National Institute for Health and Care Excellence

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Oesophago-gastric cancer: assessment and management in adults

Appendix H

NICE Guideline NG83 Forest plots January 2018

Final

Developed by the National Guideline Alliance, hosted by the Royal College of Obstetricians and Gynaecologists

Disclaimer

Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

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Appendix H:

H.1 Radical treatment

What are the specific information and support needs before and after treatment for adults with oesophago-gastric cancer who are suitable for radical treatment and their carers?

Not applicable to this review.

H.2 Palliative management

What are the specific information and support needs of adults with oesophago-gastric cancer who are suitable for palliative treatments and care only?

Not applicable to this review

H.3 MDT

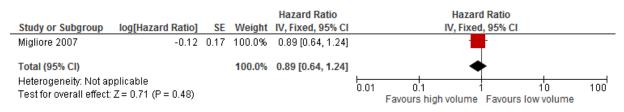
What is the most effective organisation of local and specialist MDT services for adults with oesophago-gastric cancer?

Not applicable to this review.

H.4 Surgical services

What is the optimal provision and organisation of surgical services for people with oesophago-gastric cancer?

Figure 1: Overall survival high surgeon volume vs. low surgeon volume



H.5 Staging investigations

What are the optimal staging investigations to determine suitability for curative treatment of oesophageal or gastro-oesophageal junctional cancer after diagnosis with endoscopy and whole-body CT scan?

H.5.1 Endoscopic ultrasound for gastric cancers

Figure 2: Endoscopic ultrasound to distinguish superficial (T1-2) from deeper (T3-4) stage gastric cancer

Study	тр	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Akahoshi 1991	59	0	2	13	0.97 [0.89, 1.00]	1.00 [0.75, 1.00]	-	
Ang 2006	19	7	2	29	0.90 [0.70, 0.99]	0.81 [0.64, 0.92]		
Arocena 2006	6	3	3	5	0.67 [0.30, 0.93]	0.63 [0.24, 0.91]	_	_
Barbour 2007	74	5	26	79	0.74 [0.64, 0.82]	0.94 [0.87, 0.98]		-
Bentrem 2007	85	9	48	69	0.64 [0.55, 0.72]	0.88 [0.79, 0.95]	-	
Bhandari 2004	29	1	4	14	0.88 [0.72, 0.97]	0.93 [0.68, 1.00]		
Blackshaw 2008	5	0	4	35	0.56 [0.21, 0.86]	1.00 [0.90, 1.00]	_	
Bohle 2011	22	2	18	20	0.55 [0.38, 0.71]	0.91 [0.71, 0.99]	-	
Botet 1991	11	1	1	37	0.92 [0.62, 1.00]	0.97 [0.86, 1.00]		-1
Caletti 1993	10	1	2	22	0.83 [0.52, 0.98]	0.96 [0.78, 1.00]	_ _	
Cerizzi 1991	3	0	1	17	0.75 [0.19, 0.99]	1.00 [0.80, 1.00]	_	
Chen 2002	10	3	3	41	0.77 [0.46, 0.95]	0.93 [0.81, 0.99]	_ _	-
De Manzoni 1999	11	3	7	8	0.61 [0.36, 0.83]	0.73 [0.39, 0.94]	_	
Dittler 1993	65	11	14	164	0.82 [0.72, 0.90]	0.94 [0.89, 0.97]	-	
François 1996	11	2	1	15	0.92 [0.62, 1.00]	0.88 [0.64, 0.99]		
Furukawa 2011	105	8	1	4	0.99 [0.95, 1.00]	0.33 [0.10, 0.65]		—• —
Ganpathi 2006	37	5	5	55	0.88 [0.74, 0.96]	0.92 [0.82, 0.97]		-+
Garlipp 2011	51	1	43	70	0.54 [0.44, 0.65]	0.99 [0.92, 1.00]		-
Grimm 1993	80	3	14	50	0.85 [0.76, 0.92]	0.94 [0.84, 0.99]	-	-
Habermann 2004	26	4	3	18	0.90 [0.73, 0.98]	0.82 [0.60, 0.95]		—
Heye 2009	20	3	4	0	0.64 [0.31, 0.89]	0.00 [0.00, 0.33]	_	
Hwang 2010	233	9	19	16	0.92 [0.88, 0.95]	0.64 [0.43, 0.82]		—• –
Hünerbein 1998	12	2	0	8	1.00 [0.74, 1.00]	0.80 [0.44, 0.97]		_
Hünerbein 2004	32	0	1	16	0.97 [0.84, 1.00]	1.00 [0.79, 1.00]		
Javaid 2004	29	6	3	74	0.91 [0.75, 0.98]	0.93 [0.84, 0.97]		-
Kim 2007	199	4	0	3	1.00 [0.98, 1.00]	0.43 [0.10, 0.82]		_
Kutup 2012	41	8	41	33	0.50 [0.39, 0.61]	0.80 [0.65, 0.91]		
Lee 2012	237	8	25	39	0.90 [0.86, 0.94]	0.83 [0.69, 0.92]	+	
Lok 2008	14	2	13	46	0.52 [0.32, 0.71]	0.96 [0.86, 0.99]	—	
Mancino 2000	35	10	1	33	0.97 [0.85, 1.00]	0.77 [0.61, 0.88]		
Massari 1996	24	5	2	34	0.92 [0.75, 0.99]	0.87 [0.73, 0.96]		
Murata 1988	100	3	5	38	0.95 [0.89, 0.98]	0.93 [0.80, 0.98]	-	-
Nomura 1999	18	0	2	10	0.90 [0.68, 0.99]	1.00 [0.69, 1.00]		
Park 2008	2	1	15	22	0.12 [0.01, 0.36]	0.96 [0.78, 1.00]		
Pedrazzani 2005	16	4	14	17	0.53 [0.34, 0.72]	0.81 [0.58, 0.95]		— —
Perng 1996	33	4	3	36	0.92 [0.78, 0.98]	0.90 [0.76, 0.97]		
Polkowski 2004	14	7	6	61	0.70 [0.46, 0.88]	0.90 [0.80, 0.96]		-
Potrc 2006	42	6	6	28	0.88 [0.75, 0.95]	0.82 [0.65, 0.93]		
Repiso 2010	15	3	1	17	0.94 [0.70, 1.00]	0.85 [0.62, 0.97]		
Saito 1991	56	1	4	49	0.93 [0.84, 0.98]	0.98 [0.89, 1.00]		-1
Shimizu 1994	84	2	6	36	0.93 [0.86, 0.98]	0.95 [0.82, 0.99]	-	-+
Shimoyama 2004	27	2	10	6	0.73 [0.56, 0.86]	0.75 [0.35, 0.97]		_
Tan 2007	18	5	7	33	0.72 [0.51, 0.88]	0.87 [0.72, 0.96]		
Tio 1989	30	3	1	42	0.97 [0.83, 1.00]	0.93 [0.82, 0.99]		-
Tsendsuren 2006	24	2	8	7	0.75 [0.57, 0.89]	0.78 [0.40, 0.97]		
Tseng 2000	31	0	4	39	0.89 [0.73, 0.97]	1.00 [0.91, 1.00]		
Wang 1998	50	6	8	55	0.86 [0.75, 0.94]	0.90 [0.80, 0.96]		-
Willis 2000	42	4	14	56	0.75 [0.62, 0.86]	0.93 [0.84, 0.98]		-
Xi 2003	7	1	2	22	0.78 [0.40, 0.97]	0.96 [0.78, 1.00]		
Zheng 2011	80	13	8	58	0.91 [0.83, 0.96]	0.82 [0.71, 0.90]	-	-
Ziegler 1993	50	4	4	50	0.93 [0.82, 0.98]	0.93 [0.82, 0.98]	_	
							0 0.2 0.4 0.6 0.8 1	

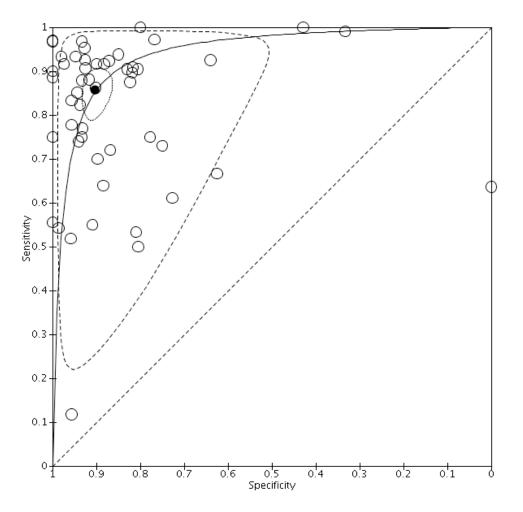


Figure 3: ROC curve for endoscopic ultrasound to distinguish superficial (T1-2) from deeper (T3-4) stage cancer

Figure 4: Endoscopic ultrasound	to distinguish T1 from	m T2 gastric cancer
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Study	ТР	FP	FN	τN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Ahn 2009	64	4	3	0	0.96 [0.87, 0.99]	0.00 [0.00, 0.60]		(00// 01/
Akahoshi 1991	37	7	3	14	0.93 [0.80, 0.98]	0.67 [0.43, 0.85]		
Akahoshi 1998	61	2	5	5	0.92 [0.83, 0.97]	0.71 [0.29, 0.96]		_
Akashi 2006	161	6	3	24	0.98 [0.95, 1.00]	0.80 [0.61, 0.92]		
Ang 2006	13	1	1	6	0.93 [0.66, 1.00]	0.86 [0.42, 1.00]		_
Barbour 2007	42	9	י 17	32	0.71 [0.58, 0.82]	0.78 [0.62, 0.89]		
Bentrem 2007	42	9 8	21	52 63		0.89 [0.79, 0.95]		-
Bhandari 2004	27	0	21	4	0.66 [0.53, 0.78]			_
Bohle 2011	3	1	12	4 24	0.93 [0.77, 0.99]	1.00 [0.40, 1.00]		
				24 7	0.20 [0.04, 0.48]	0.96 [0.80, 1.00]		
Botet 1991	4	1	0		1.00 [0.40, 1.00]	0.88 [0.47, 1.00]		
Caletti 1993	5	0	2	5	0.71 [0.29, 0.96]	1.00 [0.48, 1.00]		
Chen 2002	7	1	0	5	1.00 [0.59, 1.00]	0.83 [0.36, 1.00]		
Dittler 1993	22	1	5	51	0.81 [0.62, 0.94]	0.98 [0.90, 1.00]		
François 1996	7	0	1	4	0.88 [0.47, 1.00]	1.00 [0.40, 1.00]		
Furukawa 2011	94	0	4	8	0.96 [0.90, 0.99]	1.00 [0.63, 1.00]		
Ganpathi 2006	15	2	4	21	0.79 [0.54, 0.94]	0.91 [0.72, 0.99]		-
Garlipp 2011	11	2	16	65	0.41 [0.22, 0.61]	0.97 [0.90, 1.00]		_
Grimm 1993	28	2	10	54	0.74 [0.57, 0.87]	0.96 [0.88, 1.00]		
Heye 2009	1	1	0	9	1.00 [0.03, 1.00]	0.90 [0.55, 1.00]		`
Hwang 2010	162	21	18	51	0.90 [0.85, 0.94]	0.71 [0.59, 0.81]		
Hünerbein 1998	5	0	2	5	0.71 [0.29, 0.96]	1.00 [0.48, 1.00]		
Hünerbein 2004	14	1	4	15	0.78 [0.52, 0.94]	0.94 [0.70, 1.00]		_
Javaid 2004	7	2	1	22	0.88 [0.47, 1.00]	0.92 [0.73, 0.99]		
Kim 2007	179	10	1	9	0.99 [0.97, 1.00]	0.47 [0.24, 0.71]		
Kutup 2012	11	4	15	52	0.42 [0.23, 0.63]	0.93 [0.83, 0.98]		-
Lee 2012	155	9	37	61	0.81 [0.74, 0.86]	0.87 [0.77, 0.94]		
Lok 2008	3	0	10	14	0.23 [0.05, 0.54]	1.00 [0.77, 1.00]		
Mancino 2000	24	3	3	6	0.89 [0.71, 0.98]	0.67 [0.30, 0.93]		
Massari 1996	12	2	0	12	1.00 [0.74, 1.00]	0.86 [0.57, 0.98]		
Murata 1988	85	5	6	9	0.93 [0.86, 0.98]	0.64 [0.35, 0.87]		
Nomura 1999	16	3	0	1	1.00 [0.79, 1.00]	0.25 [0.01, 0.81]		
Pedrazzani 2005	6	1	2	21	0.75 [0.35, 0.97]	0.95 [0.77, 1.00]		
Perng 1996	14	7	8	7	0.64 [0.41, 0.83]	0.50 [0.23, 0.77]		
Polkowski 2004	4	0	5	11	0.44 [0.14, 0.79]	1.00 [0.72, 1.00]		
Potrc 2006	2	0	9	37	0.18 [0.02, 0.52]	1.00 [0.91, 1.00]	-	
Repiso 2010	5	0	5	6	0.50 [0.19, 0.81]	1.00 [0.54, 1.00]		
Saito 1991	41	2	5	12	0.89 [0.76, 0.96]	0.86 [0.57, 0.98]		
Shimizu 1994	72	1	8	9	0.90 [0.81, 0.96]	0.90 [0.55, 1.00]	-	-
Shimoyama 2004	21	1	0	15	1.00 [0.84, 1.00]	0.94 [0.70, 1.00]		
Tan 2007	7	1	1	16	0.88 [0.47, 1.00]	0.94 [0.71, 1.00]		
Tio 1989	10	1	3	17	0.77 [0.46, 0.95]	0.94 [0.73, 1.00]		
Tsendsuren 2006	10	0	2	20	0.83 [0.52, 0.98]	1.00 [0.83, 1.00]		
Tseng 2000	12	2	0	21	1.00 [0.74, 1.00]	0.91 [0.72, 0.99]		
Wang 1998	19	3	8	28	0.70 [0.50, 0.86]	0.90 [0.74, 0.98]		
Willis 2000	8	4	2	42	0.80 [0.44, 0.97]	0.91 [0.79, 0.98]		-
Zheng 2011	33	2	7	46	0.82 [0.67, 0.93]	0.96 [0.86, 0.99]		
Ziegler 1993	20	2	2	30	0.91 [0.71, 0.99]	0.94 [0.79, 0.99]		
					-	- 1	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Figure 5: ROC curve of endoscopic ultrasound to distinguish between T1 and T2 stage gastric cancer

