharya, K., and Cave, D. R. Timing of video capsule endoscopy relative to overt obscure GI bleeding: Implications from a retrospective study. Gastrointest. Endosc. 2013; 77(5):761-766
8. Yamada, A.; Watabe, H.; Kobayashi, Y.; Yamaji, Y.; Yoshida, H., and Koike, K. Timing of capsule endoscopy influences the diagnosis and outcome in obscure-overt gastrointestinal bleeding. Hepato-Gastroenterology. 2012; 59(115):676-679

PRISMA 2009 Flow Diagram



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Use of Preparation CE

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

14.1 (St. 17.1-17.2) **Use of Preparation (any)**

P: Patients having CE small bowel
I: preparation
C: no preparation
O: increased visualization OR higher diagnostic yield

Bibliographic searches

Bibliographic searches were performed on Cochrane Library, PubMed, Embase, since 1/1/2000 to 15/2/2016 separately for systematic reviews and randomized controlled trials using the following search strategies:

Systematic reviews and meta-analysis

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** (Preparation[Text Word] OR cleansing[Text Word] OR regimen[Text Word] OR preparations[Title/Abstract] OR regiments[Title/Abstract] OR "Cathartics"[Mesh] OR fasting[Text Word] OR "Laxatives"[Mesh] OR Laxatives[Title/Abstract] OR Laxative [Title/Abstract]) **AND** ("Diagnostic yield"[Title/Abstract] OR "Intestinal Diseases/diagnosis"[Mesh] OR findings[Title/Abstract] OR finding[Title/Abstract]) **AND** ("systematic review"[Title/Abstract] OR "systematic reviews"[Title/Abstract] OR cochrane[Title/Abstract] OR meta-analysis[Publication Type] OR "meta analysis"[Title/Abstract] OR metanalysis[Title/Abstract])

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** ('intestine preparation'/exp OR preparation:ab,ti OR preparations:ab,ti OR 'cleaning'/exp OR cleansing:ab,ti OR regimen:ab,ti OR cleansings:ab,ti OR regimens:ab,ti OR fasting:ab,ti OR 'laxative'/exp OR laxative:ab,ti OR laxatives:ab,ti) **AND** ('diagnostic yield':ti,ab OR 'small intestine disease'/exp/dm_di OR findings:ab,ti OR finding:ab,ti) **AND** (cochrane OR 'systematic review'/de OR 'systematic review' OR 'systematic reviews'/de OR

'systematic reviews' OR 'meta analysis'/de OR 'meta analysis' OR metanalysis OR [cochrane review]/lim OR [meta analysis]/lim OR [systematic review]/lim)

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

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 MeSH descriptor: [Cathartics] explode all trees
#4 MeSH descriptor: [Laxatives] explode all trees
#5 preparation or cleansing or regimen or laxative or fasting or Cathartics:ti,ab,kw (Word variations have been searched)
#6 #1 or #2
#7 #3 or #4 or #5
#8 diagnostic yield:ti,ab,kw (Word variations have been searched)
#9 MeSH descriptor: [Intestinal Diseases] explode all trees and with qualifier(s): [Diagnosis - DI]
#10 finding:ti,ab,kw (Word variations have been searched)
#11 #8 or #9or #10
#12 MeSH descriptor: [Intestine, Small] explode all trees
#13 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#14 #12 or #13
#15 #6 and #7 and #11 and #14 Publication Year from 2000 to 2016

Randomized controlled trials

PubMed

("Capsule Endoscopy"[Text Word] OR CE[Title/Abstract] OR capsule[Title/Abstract]) **AND** ("Intestine, Small"[Mesh] OR "small bowel"[Title/Abstract] OR "small intestine*"[Title/Abstract]) **AND** (Preparation[Text Word] OR cleansing[Text Word] OR regimen[Text Word] OR preparations[Title/Abstract] OR regiments[Title/Abstract] OR "Cathartics"[Mesh] OR fasting[Text Word] OR "Laxatives"[Mesh] OR Laxatives[Title/Abstract] OR Laxative [Title/Abstract]) **AND** ("Diagnostic yield"[Title/Abstract] OR "Intestinal Diseases/diagnosis"[Mesh] OR findings[Title/Abstract] OR finding[Title/Abstract]) **AND** ((Randomized Controlled Trial[ptyp] OR Controlled Clinical Trial[ptyp] OR randomized[Title/Abstract] OR placebo[Title/Abstract] OR "drug therapy" [Subheading] OR randomly [Title/Abstract] OR trial[Title/Abstract] OR group[Title/Abstract]) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]))