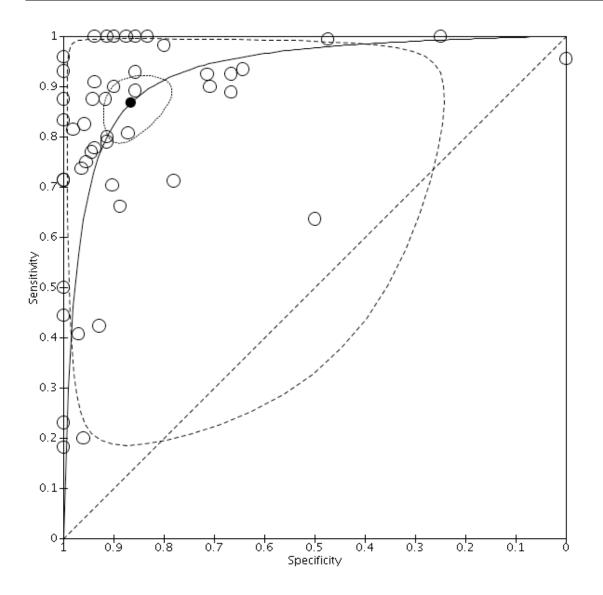


Figure 6: Endoscopic ultrasound to distinguish T1a from T1b stage gastric cancer

Study TP FP FN TN Sensitivity (95% Cl) Specificity (95% Cl) Specificity (95% Cl) Specificity (95% Cl) Specificity (95% Cl) Akahoshi 1998 40 2 13 11 0.75 [0.62, 0.86] 0.85 [0.55, 0.98] Image: the symbol of the symbol o									
Akashi 2006 125 15 4 20 0.97 [0.92, 0.99] 0.57 [0.39, 0.74] Choi 2010 487 139 147 157 0.77 [0.73, 0.80] 0.53 [0.47, 0.59] Hizawa 2002 147 24 18 31 0.89 [0.83, 0.93] 0.56 [0.42, 0.70] Hünerbein 2004 4 0 0 14 1.00 [0.40, 1.00] 1.00 [0.77, 1.00] Kim 2007 70 3 40 67 0.64 [0.54, 0.73] 0.96 [0.88, 0.99] Kim 2010 105 10 20 34 0.84 [0.76, 0.90] 0.77 [0.52, 0.89] Lee 2012 34 11 73 74 0.32 [0.23, 0.41] 0.87 [0.78, 0.93] Mitsunaga 2012 68 6 3 15 0.96 [0.88, 0.99] 0.71 [0.48, 0.83] Mouri 2009 147 13 1 30 0.99 [0.96, 1.00] 0.70 [0.54, 0.83] Murata 1988 47 7 9 28 0.84 [0.72, 0.92] 0.80 [0.63, 0.92] 4 Okada 2011 344 85 25 72 0.93 [0.90, 0.96] 0.73 [0.39, 0.94]	Study	TP	FP	FN	ΤN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Choi 2010 487 139 147 157 0.77 [0.73, 0.80] 0.53 [0.47, 0.59] Hizawa 2002 147 24 18 31 0.88 [0.83, 0.93] 0.56 [0.42, 0.70] Hünerbein 2004 4 0 0 144 1.00 [0.40, 1.00] 1.00 [0.77, 1.00] Kim 2007 70 3 40 67 0.64 [0.54, 0.73] 0.96 [0.88, 0.99] Kim 2010 105 10 20 34 0.84 [0.76, 0.90] 0.77 [0.62, 0.89] Lee 2012 34 11 73 74 0.32 [0.23, 0.41] 0.87 [0.78, 0.93] Mitsunaga 2012 68 6 3 15 0.96 [0.88, 0.99] 0.71 [0.48, 0.89] Murata 1988 47 7 9 28 0.84 [0.72, 0.92] 0.80 [0.63, 0.92] Nomura 1999 4 3 1 8 0.80 [0.28, 0.99] 0.73 [0.39, 0.94] Ohashi 1999 37 9 1 2 0.97 [0.86, 1.00] 0.18 [0.02, 0.52] Okada 2011 344 85 25 72 0.93 [0.90, 0.96] 0.46 [0.38, 0.54] <td< td=""><td>Akahoshi 1998</td><td>40</td><td>2</td><td>13</td><td>11</td><td>0.75 [0.62, 0.86]</td><td>0.85 [0.55, 0.98]</td><td></td><td></td></td<>	Akahoshi 1998	40	2	13	11	0.75 [0.62, 0.86]	0.85 [0.55, 0.98]		
Hizawa 2002 147 24 18 31 0.89 [0.83, 0.93] 0.56 [0.42, 0.70] Hünerbein 2004 4 0 0 14 1.00 [0.40, 1.00] 1.00 [0.77, 1.00] Kim 2007 70 3 40 67 0.64 [0.54, 0.73] 0.96 [0.88, 0.99] Kim 2010 105 10 20 34 0.84 [0.76, 0.90] 0.77 [0.62, 0.89] Lee 2012 34 11 73 74 0.32 [0.23, 0.41] 0.87 [0.78, 0.93] Mitsunaga 2012 68 6 3 15 0.96 [0.88, 0.99] 0.71 [0.48, 0.89] Mouri 2009 147 13 1 30 0.99 [0.96, 1.00] 0.70 [0.54, 0.83] Murata 1988 47 7 9 28 0.84 [0.72, 0.92] 0.80 [0.63, 0.92] Nomura 1999 4 3 1 8 0.80 [0.28, 0.99] 0.73 [0.39, 0.94] Ohashi 1999 37 9 1 2 0.97 [0.86, 1.00] 0.18 [0.02, 0.52] Okada 2011 344 85 25 72 0.93 [0.90, 0.96] 0.46 [0.38, 0.54] Oka	Akashi 2006	125	15	4	20	0.97 [0.92, 0.99]	0.57 [0.39, 0.74]	-	-
Hünerbein 2004 4 0 0 14 1.00 [0.40, 1.00] 1.00 [0.77, 1.00] Kim 2007 70 3 40 67 0.64 [0.54, 0.73] 0.96 [0.88, 0.99] Kim 2010 105 10 20 34 0.84 [0.76, 0.90] 0.77 [0.62, 0.89] Lee 2012 34 11 73 74 0.32 [0.23, 0.41] 0.87 [0.78, 0.93] Mitsunaga 2012 68 6 3 15 0.96 [0.88, 0.99] 0.71 [0.48, 0.89] Mouri 2009 147 13 1 30 0.99 [0.96, 1.00] 0.70 [0.54, 0.83] Murata 1988 47 7 9 28 0.84 [0.72, 0.92] 0.80 [0.63, 0.92] Nomura 1999 4 3 1 8 0.80 [0.28, 0.99] 0.73 [0.39, 0.94] Ohashi 1999 37 9 1 2 0.97 [0.86, 1.00] 0.18 [0.02, 0.52] Okada 2011 344 85 25 72 0.93 [0.90, 0.96] 0.46 [0.38, 0.54] Okamura 1999 22 2 7 10 0.76 [0.56, 0.93] 0.96 [0.78, 1.00] Shimi	Choi 2010	487	139	147	157	0.77 [0.73, 0.80]	0.53 [0.47, 0.59]		+
Kim 2007 70 3 40 67 0.64 0.54 0.73 0.96 0.88 0.99 Kim 2010 105 10 20 34 0.84 0.77 0.62, 0.89	Hizawa 2002	147	24	18	31	0.89 [0.83, 0.93]	0.56 [0.42, 0.70]	-	
Kim 2010 105 10 20 34 0.84 [0.76, 0.90] 0.77 [0.62, 0.89] Lee 2012 34 11 73 74 0.32 [0.23, 0.41] 0.87 [0.78, 0.93] Mitsunaga 2012 68 6 3 15 0.96 [0.88, 0.99] 0.71 [0.48, 0.89] Mouri 2009 147 13 1 30 0.99 [0.96, 1.00] 0.70 [0.54, 0.83] Murata 1988 47 7 9 28 0.84 [0.72, 0.92] 0.80 [0.63, 0.92] Nomura 1999 4 3 1 8 0.80 [0.28, 0.99] 0.73 [0.39, 0.94] Ohashi 1999 37 9 1 2 0.97 [0.86, 1.00] 0.18 [0.02, 0.52] Okada 2011 344 85 25 72 0.93 [0.90, 0.96] 0.46 [0.38, 0.54] Okamura 1999 22 2 7 10 0.76 [0.56, 0.93] 0.96 [0.78, 1.00] Saito 1991 18 1 5 22 0.78 [0.66, 0.99] 0.25 [0.07, 0.52] Yamamoto 2012 56 12 3 4 0.95 [0.86, 0.99] 0.25 [0.07, 0.52] Yanai 199	Hünerbein 2004	4	0	0	14	1.00 [0.40, 1.00]	1.00 [0.77, 1.00]		
Lee 2012 34 11 73 74 0.32 [0.23, 0.41] 0.87 [0.78, 0.93] Mitsunaga 2012 68 6 3 15 0.96 [0.88, 0.99] 0.71 [0.48, 0.89] Mouri 2009 147 13 1 30 0.99 [0.96, 1.00] 0.70 [0.54, 0.83] Murata 1988 47 7 9 28 0.84 [0.72, 0.92] 0.80 [0.63, 0.92] Nomura 1999 4 3 1 8 0.80 [0.28, 0.99] 0.73 [0.39, 0.94] Ohashi 1999 37 9 1 2 0.97 [0.86, 1.00] 0.18 [0.02, 0.52] Okada 2011 344 85 25 72 0.93 [0.90, 0.96] 0.46 [0.38, 0.54] Okamura 1999 22 2 7 10 0.76 [0.56, 0.90] 0.83 [0.52, 0.98] Saito 1991 18 1 5 22 0.78 [0.56, 0.93] 0.96 [0.78, 1.00] Shimizu 1994 37 2 9 32 0.80 [0.66, 0.91] 0.94 [0.80, 0.99] Yamamoto 2012 56 12 3 4 0.95 [0.86, 0.99] 0.25 [0.07, 0.52] Yanai 19	Kim 2007	70	3	40	67	0.64 [0.54, 0.73]	0.96 [0.88, 0.99]		-
Mitsunaga 2012 68 6 3 15 0.96 [0.88, 0.99] 0.71 [0.48, 0.89] Mouri 2009 147 13 1 30 0.99 [0.96, 1.00] 0.70 [0.54, 0.83] Murata 1988 47 7 9 28 0.84 [0.72, 0.92] 0.80 [0.63, 0.92] Nomura 1999 4 3 1 8 0.80 [0.28, 0.99] 0.73 [0.39, 0.94] Ohashi 1999 37 9 1 2 0.97 [0.86, 1.00] 0.18 [0.02, 0.52] Okada 2011 344 85 25 72 0.93 [0.90, 0.96] 0.46 [0.38, 0.54] Okamura 1999 22 2 7 10 0.76 [0.56, 0.90] 0.83 [0.52, 0.98] Saito 1991 18 1 5 22 0.78 [0.56, 0.93] 0.96 [0.78, 1.00] Shimizu 1994 37 2 9 32 0.80 [0.66, 0.91] 0.94 [0.80, 0.99] Yamamoto 2012 56 12 3 4 0.95 [0.86, 0.99] 0.25 [0.07, 0.52] Yanai 1997 48 4 23 21 0.68 [0.55, 0.78] 0.84 [0.64, 0.95] </td <td>Kim 2010</td> <td>105</td> <td>10</td> <td>20</td> <td>34</td> <td>0.84 [0.76, 0.90]</td> <td>0.77 [0.62, 0.89]</td> <td>+</td> <td></td>	Kim 2010	105	10	20	34	0.84 [0.76, 0.90]	0.77 [0.62, 0.89]	+	
Mouri 2009 147 13 1 30 0.99 [0.96, 1.00] 0.70 [0.54, 0.83] Murata 1988 47 7 9 28 0.84 [0.72, 0.92] 0.80 [0.63, 0.92] Nomura 1999 4 3 1 8 0.80 [0.28, 0.99] 0.73 [0.39, 0.94] Ohashi 1999 37 9 1 2 0.97 [0.86, 1.00] 0.18 [0.02, 0.52] Okada 2011 344 85 25 72 0.93 [0.90, 0.96] 0.46 [0.38, 0.54] Okamura 1999 22 2 7 10 0.76 [0.56, 0.90] 0.83 [0.52, 0.98] Saito 1991 18 1 5 22 0.78 [0.56, 0.93] 0.96 [0.78, 1.00] Shimizu 1994 37 2 9 32 0.80 [0.66, 0.91] 0.94 [0.80, 0.99] Shimoyama 2004 2 2 2 15 0.50 [0.07, 0.93] 0.88 [0.64, 0.99] Yamamoto 2012 56 12 3 4 0.95 [0.86, 0.99] 0.25 [0.07, 0.52] Yanai 1997 48 4 23 21 0.68 [0.55, 0.78] 0.84 [0.64, 0.95] Yanai 19	Lee 2012	34	11	73	74	0.32 [0.23, 0.41]	0.87 [0.78, 0.93]	-	-
Moun 2009 147 13 1 30 0.99 [0.96, 1.00] 0.70 [0.54, 0.83] Murata 1988 47 7 9 28 0.84 [0.72, 0.92] 0.80 [0.63, 0.92] Nomura 1999 4 3 1 8 0.80 [0.28, 0.99] 0.73 [0.39, 0.94] Ohashi 1999 37 9 1 2 0.97 [0.86, 1.00] 0.18 [0.02, 0.52] Okada 2011 344 85 25 72 0.93 [0.90, 0.96] 0.46 [0.38, 0.54] Okamura 1999 22 2 7 10 0.76 [0.56, 0.90] 0.83 [0.52, 0.98] Saito 1991 18 1 5 22 0.78 [0.56, 0.93] 0.96 [0.78, 1.00] Shimizu 1994 37 2 9 32 0.80 [0.66, 0.91] 0.94 [0.80, 0.99] Shimoyama 2004 2 2 15 0.50 [0.07, 0.93] 0.88 [0.64, 0.99] Yamamoto 2012 56 12 3 4 0.95 [0.86, 0.99] 0.25 [0.07, 0.52] Yanai 1997 48 4 23 21 0.68 [0.55, 0.78] 0.84 [0.64, 0.95] Yanai 1999	Mitsunaga 2012	68	6	3	15	0.96 [0.88, 0.99]	0.71 [0.48, 0.89]	-	
Nomura 1999 4 3 1 8 0.80 [0.28, 0.99] 0.73 [0.39, 0.94] Ohashi 1999 37 9 1 2 0.97 [0.86, 1.00] 0.18 [0.02, 0.52] Okada 2011 344 85 25 72 0.93 [0.90, 0.96] 0.46 [0.38, 0.54] Okamura 1999 22 2 7 10 0.76 [0.56, 0.90] 0.83 [0.52, 0.98] Saito 1991 18 1 5 22 0.78 [0.56, 0.93] 0.96 [0.78, 1.00] Shimizu 1994 37 2 9 32 0.80 [0.66, 0.91] 0.94 [0.80, 0.99] Shimoyama 2004 2 2 15 0.50 [0.07, 0.93] 0.88 [0.64, 0.99] Yamamoto 2012 56 12 3 4 0.95 [0.86, 0.99] 0.25 [0.07, 0.52] Yanai 1997 48 4 23 21 0.68 [0.55, 0.78] 0.84 [0.64, 0.95] Yanai 1999 21 12 1 15 0.95 [0.77, 1.00] 0.56 [0.35, 0.75] Yoshida 2005 246 11 17 19 0.94 [0.90, 0.96] 0.63 [0.44, 0.80]	Mouri 2009	147	13	1	30	0.99 [0.96, 1.00]	0.70 [0.54, 0.83]	-	
Ohashi 1999 37 9 1 2 0.97 [0.86, 1.00] 0.18 [0.02, 0.52] Okada 2011 344 85 25 72 0.93 [0.90, 0.96] 0.46 [0.38, 0.54] Okamura 1999 22 2 7 10 0.76 [0.56, 0.90] 0.83 [0.52, 0.98] Saito 1991 18 1 5 22 0.78 [0.56, 0.93] 0.96 [0.78, 1.00] Shimizu 1994 37 2 9 32 0.80 [0.66, 0.91] 0.94 [0.80, 0.99] Shimoyama 2004 2 2 2 15 0.50 [0.07, 0.93] 0.88 [0.64, 0.99] Yamamoto 2012 56 12 3 4 0.95 [0.86, 0.99] 0.25 [0.07, 0.52] Yanai 1997 48 4 23 21 0.68 [0.55, 0.78] 0.84 [0.64, 0.95] Yanai 1999 21 12 1 15 0.95 [0.77, 1.00] 0.56 [0.35, 0.75] Yoshida 2005 246 11 17 19 0.94 [0.90, 0.96] 0.63 [0.44, 0.80]	Murata 1988	47	7	9	28	0.84 [0.72, 0.92]	0.80 [0.63, 0.92]		
Okada 2011 344 85 25 72 0.93 [0.90, 0.96] 0.46 [0.38, 0.54] Okamura 1999 22 2 7 10 0.76 [0.56, 0.90] 0.83 [0.32, 0.98] Saito 1991 18 1 5 22 0.78 [0.56, 0.93] 0.96 [0.78, 1.00] Shimizu 1994 37 2 9 32 0.80 [0.66, 0.91] 0.94 [0.80, 0.99] Shimoyama 2004 2 2 2 15 0.50 [0.07, 0.93] 0.88 [0.64, 0.99] Yamamoto 2012 56 12 3 4 0.95 [0.86, 0.99] 0.25 [0.07, 0.52] Yanai 1997 48 4 23 21 0.68 [0.55, 0.78] 0.84 [0.64, 0.95] Yanai 1999 21 12 1 15 0.95 [0.77, 1.00] 0.56 [0.35, 0.75] Yoshida 2005 246 11 17 19 0.94 [0.90, 0.96] 0.63 [0.44, 0.80]	Nomura 1999	4	3	1	8	0.80 [0.28, 0.99]	0.73 [0.39, 0.94]		
Okada 2011 344 85 25 72 0.39 [0.90, 0.96] 0.46 [0.38, 0.34] Okamura 1999 22 2 7 10 0.76 [0.56, 0.90] 0.83 [0.52, 0.98] Saito 1991 18 1 5 22 0.78 [0.56, 0.93] 0.96 [0.78, 1.00] Shimizu 1994 37 2 9 32 0.80 [0.66, 0.91] 0.94 [0.80, 0.99] Shimoyama 2004 2 2 15 0.50 [0.07, 0.93] 0.88 [0.64, 0.99] Yamamoto 2012 56 12 3 4 0.95 [0.86, 0.99] 0.25 [0.07, 0.52] Yanai 1997 48 4 23 21 0.68 [0.55, 0.78] 0.84 [0.64, 0.95] Yanai 1999 21 12 1 15 0.95 [0.77, 1.00] 0.56 [0.35, 0.75] Yoshida 2005 246 11 17 19 0.94 [0.90, 0.96] 0.63 [0.44, 0.80]	Ohashi 1999	37	9	1	2	0.97 [0.86, 1.00]	0.18 [0.02, 0.52]		
Saito 1991 18 1 5 22 0.78 [0.56, 0.93] 0.96 [0.78, 1.00] Shimizu 1994 37 2 9 32 0.80 [0.66, 0.91] 0.94 [0.80, 0.99] Shimoyama 2004 2 2 2 15 0.50 [0.07, 0.93] 0.88 [0.64, 0.99] Yamamoto 2012 56 12 3 4 0.95 [0.86, 0.99] 0.25 [0.07, 0.52] Yanai 1997 48 4 23 21 0.68 [0.55, 0.78] 0.84 [0.64, 0.95] Yanai 1999 21 12 1 15 0.95 [0.77, 1.00] 0.56 [0.35, 0.75] Yoshida 2005 246 11 17 19 0.94 [0.90, 0.96] 0.63 [0.44, 0.80]	Okada 2011	344	85	25	72	0.93 [0.90, 0.96]	0.46 [0.38, 0.54]		
Shimizu 1994 37 2 9 32 0.80 [0.66, 0.91] 0.94 [0.80, 0.99] Shimiyama 2004 2 2 2 15 0.50 [0.07, 0.93] 0.88 [0.64, 0.99] Yamamoto 2012 56 12 3 4 0.95 [0.86, 0.99] 0.25 [0.07, 0.52] Yanai 1997 48 4 23 21 0.68 [0.55, 0.78] 0.84 [0.64, 0.95] Yanai 1999 21 12 1 15 0.95 [0.77, 1.00] 0.56 [0.35, 0.75] Yoshida 2005 246 11 17 19 0.94 [0.90, 0.96] 0.63 [0.44, 0.80]	Okamura 1999	22	2	7	10	0.76 [0.56, 0.90]	0.83 [0.52, 0.98]		
Shimoyama 2004 2 2 2 15 0.50 [0.07, 0.93] 0.88 [0.64, 0.99] Yamamoto 2012 56 12 3 4 0.95 [0.86, 0.99] 0.25 [0.07, 0.52] Yanai 1997 48 4 23 21 0.68 [0.55, 0.78] 0.84 [0.64, 0.95] Yanai 1999 21 12 1 15 0.95 [0.77, 1.00] 0.56 [0.35, 0.75] Yoshida 2005 246 11 17 19 0.94 [0.90, 0.96] 0.63 [0.44, 0.80]	Saito 1991	18	1	5	22	0.78 [0.56, 0.93]	0.96 [0.78, 1.00]		
Yamamoto 2012 56 12 3 4 0.95 [0.86, 0.99] 0.25 [0.07, 0.52] Yanai 1997 48 4 23 21 0.68 [0.55, 0.78] 0.84 [0.64, 0.95] Yanai 1999 21 12 1 15 0.95 [0.77, 1.00] 0.56 [0.35, 0.75] Yoshida 2005 246 11 17 19 0.94 [0.90, 0.96] 0.63 [0.44, 0.80]	Shimizu 1994	37	2	9	32	0.80 [0.66, 0.91]	0.94 [0.80, 0.99]		
Yanai 1997 48 4 23 21 0.68 [0.55, 0.78] 0.84 [0.64, 0.95] Yanai 1999 21 12 1 15 0.95 [0.77, 1.00] 0.56 [0.35, 0.75] Yoshida 2005 246 11 17 19 0.94 [0.90, 0.96] 0.63 [0.44, 0.80] ++++++++++++++++++++++++++++++++++++	Shimoyama 2004	2	2	2	15	0.50 [0.07, 0.93]	0.88 [0.64, 0.99]		
Yanai 1999 21 12 1 15 0.95 [0.77, 1.00] 0.56 [0.35, 0.75]	Yamamoto 2012	56	12	3	4	0.95 [0.86, 0.99]	0.25 [0.07, 0.52]	-	
Yoshida 2005 246 11 17 19 0.94 [0.90, 0.96] 0.63 [0.44, 0.80]	Yanai 1997	48	4	23	21	0.68 [0.55, 0.78]	0.84 [0.64, 0.95]		
	Yanai 1999	21	12	1	15	0.95 [0.77, 1.00]	0.56 [0.35, 0.75]		
	Yoshida 2005	246	11	17	19	0.94 [0.90, 0.96]	0.63 [0.44, 0.80]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Figure 7: ROC curve of endoscopic ultrasound to distinguish between T1a and T1b stage gastric cancer