Embase

('capsule endoscopy'/exp OR capsule:ab,ti OR CE:ab,ti) **AND** ('small intestine'/exp OR 'small intestine*':ab,ti OR 'small bowel':ab,ti) **AND** ('intestine preparation'/exp OR preparation:ab,ti OR preparations:ab,ti OR 'cleaning'/exp OR cleansing:ab,ti OR regimen:ab,ti OR cleansings:ab,ti OR regimens:ab,ti OR fasting:ab,ti OR 'laxative'/exp OR laxative:ab,ti OR laxatives:ab,ti) **AND** ('diagnostic yield':ti,ab OR 'small intestine disease'/exp/dm_di OR findings:ab,ti OR finding:ab,ti) **AND** ('randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind

procedure'/exp OR 'single blind procedure'/exp OR 'controlled clinical trial'/exp OR 'clinical trial'/exp OR placebo:ab,ti OR 'double blind':ab,ti OR 'single blind':ab,ti OR assign*:ab,ti OR allocat*:ab,ti OR volunteer*:ab,ti OR random*:ab,ti OR factorial*:ab,ti OR crossover:ab,ti OR (cross:ab,ti AND over:ab,ti))

Cochrane Central Register of Controlled Trials (CENTRAL)

#1 MeSH descriptor: [Capsule Endoscopy] explode all trees
#2 capsule endoscopy or CE:ti,ab,kw (Word variations have been searched)
#3 MeSH descriptor: [Cathartics] explode all trees
#4 MeSH descriptor: [Laxatives] explode all trees
#5 preparation or cleansing or regimen or laxative or fasting or Cathartics:ti,ab,kw (Word variations have been searched)
#6 #1 or #2
#7 #3 or #4 or #5
#8 diagnostic yield:ti,ab,kw (Word variations have been searched)
#9 MeSH descriptor: [Intestinal Diseases] explode all trees and with qualifier(s): [Diagnosis - DI]
#10 finding:ti,ab,kw (Word variations have been searched)
#11 #8 or #9or #10
#12 MeSH descriptor: [Intestine, Small] explode all trees
#13 small bowel or small intestine:ti,ab,kw (Word variations have been searched)
#14 #12 or #13
#15 #6 and #7 and #11 and #14 Publication Year from 2000 to 2016

Results

Results of the bibliographic searches

After removing duplicates, 123 articles (16 reviews and 107 RCTs) were found. 5 systematic reviews and 16 RCTs (17 articles) were considered potentially relevant and acquired in full text (See flow chart).

Included studies
5 rewiews were included (Belsey 2012, Kotwal 2014, Koulaouzidis 2013, Rokkas 2009, Wu 2011). We divided the primary studies in all these reviews into four groups on the basis of the intervention examined: (a) purgatives, (b) antifoaming agents, (c) combination of purgative and antifoaming agent, and (d) prokinetics.

Systematic reviews

Overlapping of primary studies included in the reviews

	Kotwal	**Koulaouzidis**	**Belsey 2012**	**Wu 2011**	**Rokkas**

	2014	2013			2009
purgative					
Ben Soussan 2005					X
Lapalus 2006					X
Lapalus 2008	X		X		
Niv 2004					X
Niv 2005					X
Park 2011	X				
pons 2006					X
Pons Beltran 2011	X				
Van Tuyl 2007	X		X		X
Viazis 2004	X		X		
wei 2008	X			X	X
wi 2006					X
wi 2009	X		X		
antifoaming agents					
Albert 2004				X	
Ge 2006	X			X	
purgative plus antifoaming agent					
Nouda 2010	X				
spada 2010	X		X	X	
wei 2008	X			X	
prokinetics					
Almeida 2010	X	X			
Hosono 2011		X			
Iwamoto 2010		X			
Postgate 2009		X			
Selby 2005		X			
Shiotani 2011		X			
wei 2007	X	X			

Reviews inclusion process results

Belsey 2012 overlapped completely with Kotwal 2014; Wu 2011 did not overlap with Kotwal 2014 only for one study (Albert 2004) which included only 36 patients. Rokkas 2009 overlapped with Kotwal 2014 only for two studies.
For purgative preparation, we reported results of Kotwal 2014 and Rokkas 2009.
For antifoaming agents and for purgative plus antifoaming agent as preparation, we reported results of Kotwal 2014.
For prokinetics preparation we reported results of Koulaouzidis 2013 because included more studies than Kotwal 2014.