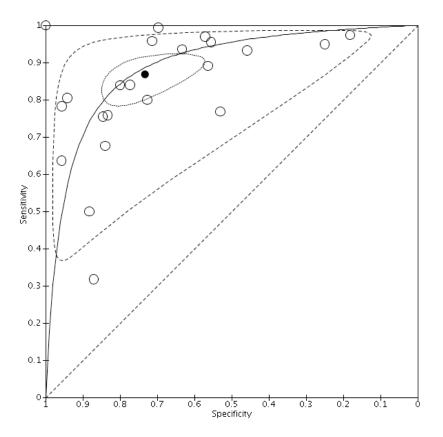


Figure 8: Endoscopic ultrasound to detect nodal metastasis of gastric cancer

Study	тр	FP	FN	ΤN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Ahn 2009	63	5	2	1	0.97 [0.89, 1.00]	0.17 [0.00, 0.64]	-	-
Akahoshi 1998	36	5	4	1	0.90 [0.76, 0.97]	0.17 [0.00, 0.64]	-+	
Ang 2006	20	12	6	19	0.77 [0.56, 0.91]	0.61 [0.42, 0.78]		
Arocena 2006	4	3	2	8	0.67 [0.22, 0.96]	0.73 [0.39, 0.94]	_	
Barbour 2007	85	25	27	69	0.76 [0.67, 0.83]	0.73 [0.63, 0.82]		
Bentrem 2007	71	27	37	83	0.66 [0.56, 0.75]	0.75 [0.66, 0.83]		
Bhandari 2004	27	6	1	14	0.96 [0.82, 1.00]	0.70 [0.46, 0.88]		—
Blackshaw 2008	9	4	1	30	0.90 [0.55, 1.00]	0.88 [0.73, 0.97]		
Bohle 2011	18	9	5	30	0.78 [0.56, 0.93]	0.77 [0.61, 0.89]		
Botet 1991	10	8	1	31	0.91 [0.59, 1.00]	0.79 [0.64, 0.91]		
Caletti 1993	5	11	2	14	0.71 [0.29, 0.96]	0.56 [0.35, 0.76]		
Cerizzi 1991	2	3	3	13	0.40 [0.05, 0.85]	0.81 [0.54, 0.96]		
Chen 2002	12	9	3	33	0.80 [0.52, 0.96]	0.79 [0.63, 0.90]		
De Manzoni 1999	5	8	0	16	1.00 [0.48, 1.00]	0.67 [0.45, 0.84]		
Dittler 1993	66	53	5	130	0.93 [0.84, 0.98]	0.71 [0.64, 0.77]	-	-
François 1996	10	3	0	16	1.00 [0.69, 1.00]	0.84 [0.60, 0.97]		
Ganpathi 2006	26	11	9	53	0.74 [0.57, 0.88]	0.83 [0.71, 0.91]		
Grimm 1993	49	16	9	74	0.84 [0.73, 0.93]	0.82 [0.73, 0.89]		
Habermann 2004	19	1	0	30	1.00 [0.82, 1.00]	0.97 [0.83, 1.00]		
Hamada 1997	90	17	12	30	0.88 [0.80, 0.94]	0.64 [0.49, 0.77]	-	
Hwang 2010	158	67	6	16	0.96 [0.92, 0.99]	0.19 [0.11, 0.29]	•	-
Hünerbein 1998	8	3	1	8	0.89 [0.52, 1.00]	0.73 [0.39, 0.94]		
Javaid 2004	28	46	4	34	0.88 [0.71, 0.96]	0.42 [0.32, 0.54]		
Kutup 2012	24	17	18	64	0.57 [0.41, 0.72]	0.79 [0.69, 0.87]		
Lee 2012	50	23	46	190	0.52 [0.42, 0.62]	0.89 [0.84, 0.93]		_ *
Lok 2008	22	15	4	34	0.85 [0.65, 0.96]	0.69 [0.55, 0.82]		
Mancino 2000	29	19	4	25	0.88 [0.72, 0.97]	0.57 [0.41, 0.72]		
Massari 1996	7	13	5	0	0.58 [0.28, 0.85]	0.00 [0.00, 0.25]		- <u>.</u>
Nakamura 1999a	15	8	3	5	0.83 [0.59, 0.96]	0.38 [0.14, 0.68]		
Park 2008	5	10	2	21	0.71 [0.29, 0.96]	0.68 [0.49, 0.83]		
Pedrazzani 2005	10	12	4	25	0.71 [0.42, 0.92]	0.68 [0.50, 0.82]		
Perng 1996	24	12	8	25	0.75 [0.57, 0.89]	0.68 [0.50, 0.82]		
Polkowski 2004	9	15	5	31	0.64 [0.35, 0.87]	0.67 [0.52, 0.80]		
Potrc 2006	21	32	3	26	0.88 [0.68, 0.97]	0.45 [0.32, 0.58]		
Repiso 2010	11	8	2	15	0.85 [0.55, 0.98]	0.65 [0.43, 0.84]		
Shimoyama 2004	22	6	3	14	0.88 [0.69, 0.97]	0.70 [0.46, 0.88]		
Tan 2007	20	12	5	26	0.80 [0.59, 0.93]	0.68 [0.51, 0.82]		
Tio 1989	14	7	16	43	0.47 [0.28, 0.66]	0.86 [0.73, 0.94]		
Tsendsuren 2006	17	14	0	10	1.00 [0.80, 1.00]	0.42 [0.22, 0.63]		
Tseng 2000	30	10 17	5 12	29 57	0.86 [0.70, 0.95]	0.74 [0.58, 0.87]		
Wang 1998	33	17			0.73 [0.58, 0.85]	0.77 [0.66, 0.86]		
Willis 2000 Xi 2003	52 14	17 6	10 5	37 7	0.84 [0.72, 0.92]	0.69 [0.54, 0.80]		
Zheng 2011	14 45	ь 49	5 20	7 48	0.74 [0.49, 0.91] 0.69 [0.57, 0.80]	0.54 [0.25, 0.81] 0.49 [0.39, 0.60]		-
Ziegler 1993	45 44	49 18	20	40 40	0.88 [0.76, 0.95]	0.49 [0.55, 0.80]		. . .
2109101 1993		10	0	40	0.00 [0.70, 0.95]		0 0.2 0.4 0.6 0.8 1	
							5 5.2 0. 4 0.0 0.0 1	0 0.2 0.7 0.0 0.0 1

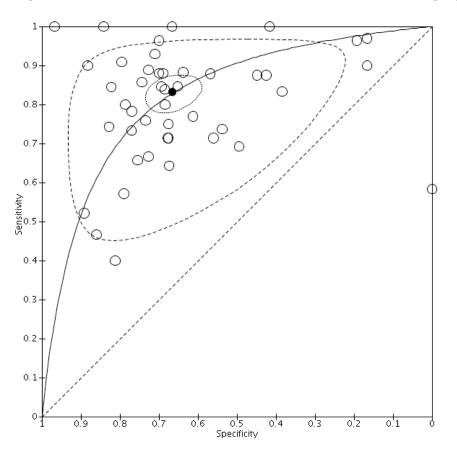


Figure 9: ROC curve of endoscopic ultrasound for nodal staging of gastric cancers

H.5.2 Endoscopic ultrasound in oesophageal cancers

Figure 10: Endoscopic ultrasound to detect T1 disease in oesophageal cancer

Study	TP	FP	FΝ	ΤN	Sensitivity (95% CI)	Specificity (95% CI) Sensitivity (95% CI)Specificity (95% CI)
Catalano(End)	6	2	12	80	0.33 [0.13, 0.59]	0.98 [0.91, 1.00]
Catalan o (Eva)	18	2	3	122	0.86 [0.64, 0.97]	0.98 [0.94, 1.00]
Choi	39	1	10	59	0.80 [0.66, 0.90]	0.98 [0.91, 1.00]
Gheorghe	2	0	1	38	0.67 [0.09, 0.99]	1.00 [0.91, 1.00]
Grimm	9	36	1	17	0.90 [0.55, 1.00]	0.32 [0.20, 0.46]
Heintz	2	0	2	18	0.50 [0.07, 0.93]	1.00 [0.81, 1.00]
Hunerbein.C	9	1	- 7	80	0.56 [0.30, 0.80]	0.99 [0.93, 1.00]
Hunerbein.M	0	2	2	15	0.00 [0.00, 0.84]	0.88 [0.64, 0.99]
Kienle	12	1	- 7	97	0.63 [0.38, 0.84]	0.99 [0.94, 1.00]
Lee	8	1	1	5	0.89 [0.52, 1.00]	0.83 [0.36, 1.00]
Lok	0	0	2	57	0.00 [0.00, 0.84]	1.00 [0.94, 1.00]
Massari	3	0	1	36	0.75 [0.19, 0.99]	1.00 [0.90, 1.00]
Nesje	2	1	2	48	0.50 [0.07, 0.93]	0.98 [0.89, 1.00]
Nishimaki	48	7	12	108	0.80 [0.68, 0.89]	0.94 [0.88, 0.98]
Pech	81	7	18	73	0.82 [0.73, 0.89]	0.91 [0.83, 0.96]
Pham	4	З	1	20	0.80 [0.28, 0.99]	0.87 [0.66, 0.97]
Sandha	4	0	1	10	0.80 [0.28, 0.99]	1.00 [0.69, 1.00]
Shin	162	12	40	26	0.80 [0.74, 0.85]	0.68 [0.51, 0.82]
Tio(End)	10	1	2	91	0.83 [0.52, 0.98]	0.99 [0.94, 1.00]
Tio(Endo)	7	1	1	57	0.88 [0.47, 1.00]	0.98 [0.91, 1.00]
Tio(Eso)	9	1	2	71	0.82 [0.48, 0.98]	0.99 [0.93, 1.00]
Vazquez	1	2	1	33	0.50 [0.01, 0.99]	0.94 [0.81, 0.99]
Vickers I	1	0	0	49	1.00 [0.03, 1.00]	1.00 [0.93, 1.00]
Wu	4	3	ō	77	1.00 [0.40, 1.00]	0.96 [0.89, 0.99]
Yen	12	2	2	11	0.86 [0.57, 0.98]	0.85 [0.55, 0.98]
Ziegler		ō	1	32	0.80 [0.28, 0.99]	
		-	-			0 0.2 0.4 0.6 0.8 1 0 0.2 0.4 0.6 0.8 1

Figure 11: ROC curve of endoscopic ultrasound for detection of T1 disease in oesophageal cancer

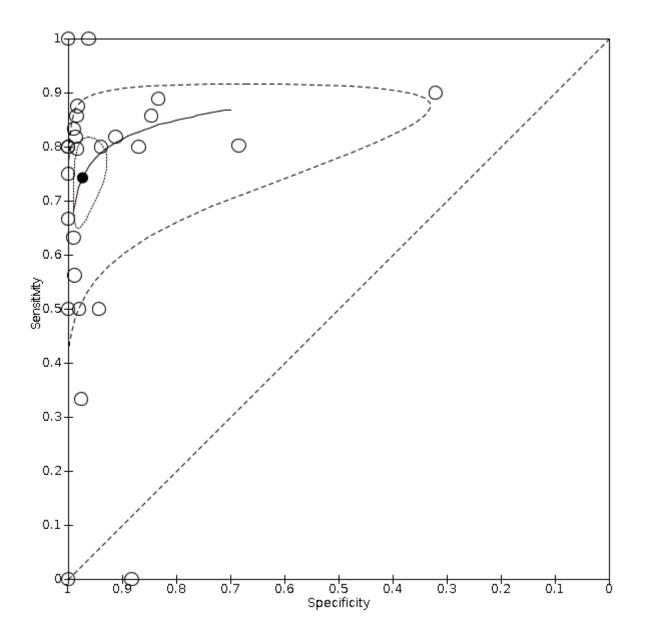
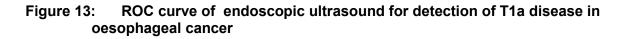
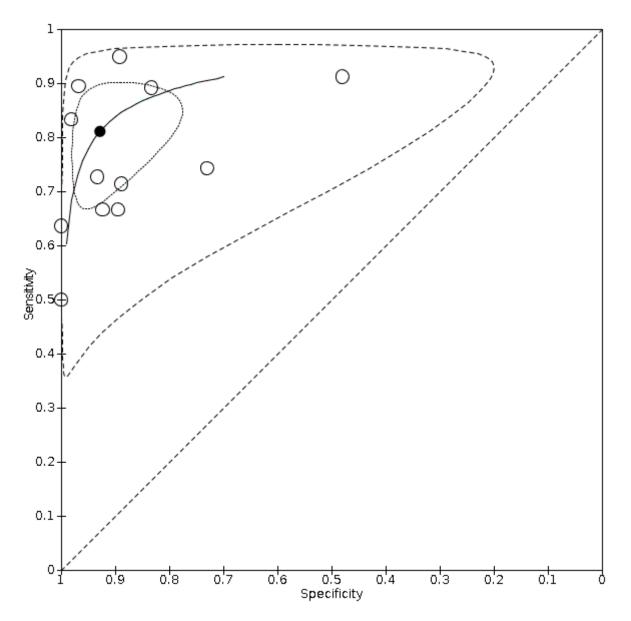
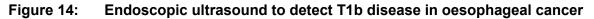


Figure 12: Endoscopic ultrasound to detect T1a disease in oesophageal cancer

Study	ΤР	FP	FN	ΤN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)Specificity (95% CI)
Goda	74	3	9	15	0.89 [0.80, 0.95]	0.83 [0.59, 0.96]	
Hasegawa	5	2	2	16	0.71 [0.29, 0.96]	0.89 [0.65, 0.99]	_
He	26	10	9	27	0.74 [0.57, 0.88]	0.73 [0.56, 0.86]	
Kawano	56	4	3	33	0.95 [0.86, 0.99]	0.89 [0.75, 0.97]	
May	62	13	6	12	0.91 [0.82, 0.97]	0.48 [0.28, 0.69]	
Murata	10	З	2	158	0.83 [0.52, 0.98]	0.98 [0.95, 1.00]	
Murata. Y	- 7	0	- 4	42	0.64 [0.31, 0.89]	1.00 [0.92, 1.00]	
Shinkai	17	З	2	91	0.89 [0.67, 0.99]	0.97 [0.91, 0.99]	
Takemoto	2	1	1	12	0.67 [0.09, 0.99]	0.92 [0.64, 1.00]	- _
Toh	8	1	3	14	0.73 [0.39, 0.94]	0.93 [0.68, 1.00]	_
Yanai. H	6	0	6	5	0.50 [0.21, 0.79]	1.00 [0.48, 1.00]	_
Y o shikane	6	2	3	17	0.67 [0.30, 0.93]	0.89 [0.67, 0.99]	
							0 0.2 0.4 0.0 0.8 1 0 0.2 0.4 0.0 0.8 1







Study	ТР	FP	FN	ΤN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)Specificity (95% CI)
Goda	15	9	3	74	0.83 [0.59, 0.96]	0.89 [0.80, 0.95]	
Hasegawa	14	2	4	5	0.78 [0.52, 0.94]	0.71 [0.29, 0.96]	_ --
He	27	9	10	26	0.73 [0.56, 0.86]	0.74 [0.57, 0.88]	
Kawano	33	3	4	56	0.89 [0.75, 0.97]	0.95 [0.86, 0.99]	
Мау	12	6	13	62	0.48 [0.28, 0.69]	0.91 [0.82, 0.97]	
Murata	38	4	- 7	124	0.84 [0.71, 0.94]	0.97 [0.92, 0.99]	
Murata. Y	20	29	4	0	0.83 [0.63, 0.95]	0.00 [0.00, 0.12]	
Shinkai	26	4	8	75	0.76 [0.59, 0.89]	0.95 [0.88, 0.99]	
Takemoto	5	1	3	7	0.63 [0.24, 0.91]	0.88 [0.47, 1.00]	
Toh	12	4	1	9	0.92 [0.64, 1.00]	0.69 [0.39, 0.91]	++
Yanai. H	5	6	0	6	1.00 [0.48, 1.00]	0.50 [0.21, 0.79]	
Yoshikane	15	3	4	6	0.79 [0.54, 0.94]	0.67 [0.30, 0.93]	

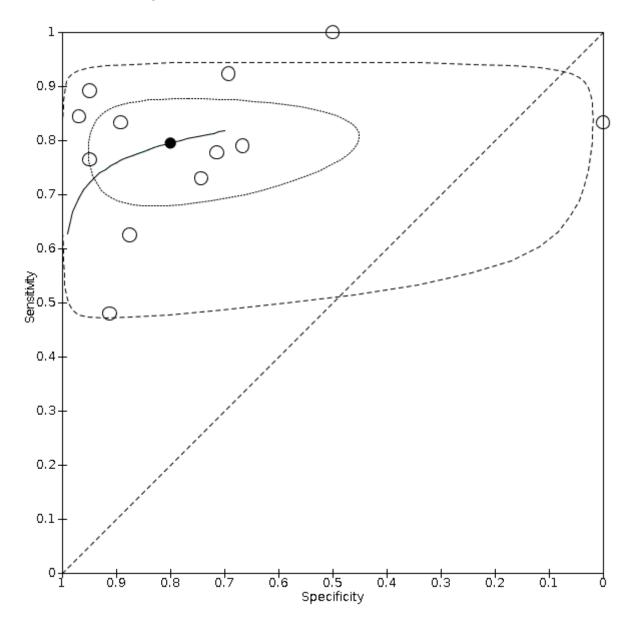
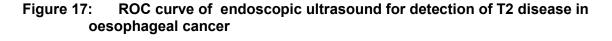


Figure 15: ROC curve of endoscopic ultrasound for detection of T1b disease in oesophageal cancer

Figure 16: Endoscopic ultrasound to detect T2 disease in oesophageal cancer

Study	тр	FP	ΕN	ты	Sensitivity (95% CI)	Specificity (95% CI) Sensitivity (95% CI)Specificity (95% CI)
Binmoeller	8	1	2	27	0.80 [0.44, 0.97]	0.96 [0.82, 1.00]
Catalano(End)	12	17	4	67	0.75 [0.48, 0.93]	0.80 [0.70, 0.88]
Catalano(Eva)	43	4	8	90	0.84 [0.71, 0.93]	
Choi		17	7	77	0.53 [0.27, 0.79]	0.82 [0.73, 0.89]
Gheorahe	6	Ó	í	34	0.86 [0.42, 1.00]	
Grimm	13	ž	2	45	0.87 [0.60, 0.98]	0.94 [0.83, 0.99]
Heintz	4	1	1	16	0.80 [0.28, 0.99]	0.94 [0.03, 0.99]
Hunerbein.C	20	7	6	64	0.77 [0.56, 0.91]	0.90 [0.81, 0.96]
Hunerbein.M	20	2	ĭ	14	0.67 [0.09, 0.99]	
Kienle	17	21	16	63	0.52 [0.34, 0.69]	0.75 [0.64, 0.84]
Kutup	27	28	39	130	0.41 [0.29, 0.54]	0.82 [0.75, 0.88]
Lee	1	1	1	12	0.50 [0.01, 0.99]	
Lok	4	6	8	41	0.33 [0.10, 0.65]	0.87 [0.74, 0.95]
Massari	9	ĩ	2	28	0.82 [0.48, 0.98]	0.97 [0.82, 1.00]
Murata	24	6	7		0.77 [0.59, 0.90]	0.96 [0.91, 0.98]
Nesje	- 3	4	4	42	0.43 [0.10, 0.82]	
Nishimaki	11	6	9	149	0.55 [0.32, 0.77]	0.96 [0.92, 0.99]
Pech	13	22	17	127	0.43 [0.25, 0.63]	0.85 [0.79, 0.91]
Pham	2	3	4	19	0.33 [0.04, 0.78]	0.86 [0.65, 0.97]
Sandha	3	1	2	- 9	0.60 [0.15, 0.95]	
Shin	15	51	3	171	0.83 [0.59, 0.96]	0.77 [0.71, 0.82]
Shinkai	10	4	8	91	0.56 [0.31, 0.78]	0.96 [0.90, 0.99]
Takemoto	ĩ	3	ŏ	8	1.00 [0.03, 1.00]	0.73 [0.39, 0.94]
Tekola	5	30	1	2	0.83 [0.36, 1.00]	
Tio(End)	8	3	5	88	0.62 [0.32, 0.86]	0.97 [0.91, 0.99]
Tio(Endo)	6	15	3	42	0.67 [0.30, 0.93]	0.74 [0.60, 0.84]
Tio(Eso)	11	2	2	68	0.85 [0.55, 0.98]	0.97 [0.90, 1.00]
Toh	1	1	2	22	0.33 [0.01, 0.91]	0.96 [0.78, 1.00]
Vazquez	8	ī	2	26	0.80 [0.44, 0.97]	0.96 [0.81, 1.00]
Vickers	8	ī	2	39	0.80 [0.44, 0.97]	0.97 [0.87, 1.00]
Wu	5	3	2	74	0.71 [0.29, 0.96]	0.96 [0.89, 0.99]
Yen	5	2	2	18	0.71 [0.29, 0.96]	0.90 [0.68, 0.99]
Ziegler	3	ĩ	ĩ	32	0.75 [0.19, 0.99]	0.97 [0.84, 1.00]
	2	-	-		2	0 0.2 0.4 0.6 0.8 1 0 0.2 0.4 0.6 0.8 1



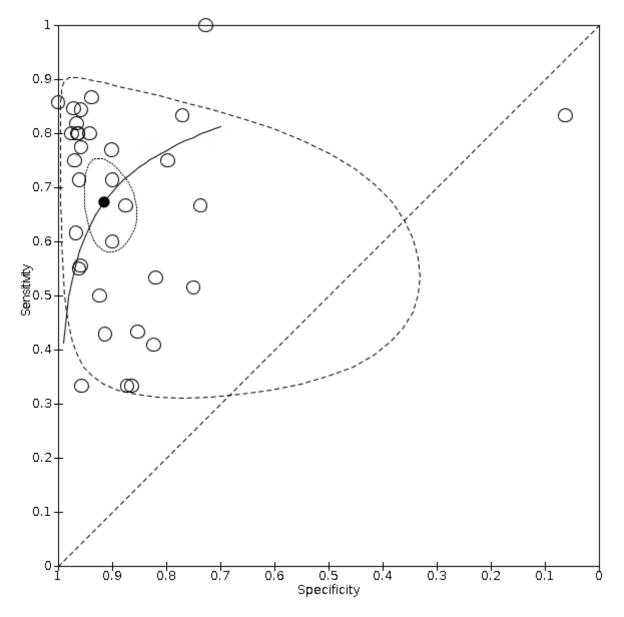


Figure 18: Endoscopic ultrasound to detect T3 disease in oesophageal cancer

						- 10 1. (
Study	ΤР	FP	FN	ΤN			Sensitivity (95% CI)Specificity (95% CI)
Binmoeller	19	3	1	15	0.95 [0.75, 1.00]	0.83 [0.59, 0.96]	
Catalano(End)	47	4	10	39	0.82 [0.70, 0.91]	0.91 [0.78, 0.97]	
Catalano(Eva)	61	8	4	72	0.94 [0.85, 0.98]	0.90 [0.81, 0.96]	
Choi	32	13	9	55	0.78 [0.62, 0.89]	0.81 [0.70, 0.89]	
Gheorghe	9	13	2	17	0.82 [0.48, 0.98]	0.57 [0.37, 0.75]	_
Grimm	26	2	5	31	0.84 [0.66, 0.95]	0.94 [0.80, 0.99]	
Heintz	9	1	2	10	0.82 [0.48, 0.98]	0.91 [0.59, 1.00]	
Hunerbein.C	47	8	4	38	0.92 [0.81, 0.98]	0.83 [0.69, 0.92]	-+ -+
Hunerbein.M	9	1	0	9	1.00 [0.66, 1.00]	0.90 [0.55, 1.00]	——————————————————————————————————————
Kienle	42	16	12	47	0.78 [0.64, 0.88]	0.75 [0.62, 0.85]	
Lok	37	11	4	7	0.90 [0.77, 0.97]	0.39 [0.17, 0.64]	
Massari	14	2	1	23	0.93 [0.68, 1.00]	0.92 [0.74, 0.99]	
Murata	74	5	4	90	0.95 [0.87, 0.99]	0.95 (0.88, 0.98)	
Nesie	28	4	4	17	0.88 [0.71, 0.96]	0.81 (0.58, 0.95)	—
Nishimaki	66	5	18	86	0.79 [0.68, 0.87]	0.95 [0.88, 0.98]	
Pech	38	18	8	115	0.83 [0.69, 0.92]	0.86 [0.79, 0.92]	
Pham	4	4	2	18	0.67 [0.22, 0.96]	0.82 [0.60, 0.95]	_
Sandha	6	1	1	7	0.86 [0.42, 1.00]	0.88 [0.47, 1.00]	_
Takemoto	2	0	1	9	0.67 [0.09, 0.99]	1.00 [0.66, 1.00]	
Tio(End)	40	5	8	51	0.83 [0.70, 0.93]	0.91 [0.80, 0.97]	
Tio(Endo)	25	2	2	37	0.93 [0.76, 0.99]	0.95 [0.83, 0.99]	
Tio(Eso)	32	4	2	45	0.94 [0.80, 0.99]	0.92 [0.80, 0.98]	-+ -+
Vazquez	22	3	3	9	0.88 [0.69, 0.97]	0.75 [0.43, 0.95]	
Vickers	37	3	1	9	0.97 [0.86, 1.00]	0.75 [0.43, 0.95]	_
Vickers & D	10	-	ī	29	0.91 [0.59, 1.00]	0.74 [0.58, 0.87]	
Wu	8	11	1	29 65	0.89 [0.52, 1.00]	0.86 [0.76, 0.93]	
	7	1	1	28	0.89 [0.32, 1.00]	0.97 [0.82, 1.00]	
Ziegler		T	T	20	0.00 [0.47, 1.00]	0.87 [0.82, 1.00]	0 0.2 0.4 0.6 0.8 1 0 0.2 0.4 0.6 0.8 1
							0 0.2 0.4 0.6 0.8 1 0 0.2 0.4 0.6 0.8 1

Figure 19: ROC curve of endoscopic ultrasound for detection of T3 disease in oesophageal cancer