Primary studies

Among the 16 RCTs: 8 were already included in systematic reviews (Lapalus 2008 , Postgate 2009, Spada 2010, van Tuyl 2007, Viazis 2004, Wei 2007, Wei 2008, Wi 2009); 5 were conference abstracts without useful data (Hansel 2014, Nouda 2010, Rayner-Hartley 2014, Tan 2010, Tan 2011); one because not comparison of interest (Niv 2013).

So we reported results only of 2 studies (3 articles) (Maqboul 2012 Gastrointest. Endosc 2012 AB267, Maqboul 2012 Gut. A282-A283, Rosa 2013).

a. Purgative

Authors, publication year	N of studies and participants	Intervention	Control	Visualization	Diagnostic yield
Kotwal 2014	5 studies, 511 patients	PEG administered before VCE	clear liquid diet and then fasting		Peg: 46.4 % Fasting: 36.2% OR: 1.68; 95% CI: 1.16–2.42; I^2=37%
	5 studies, 503 patients	PEG administered before VCE	clear liquid diet and then fasting	adequate or excellent/good = Peg: 68.5% Fasting 48.3%, OR:3.13; 95% CI: 1.70–5.75 I^2=51%	
	3 studies, 392 patients	Na (sodium) phosphate administered before VCE	clear liquid diet and then fasting		Na (sodium) phosphate:53.8 % Fasting: 40% OR: 1.77; 95% CI: 1.18–2.64, I^2=0%
	2 studies, 270 patients	Na (sodium) phosphate administered before VCE	clear liquid diet and then fasting	adequate or excellent/good= Na (sodium) phosphate : 75.3 % Fasting 62.5%, OR: 2.06; 95% CI: 0.74–5.70, I^2=70%	
Rokkas 2009	5 studies, 476 patients	PEG (polyethylene glycol)or PS (sodium phosphate)	clear liquid diet		Peg or sodium phosphate: 122 / 263 (46.3 %) Fasting: 80/213 (37.5 %) OR = 1.813 (95% CI 1.251 – 2.628) I^2 = 39%
	7 studies, 653 patients	PEG (polyethylene glycol)or PS (sodium phosphate)	clear liquid diet	Adequate or excellent / good small bowel mucosa visualization: Peg or PS: 281 / 404 (69.5 %) clear liquid diet:	

				135 / 249 (54.2 %), OR = 2.113 (95%CI 1.252 – 3.566) I^2 = 59.58	
Rosa 2013	38 patients	Diet as control + 2 L of polyethylene glycol (PEG) the evening before the procedure(n=18)	24 h liquid diet and overnight fasting(n=20)	**Bubbles, as quality of visualization** Liquid diet =10 (50%) Peg: = 3 (15.8%) *P* = 0.026	relevant small bowel endoscopic lesions Liquid diet =12(60%) Peg = 11 (57.8%) (*P* = ns)
Maqboul 2012	51 patients	Peg: Clear fluid day before procedure. 2L PEG in afternoon of day prior to procedure. Overnight fast (n=12) Peg+Picoprep: Clear fluid day before procedure. 1L PEG and 1 sachet Picoprep in afternoon of day prior to procedure. Overnight fast. (n=20)	Group 1: Clear fluid day before procedureOvernight fast (n=19)	**Good SB views, %** Liquid diet=100 Peg= 81.2 Peg +Picoprep= 79	Liquid diet= 42.1 Peg= 41.6 Peg +Picoprep= 35 P=ns

b. Antifoaming agents

Authors, publication year	N of studies and participants	Intervention	Control	Visualization	Diagnostic yield, I vs C
Kotwal 2014	1 study, 56 patients	Simethicone	overnight fasting	simethicone showed better VQ in proximal small bowel because of fewer intraluminal bubbles (P=0.02). There was no statistically significant difference in VQ for distal small bowel among the two groups	