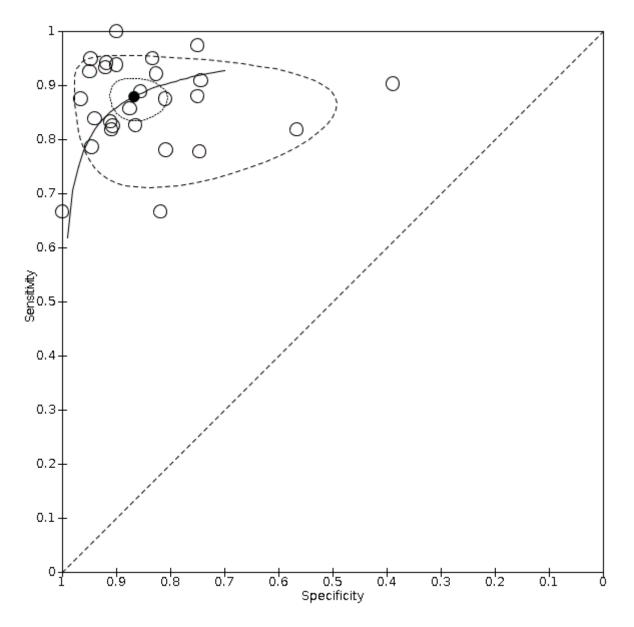
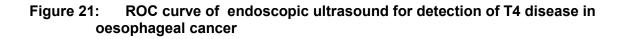


Figure 20: Endoscopic ultrasound to detect T4 disease in oesophageal cancer

Study	тр	FP	FN	ты	Sonsitivity (05% CI)	Specificity (95% CI) Sensitivity (95% CI)Specificity (95% CI)
		FP				
Binmoeller	7	1	1	29	0.88 [0.47, 1.00]	0.97 [0.83, 1.00]
Catalano(End)	8	4	1	87	0.89 [0.52, 1.00]	0.96 [0.89, 0.99]
Catalano(Eva)	7	1	1	136	0.88 [0.47, 1.00]	0.99 [0.96, 1.00]
Gheorghe	1	9	1	30	0.50 [0.01, 0.99]	0.77 [0.61, 0.89]
Grimm	- 7	3	1	52	0.88 [0.47, 1.00]	0.95 [0.85, 0.99]
Heintz	2	0	0	20	1.00 [0.16, 1.00]	1.00 [0.83, 1.00] —
Hunerbein.C	3	2	1	91	0.75 [0.19, 0.99]	0.98 [0.92, 1.00]
Hunerbein.M	5	0	0	14	1.00 [0.48, 1.00]	1.00 [0.77, 1.00]
Kienle	1	0	1	115	0.50 [0.01, 0.99]	1.00 [0.97, 1.00]
Lok	1	1	3	54	0.25 [0.01, 0.81]	0.98 [0.90, 1.00]
Massari	9	1	1	29	0.90 [0.55, 1.00]	0.97 [0.83, 1.00]
Murata	7	2	0	164	1.00 [0.59, 1.00]	0.99 [0.96, 1.00]
Nesje	5	1	5	42	0.50 [0.19, 0.81]	0.98 [0.88, 1.00]
Nishimaki	3	5	8	159	0.27 [0.06, 0.61]	0.97 [0.93, 0.99]
Pham	4	3	2	19	0.67 [0.22, 0.96]	0.86 [0.65, 0.97]
Sandha	2	1	1	11	0.67 [0.09, 0.99]	0.92 [0.62, 1.00]
Shinkai	41	9	1	62	0.98 [0.87, 1.00]	0.87 [0.77, 0.94] -
Tio(End)	26	3	5	70	0.84 [0.66, 0.95]	0.96 [0.88, 0.99]
Tio(Endo)	20	1	2	43	0.91 [0.71, 0.99]	0.98 [0.88, 1.00]
Tio(Eso)	23	1	2	57	0.92 [0.74, 0.99]	0.98 [0.91, 1.00]
Vickers I	1	ō	ō	49	1.00 [0.03, 1.00]	1.00 [0.93, 1.00]
Wu	9	1	2	72	0.82 [0.48, 0.98]	0.99 [0.93, 1.00]
Ziegler	19	ī	ĩ	16	0.95 [0.75, 1.00]	0.94 [0.71, 1.00]
Liegioi	10	1	1	10	0.00 [0.70, 1.00]	0.02 0.4 0.6 0.8 1 0 0.2 0.4 0.6 0.8 1



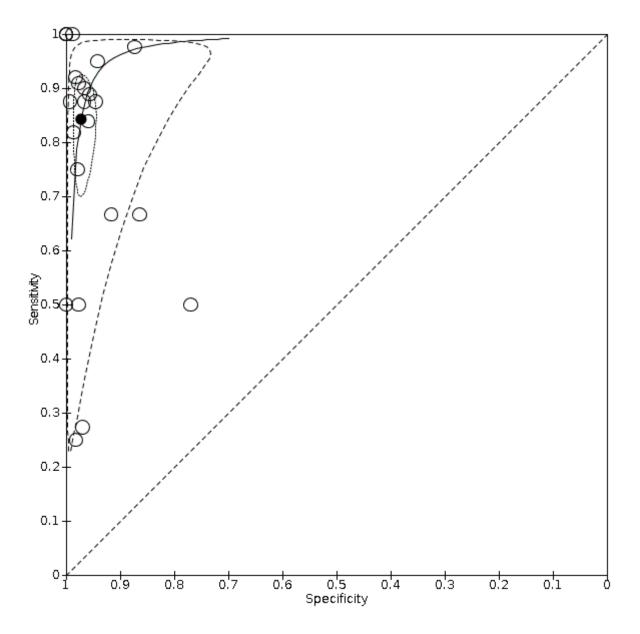
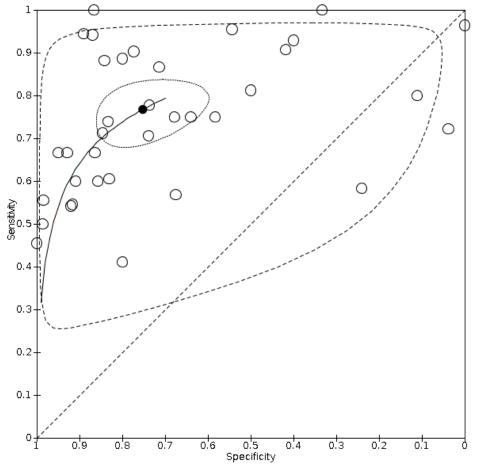


Figure 22: Endoscopic ultrasound to detect N0 (absence of nodal metastasis) in oesophageal cancer

Study	TP	FP	FN	ΤN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)Specificity (95% CI)
Catalano(End)	34	- 7	2	57	0.94 [0.81, 0.99]	0.89 [0.79, 0.95]	-+ -+
Catalano(Eva)	31	22	4	88	0.89 [0.73, 0.97]	0.80 [0.71, 0.87]	
Choi	49	32	5	23	0.91 [0.80, 0.97]	0.42 [0.29, 0.56]	
Gheorghe	6	1	5	11	0.55 [0.23, 0.83]	0.92 [0.62, 1.00]	_ _
Grimm	37	5	4	17	0.90 [0.77, 0.97]	0.77 [0.55, 0.92]	- + - + -
Heintz	4	2	0	13	1.00 [0.40, 1.00]	0.87 [0.60, 0.98]	
Hunerbein.M	2	1	1	13	0.67 [0.09, 0.99]	0.93 [0.66, 1.00]	-
Kienle	37	10	15	55	0.71 [0.57, 0.83]	0.85 [0.74, 0.92]	
Lee	13	3	1	2	0.93 [0.66, 1.00]	0.40 [0.05, 0.85]	
Lok	17	6	6	30	0.74 [0.52, 0.90]	0.83 [0.67, 0.94]	
Lowe	10	6	5	38	0.67 [0.38, 0.88]	0.86 [0.73, 0.95]	
Massari	16	З	1	20	0.94 [0.71, 1.00]	0.87 [0.66, 0.97]	
Menningen	23	10	15	49	0.61 [0.43, 0.76]	0.83 [0.71, 0.92]	
Murata	900	29	121	154	0.88 [0.86, 0.90]	0.84 [0.78, 0.89]	• •
Natsugoe	26	2	4	5	0.87 [0.69, 0.96]	0.71 [0.29, 0.96]	_
Nesje	21	21	1	25	0.95 [0.77, 1.00]	0.54 [0.39, 0.69]	
Nishimaki	23	22	33	88	0.41 [0.28, 0.55]	0.80 [0.71, 0.87]	
Pech	48	29	20	82	0.71 [0.58, 0.81]	0.74 [0.65, 0.82]	-##-
Pham	7	5	2	14	0.78 [0.40, 0.97]	0.74 [0.49, 0.91]	_
Salminen	8	1	4	19	0.67 [0.35, 0.90]	0.95 [0.75, 1.00]	
Sandha	3	1	2	10	0.60 [0.15, 0.95]	0.91 [0.59, 1.00]	_
Shin	135	51	52	2	0.72 [0.65, 0.78]	0.04 [0.00, 0.13]	
Shinkai	28	41	20	13	0.58 [0.43, 0.72]	0.24 [0.13, 0.38]	
Staiger	13	9	3	9	0.81 [0.54, 0.96]	0.50 [0.26, 0.74]	_
Takizawa	25	25	19	52	0.57 [0.41, 0.72]	0.68 [0.56, 0.78]	
Tekola	27	10	1	0	0.96 [0.82, 1.00]	0.00 [0.00, 0.31]	
Tio(End)	17	1	17	69	0.50 [0.32, 0.68]	0.99 [0.92, 1.00]	
Tio(Endo)	13	4	11	46	0.54 [0.33, 0.74]	0.92 [0.81, 0.98]	
Tio(Eso)	15	1	12	63	0.56 [0.35, 0.75]	0.98 [0.92, 1.00]	
Toh	23	2	0	1	1.00 [0.85, 1.00]	0.33 [0.01, 0.91]	
Vickers J & D	32	8	8	1	0.80 [0.64, 0.91]	0.11 [0.00, 0.48]	
Wakelin	9	2	6	12	0.60 [0.32, 0.84]	0.86 [0.57, 0.98]	_ _
Wu	9	19	3	40	0.75 [0.43, 0.95]	0.68 [0.54, 0.79]	
Yen	10	0	12	5	0.45 [0.24, 0.68]	1.00 [0.48, 1.00]	
Y o shikane	12	5	4	- 7	0.75 [0.48, 0.93]	0.58 [0.28, 0.85]	
Ziegler	9	9	З	16	0.75 [0.43, 0.95]	0.64 [0.43, 0.82]	
							0 0.2 0.4 0.6 0.8 1 0 0.2 0.4 0.6 0.8 1





H.5.3 PET-CT for oesophageal cancer

Figure 24: PET-CT for detection of nodal metastasis of oesophageal cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Berrisford 2008	12	18	4	3	0.75 [0.48, 0.93]	0.14 [0.03, 0.36]		-
Hsu 2009	12	4	9	20	0.57 [0.34, 0.78]	0.83 [0.63, 0.95]		
Hsu 2011	15	3	30	29	0.33 [0.20, 0.49]	0.91 [0.75, 0.98]		
Little 2007	0	3	6	49	0.00 [0.00, 0.46]	0.94 [0.84, 0.99]		
Liu 2016	- 77	17	12	267	0.87 [0.78, 0.93]	0.94 [0.91, 0.96]	-	•
Roedl 2008	48	- 4	- 7	22	0.87 [0.76, 0.95]	0.85 [0.65, 0.96]		
Salahudeen 2008	4	0	8	3	0.33 [0.10, 0.65]	1.00 [0.29, 1.00]		
Schreurs 2008	13	2	6	40	0.68 [0.43, 0.87]	0.95 [0.84, 0.99]		
Shen 2012	123	8	19	177	0.87 [0.80, 0.92]	0.96 [0.92, 0.98]	-	
Shum 2012	8	6	2	10	0.80 [0.44, 0.97]	0.63 [0.35, 0.85]		
Sohda 2010	- 7	8	3	3	0.70 [0.35, 0.93]	0.27 [0.06, 0.61]		
Yano 2012	12	13	25	31	0.32 [0.18, 0.50]	0.70 [0.55, 0.83]		
Yen 2012	0	2	3	6	0.00 [0.00, 0.71]	0.75 [0.35, 0.97]		
							0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

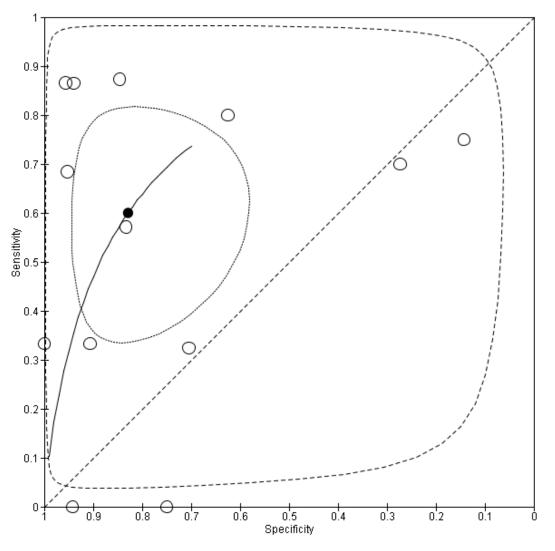


Figure 25: ROC curve of PET-CT for detection of nodal metastasis of oesophageal cancer

H.5.4 Laparoscopy for gastric cancer

Figure 26: Laparoscopy for detection of peritoneal metastasis of gastric cancer

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Asencio 1997	16	0	2	42	0.89 [0.65, 0.99]	1.00 [0.92, 1.00]		
Burke 1997	32	0	6	65	0.84 [0.69, 0.94]	1.00 [0.94, 1.00]		-
Fujimura 2002	9	0	4	18	0.69 [0.39, 0.91]	1.00 [0.81, 1.00]		
Lavonius 2002	19	0	3	25	0.86 [0.65, 0.97]	1.00 [0.86, 1.00]		
Lowy 1996	16	0	3	38	0.84 [0.60, 0.97]	1.00 [0.91, 1.00]		
Muntean 2009	14	0	2	29	0.88 [0.62, 0.98]	1.00 [0.88, 1.00]		
Sarela 2006	151	0	41	360	0.79 [0.72, 0.84]	1.00 [0.99, 1.00]		•
Stell 1996	9	0	4	52	0.69 [0.39, 0.91]	1.00 [0.93, 1.00]		
Tsuchida 2011	8	0	1	14	0.89 [0.52, 1.00]	1.00 [0.77, 1.00]		

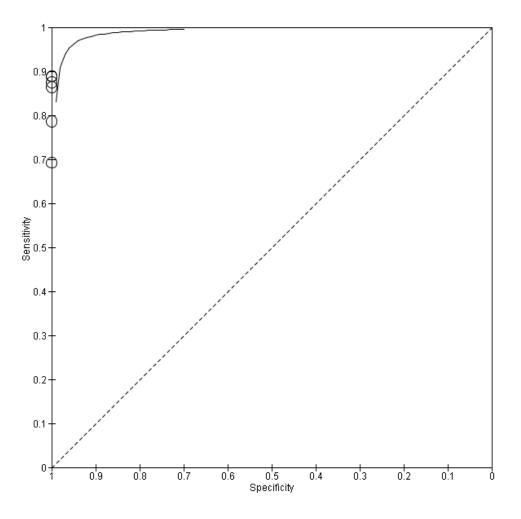


Figure 27: ROC curve of laparoscopy for detection of peritoneal metastasis of gastric cancer

H.6 Staging investigations

What are the optimal staging investigations to determine suitability for curative treatment of gastric cancer after diagnosis with endoscopy and whole-body CT scan?

See H.5

H.7 Which people with adenocarcinoma of the stomach and oesophagus should have their tumours HER2 tested?

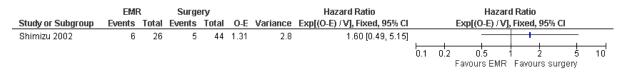
Not applicable to this review.

H.8 T1N0 oesophageal cancer

What is the optimal management of T1N0 oesophageal cancer?

Extended endoscopic mucosal resection (EMR) versus (oesophagectomy]

Figure 28: EMR versus oesophagectomy in patients with T1N0 squamous cell oesophageal cancer (median follow up 48 months). Overall survival



Extended endoscopic mucosal resection (EMR) versus endoscopic submucosal dissection (ESD)

Figure 29: EMR versus ESD in patients with T1N0 squamous cell oesophageal cancer (follow up 12 months). Disease free survival

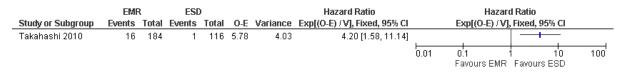


Figure 30: EMR versus ESD in patients with T1N0 squamous cell oesophageal cancer. Pathological margins free of tumour (post-treatment)

	EMF	1	ESD)	Risk Ratio			Risk	Ratio			
Study or Subgroup	Events	Total	Events	Total	M-H, Fixed, 95% Cl			M-H, Fixe	ed, 95% (CI		
Takahashi 2010	144	184	113	116	0.80 [0.74, 0.87]			+				
						0.1	0.2 Fav	0.5 ours ESD	1 2 Favour	2 Is EMR	5	10

Figure 31: EMR versus ESD in patients with T1N0 squamous cell oesophageal cancer. Perforation (post-treatment)

	EMF	ł	ESD		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Takahashi 2010	3	184	3	116	0.63 [0.13, 3.07]	0.1 0.2 0.5 1 2 5 10 Favours EMR Favours ESD

Figure 32: EMR versus ESD in patients with T1N0 squamous cell oesophageal cancer. Stenosis (post-treatment)

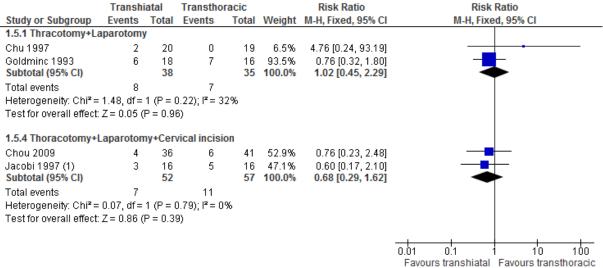
	EMF	EMR ESD		Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	M-H, Fixed, 95% Cl		M-H, Fixed, 95% Cl	
Takahashi 2010	17	184	20	116	0.54 [0.29, 0.98]			
						0.1	0.2 0.5 1 2 5 10]]
							Favours EMR Favours ESD	

H.9 Surgical treatment of oesophageal cancer

What is the most effective operative approach for the surgical treatment of oesophageal cancer?

H.9.1 Tranhiatal versus transthoracic oesophagectomy in oesophageal cancer

Figure 33: Post-operative complications: Anastomotic leak



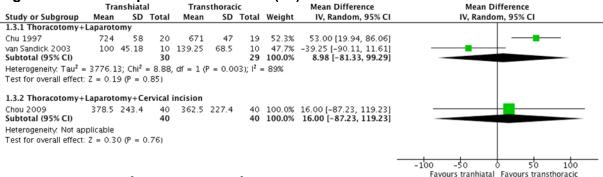
(1) Caution - double counted with pulmonary complications

Figure 34: Post-operative complications: Pneumonia

	Transhi	iatal	Transtho	racic		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
1.5.1 Thracotomy+L	aparotomy	y					
Chu 1997	2	20	0	19	6.5%	4.76 [0.24, 93.19]	
Goldminc 1993 Subtotal (95% Cl)	6	18 38	7	16 35	93.5% 100.0%	0.76 [0.32, 1.80] 1.02 [0.45, 2.29]	
Fotal events	8		7				
Heterogeneity: Chi ² =	= 1.48, df =	1 (P = 0)	0.22); I^z = 3:	2%			
Test for overall effect	: Z = 0.05 (P = 0.9	6)				
1.5.4 Thoracotomy+	Lanaroton	w.+Con	vical incisi	0.0			
-		-			50 00V		
Chou 2009	4	36	6	41	52.9%	0.76 [0.23, 2.48]	
Jacobi 1997 (1)	3	16	5	16	47.1%	0.60 [0.17, 2.10]	
Subtotal (95% CI)		52		57	100.0%	0.68 [0.29, 1.62]	
Fotal events	7		11				
Jotorogonoity: OhiZ-	:007 df=	1 (P = 0)).79); I² = 0'	%			
Heterogeneity. Chi==	0.011 41						
Test for overall effect	•	P = 0.3	3)				
	•	P = 0.3	3)				
	•	P = 0.3	3)				

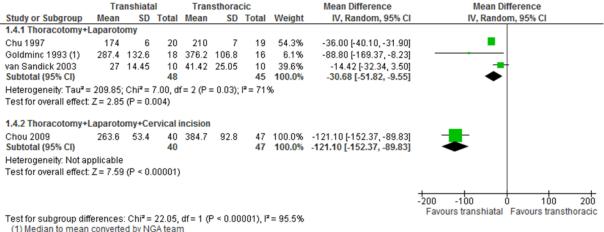
(1) Caution - double counted with pulmonary complications

Figure 35: Intraoperative blood loss (ml)



Test for subgroup differences: $Chi^2 = 0.01$, df = 1 (P = 0.92), $I^2 = 0\%$

Figure 36: Length of operation (minutes)



(1) Median to mean converted by NGA team

Figure 37: Mean lymph nodes resected

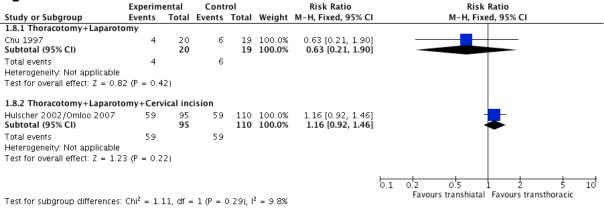
	Trar	shia	tal	Trans	sthora	acic		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
1.6.1 Thoracotomy+Laparoto	my+Ce	ervica	l incisi	on					
Hulscher 2002/Omloo 2007 Subtotal (95% CI)	16	9	94 94	31	14			-15.00 [-18.18, -11.82] -15.00 [-18.18, -11.82]	↓
Heterogeneity: Not applicable									
Test for overall effect: Z = 9.25	5 (P < 0	.000	01)						
									-20 -10 0 10 20
									Favours transthoracic Favours transhiatal

Test for subgroup differences: Not applicable

ection of	tumo	ur wi	th ma	arginal cleara	ance
Transhiatal	Transth	oracic		Risk Ratio	Risk Ratio
Events Tota	l Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
omy+Cervical	incision:R0	resecti	on		
68 9	4 79	111	71.2%	1.02 [0.86, 1.21]	•
9	4	111	71.2%	1.02 [0.86, 1.21]	◆
68	79				
9 (P = 0.85)					
omy+Cervical	incision: R	1 resecti	ion		
23 9	4 28	111	25.2%	0.97 [0.60, 1.56]	_ _
9	4	111	25.2%	0.97 [0.60, 1.56]	•
23	28				
2 (P = 0.90)					
omy+Cervical	incision: R	2 resecti	ion		
1 9	4 4	111	3.6%	0.30 [0.03, 2.60]	
9	4	111	3.6%	0.30 [0.03, 2.60]	
1	4				
0 (P = 0.27)					
28	2	333	100.0%	0.98 [0.82, 1.17]	•
92	111				
r = 2 (P = 0.51)); l ² = 0%				0.01 0.1 1 10 100
4 (P = 0.81)					Favours transthoracic Favours transhiatal
$Chi^2 = 1.26$, d	f = 2 (P = 1	0.53), I ²	= 0%		ravous transmoracie ravours transmatar
	Transhiatal Events Tota omy+Cervical 68 9 (P = 0.85) omy+Cervical i 23 2 23 9 23 9 23 2 2 (P = 0.90) omy+Cervical i 1 9 1 9 1 9 1 9 2 (P = 0.27) 28 9 92 2 2 (P = 0.27) 28 9 92 2 2 (P = 0.21)	Transhiatal Transhi Events Transhi Events bmy+Cervical incision:R0 68 94 79 94 68 79 9 (P = 0.85) 94 28 bmy+Cervical incision: R1 23 94 28 23 24 28 24 94 28 23 24 28 24 94 28 23 94 28 23 94 28 24 94 4 1 94 4 1 94 4 1 94 4 1 94 1 29 111 4 0 (P = 0.27) 282 111 92 111 4 1 9 11 1	Transhiatal Transthoracic Events Total Events Total tomy+Cervical incision:R0 resection 111 68 94 79 111 68 79 111 111 68 79 9 (P = 0.85) 111 23 94 28 111 23 24 28 111 23 24 28 111 23 28 28 111 23 28 111 111 23 28 111 111 23 28 111 111 23 28 111 111 23 28 111 111 23 28 111 111 1 94 111 111 1 94 111 111 1 94 111 111 1 94 111 111 <tr< td=""><td>Transhiatal Transthoracic Events Total Events Total Weight omy+Cervical incision:R0 resection 79 111 71.2% 68 94 79 111 71.2% 68 94 79 111 71.2% 68 79 111 71.2% 68 79 111 71.2% 68 79 111 71.2% 68 79 111 71.2% 90 (P = 0.85) </td><td>Events Total Events Total Weight M-H, Fixed, 95% CI omy+Cervical incision:R0 resection 68 94 79 111 71.2% 1.02 [0.86, 1.21] 68 79 94 111 71.2% 1.02 [0.86, 1.21] 68 79 99 (P = 0.85) 0 0.97 [0.60, 1.56] 94 111 25.2% 0.97 [0.60, 1.56] 23 94 28 111 25.2% 0.97 [0.60, 1.56] 23 23 28 2 (P = 0.90) 0.97 [0.60, 1.56] 0.97 [0.60, 1.56] 94 111 25.2% 0.97 [0.60, 1.56] 0.97 [0.60, 1.56] 23 28 2 (P = 0.90) 0.97 [0.60, 1.56] 94 111 3.6% 0.30 [0.03, 2.60] 1 94 4 111 3.6% 0.30 [0.03, 2.60] 1 4 0 (P = 0.27) 282 333 100.0% 0.98 [0.82, 1.17] 92 111 5 94 111 5</td></tr<>	Transhiatal Transthoracic Events Total Events Total Weight omy+Cervical incision:R0 resection 79 111 71.2% 68 94 79 111 71.2% 68 94 79 111 71.2% 68 79 111 71.2% 68 79 111 71.2% 68 79 111 71.2% 68 79 111 71.2% 90 (P = 0.85)	Events Total Events Total Weight M-H, Fixed, 95% CI omy+Cervical incision:R0 resection 68 94 79 111 71.2% 1.02 [0.86, 1.21] 68 79 94 111 71.2% 1.02 [0.86, 1.21] 68 79 99 (P = 0.85) 0 0.97 [0.60, 1.56] 94 111 25.2% 0.97 [0.60, 1.56] 23 94 28 111 25.2% 0.97 [0.60, 1.56] 23 23 28 2 (P = 0.90) 0.97 [0.60, 1.56] 0.97 [0.60, 1.56] 94 111 25.2% 0.97 [0.60, 1.56] 0.97 [0.60, 1.56] 23 28 2 (P = 0.90) 0.97 [0.60, 1.56] 94 111 3.6% 0.30 [0.03, 2.60] 1 94 4 111 3.6% 0.30 [0.03, 2.60] 1 4 0 (P = 0.27) 282 333 100.0% 0.98 [0.82, 1.17] 92 111 5 94 111 5