c. Purgative plus antifoaming agents

Authors, publication year	N of studies & participants	Intervention	Control	Visualization,	diagnostic yield,
Kotwal 2014	1 study, 58 patients	PEG+simethicone	fasting for 12 h		Peg+simethicone14/29 (48.2%) Fasting: 19/29 (65.5%), P=0.39
	3 studies, 158 patients	PEG+simethicone	fasting for 12 h	2 studies found significantly better with the use of PEG+simethicone in the proximal and distal small bowel (P<0.01). 1 study did not found significant difference	
Rosa 2013	39 patients	Clear liquid +Peg + 100 mg of simethicone 30 min prior to capsule ingestion(n=19)	a 24 h liquid diet and overnight fasting(n=20)	Bubbles, as quality of visualization Liquid diet =10 (50%) Peg+ simethicone = 5 (27.8%)	relevant small bowel endoscopic lesions Liquid diet =12(60%) Peg+ simethicone = 8(44.4%) P:ns

d. Prokinetics

Authors, publication year	N of studies and participants	Intervention	Control	visualization	diagnostic yield
Koulaouzidis 2013	7 studies, 835 patients	metoclopramide (6 studies) or mosapride (1 study)	no prokinetic		RR=1.10 (95%CI 0.96–1.27) (I^2 0%)

Quality of evidence

Diagnostic yield:
Study limitations (risk of bias): no
Inconsistency of results: no
Indirectness of evidence: no
Imprecision: no for purgative (one meta analysis including 5 RCTs with 511 patients for polyethylene glycol, one meta analysis including 3 studies with 392 patients for sodium phosphate, one meta analysis including 5 RCTs with 476 patients for sodium phosphate or polyethylene glycol, two RCTs including 89 patients); yes for Purgative plus antifoaming agents (one meta analysis including 1 RCT with 58 patients and one RCT including 39 patients); no for Prokinetics (one meta analysis including 7 RCTs with 835 patients)
Publication bias: undetected for purgative agents, suspected for prokinetics
Overall quality of evidence: overall quality of evidence was judged as high, it was judged as moderate for prokinetics because of publication bias suspected.

Visualization:
Study limitations (risk of bias): no
Inconsistency of results: yes (for purgative and purgative plus antifoaming agents)
Indirectness of evidence: no
Imprecision: no for purgative (one meta analysis including 5 studies with 503 patients for polyethylene glycol, one meta analysis including 2 studies with 270 patients for sodium phosphate, one meta analysis including 7 studies with 653 patients for sodium phosphate or polyethylene glycol, two RCTs including 89 patients); yes for Antifoaming agents (one meta analysis including 1 study with 56 patients); yes for Purgative plus antifoaming agents (one meta analysis including 3 studies with 158 patients and one RCT including 39 patients).
Publication bias: undetected
Overall quality of evidence: overall quality of evidence was judged as moderate for inconsistency or imprecision

Conclusions

Diagnostic yield:
Purgative vs fasting alone**:** diagnostic yield is significantly higher in patients who received purgative agents (**HIGH QUALIYY OF EVIDENCE**)
Antifoaming agents: the study did not assess this outcome
Purgative plus antifoaming agents: the administration of purgative plus antifoaming agents probably does not increase diagnostic yield (**MODERATE QUALITY OF EVIDENCE**)
Prokinetics: the administration of purgative plus antifoaming agents does not increase diagnostic yield (**MODERATE QUALIYY OF EVIDENCE**)

Visualization:
Purgative vs fasting alone: visualization is probably higher in patients who received purgative agents (**MODERATE QUALITY OF EVIDENCE**)
Antifoaming agents: simethicone probably increases visualization in proximal small bowel because of fewer intraluminal bubbles. There was no statistically significant difference visualization quality for distal small bowel among the two groups (**MODERATE QUALITY OF EVIDENCE**)
Purgative plus antifoaming agents: the administration of purgative plus antifoaming agents probably increases quality of visualization (**MODERATE QUALITY OF EVIDENCE**)
Prokinetics: the systematic review did not assess this outcome

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Systematic reviews

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Primary studies

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PRISMA 2009 Flow Diagram