Figure 38: Resection of tumour with marginal clearance

Figure 39: Recurrence



Test for subgroup differences: Chi² = 1.11, df = 1 (P = 0.29), I² = 9.8%

Figure 40: Mortality

-	Experim	ental	Contr	ol		Risk Ratio	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl		
1.10.1 Thoracotomy+	Laparotor	ny							
Chu 1997 (1)	0	20	0	19		Not estimable			
Goldminc 1993 (2) Subtotal (95% Cl)	2	32 52	3	35 54	100.0% 100.0%	0.73 [0.13, 4.09] 0.73 [0.13, 4.09]			
Total events	2		3						
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z=0.36 (F	P = 0.72)						
1.10.2 Thoracotomy+	Laparotor	ny+Cer	vical inci	sion					
Jacobi 1997 (3) Subtotal (95% CI)	1	16 16	1	16 16	100.0% 100.0%	1.00 [0.07, 14.64] 1.00 [0.07, 14.64]			
Total events	1		1						
Heterogeneity: Not ap	•								
Test for overall effect:	Z = 0.00 (F	P = 1.00)						

Test for subgroup differences: Chi² = 0.04, df = 1 (P = 0.85), l² = 0% (1) 30-day mortality

(2) hospital death (up to 80 days)

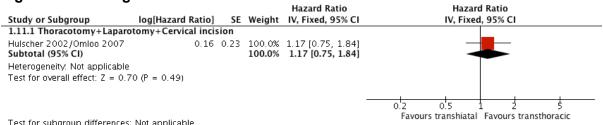
(3) 30-day mortality

Figure 41: **Overall survival**

				Hazard Ratio		Hazard Ratio	
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Fixed, 95% CI		IV, Fixed, 95% CI	
1.2.1 Thoracotomy+Laparoto	my+Cervical incisi	ion					
Hulscher 2002/Omloo 2007 Subtotal (95% CI)	0.13	0.23		1.14 [0.73, 1.79] 1.14 [0.73, 1.79]			
Heterogeneity: Not applicable Test for overall effect: $Z = 0.57$	7 (P = 0.57)						
					0.5	0.7 1 1.5	1
Test for subgroup differences	hist souties late					Favours transhiatal Favours transthoracic	

Test for subgroup differences: Not applicable

Figure 42: **Progression-free survival**



Test for subgroup differences: Not applicable

H.9.2 Totally minimally invasive versus any open oesophagectomy

MIO Open Risk Ratio Risk Ratio Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% Cl M-H, Fixed, 95% CI 2.1.1 Anastomotic leak Biere 2012 7 59 4 56 67.1% 1.66 [0.51, 5.37] 0.50 [0.05, 5.39] Guo 2013 110 32.9% 1 111 2 166 100.0% Subtotal (95% CI) 170 1.28 [0.46, 3.55] Total events 8 6 Heterogeneity: $Chi^2 = 0.80$, df = 1 (P = 0.37); $I^2 = 0\%$ Test for overall effect: Z = 0.47 (P = 0.64) 2.1.2 Pulmonary complications Biere 2012 2 59 2 56 18.5% 0.95 [0.14, 6.51] 0.33 [0.09, 1.19] Guo 2013 3 111 9 110 81.5% 166 100.0% Subtotal (95% CI) 0.44 [0.16, 1.26] 170 Total events 5 11 Heterogeneity: $Chi^2 = 0.80$, df = 1 (P = 0.37); $l^2 = 0\%$ Test for overall effect: Z = 1.53 (P = 0.13) 0.05 0.2 5 20 Favours MIO Favours open

Figure 43: Post-operative complications

Test for subgroup differences: $Chi^2 = 2.02$, df = 1 (P = 0.16), $l^2 = 50.4\%$

Figure 44: Intraoperative blood loss (ml)

		MIO		0	Open			Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Rando	m, 95% CI	
Biere 2012	408.5	313.4	59	1,009.4	786.2	56	49.4%	-600.90 [-821.80, -380.00]			
Guo 2013	590	324.4	110	219.7	194.4	111	50.6%	370.30 [299.71, 440.89]		-	
Total (95% CI)			169			167	100.0%	-109.43 [-1061.12, 842.26]			
Heterogeneity: Tau ² =	46461	9%	-500 -250	250 500							
Test for overall effect:	Z = 0.2	3 (P = 0).82)							Favours open	

Figure 45: Length of operation (minutes)

		MIO			Open			Mean Difference	Mean Difference
Study or Subgroup	Mean SD Total			Mean	SD	SD Total Weight IV, Fixed, 95%			I IV, Fixed, 95% CI
Biere 2012	326.71	123.17	59	308.67	132.71	56	15.6%	18.04 [-28.82, 64.90]]
Guo 2013	272.3	57.9	111	218.7	91	110	84.4%	53.60 [33.47, 73.73]	
Total (95% CI)			170			166	100.0%	48.06 [29.56, 66.56]	
Heterogeneity: Chi ² = Test for overall effect:									
			,						Favours MIO Favours open

Figure 46: EORTC Quality of life – Global score

-	MIO Open							Mean Difference	Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fiz	ced, 95% C	1	
Biere 2012	61	18	59	51	21	56	100.0%	10.00 [2.83, 17.17]					
Total (95% CI)			59			56	100.0%	10.00 [2.83, 17.17]			•		
Heterogeneity: Not applicable Test for overall effect: Z = 2.74 (P = 0.006)									-100	-50 Favours op	0 en Favou	50 rs MIO	100

Figure 47: Resection margin

	MIO		Ope	n		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
2.6.1 R0							
Biere 2012	54	59	47	56	90.4%	1.09 [0.95, 1.25]	
Subtotal (95% CI)		59		56	90.4%	1.09 [0.95, 1.25]	•
Total events	54		47				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z=1.23 (P = 0.2	2)				
2.6.2 R1							
Biere 2012	1	59	5	56	9.6%	0.19 [0.02, 1.57]	-
Subtotal (95% CI)		59		56	9.6%	0.19 [0.02, 1.57]	
Total events	1		5				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z=1.54 ((P = 0.1	2)				
Total (95% CI)		118		112	100.0%	1.00 [0.86, 1.18]	•
Total events	55		52				
Heterogeneity: Chi ² =	3.75, df =	1 (P =	0.05); i ² =	= 73%			
Test for overall effect:	Z=0.05 (P = 0.9	96)				0.01 0.1 1 10 10 Favours MIO Favours open
Test for subgroup diff	erences:	Chi ^z = 1	2.61, df=	1 (P =	0.11), P=	: 61.7%	Favours MIO Favours open

Figure 48: Mean number of lymph nodes resected

		MIO Open						Mean Difference		Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rar	1dom, 95	% CI
Biere 2012	21.78	10.77	59	59	10.55	56	50.0%	-37.22 [-41.12, -33.32]				
Guo 2013	24.3	21	111	19.2	12.5	110	50.0%	5.10 [0.55, 9.65]				
Total (95% CI)			170			166	100.0%	-16.08 [-57.55, 25.40]				
Heterogeneity: Tau ² :	Heterogeneity. Tau ² = 890.82; Chi ² = 191.61, df = 1 (P < 0.00001); l ² = 99%											
Test for overall effect	:Z = 0.7	6 (P = 0), 45)						Fa	avours op	en Favo	22

Figure 49: 30-day mortality

0	міо			n		Risk Ratio		Risk Ratio				
Study or Subgroup	Events Total Eve		Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixed, 95% Cl				
Biere 2012	1	59	0	56	100.0%	2.85 [0.12, 68.53]			_			
Total (95% CI)		59		56	100.0%	2.85 [0.12, 68.53]						
Total events	1		0									
Heterogeneity: Not ap Test for overall effect		(P = 0.5	52)				0.01	0.1 1 10 100 Favours MIO Favours open				

50

H.9.3 Hybrid minimally invasive versus open oesophagectomy

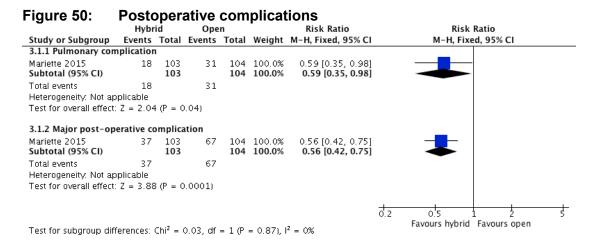
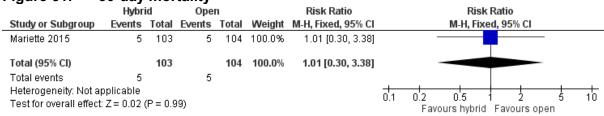


Figure 51: 30-day mortality



H.10 Lymph node dissection in oesophageal and gastric cancer

Does the extent of lymph node dissection influence outcomes in adults with oesophageal and gastric cancer?

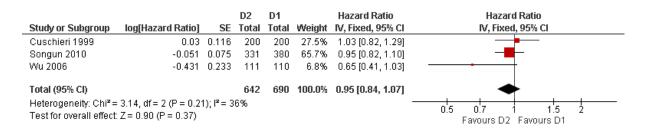
H.10.1 Overall survival following D2 versus D1 lymphadenectomy in patients with gastric cancer.

Figure 52: Overall survival

Study or Subgroup	log[Hazard Ratio]	SE	D2 Total	D1 Total	Weight	Hazard Ratio IV, Random, 95% Cl	Hazard Ratio IV, Random, 95% Cl
Cuschieri 1999	0.095	0.12	200	200	27.3%	1.10 [0.87, 1.39]	-
Degiuli 2014	0.039	0.21	134	133	18.3%	1.04 [0.69, 1.57]	- _
Robertson 1994	0.351	0.463	29	25	6.3%	1.42 [0.57, 3.52]	
Songun 2010	-0.083	0.085	331	380	31.0%	0.92 [0.78, 1.09]	
Wu 2006	-0.713	0.224	111	110	17.1%	0.49 [0.32, 0.76]	- _
Total (95% CI)			805	848	100.0%	0.91 [0.71, 1.17]	•
Heterogeneity: Tau ² = Test for overall effect		df = 4 (F	9 = 0.02); I² = 6	4%		0.2 0.5 1 2 5 Favours D2 Favours D1

H.10.2 Disease free survival following D2 versus D1 lymphadenectomy in patients with gastric cancer.

Figure 53: Disease-free survival



H.10.3 Post-operative mortality following D2 versus D1 lymphadenectomy in patients with gastric cancer.

Figure 54: Post-operative mortality

	D2		D1			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Fixed, 95% Cl	IV, Fixed, 95% Cl
Cuschieri 1999	26	200	13	200	41.3%	2.00 [1.06, 3.78]	
Degiuli 2014	3	134	4	133	7.7%	0.74 [0.17, 3.26]	
Dent 1988	0	21	0	22		Not estimable	
Li 2007	0	109	0	108		Not estimable	
Robertson 1994	1	29	0	25	1.7%	2.60 [0.11, 61.11]	
Songun 2010	32	331	15	380	47.2%	2.45 [1.35, 4.44]	-∎-
Wu 2006	1	111	1	110	2.2%	0.99 [0.06, 15.65]	
Total (95% Cl)		935		978	100.0%	2.02 [1.34, 3.04]	◆
Total events	63		33				
Heterogeneity: Chi ² =	2.44, df=	4 (P =	0.66); l² =	= 0%			
Test for overall effect:	Z = 3.37	(P = 0.0)008)				Favours D2 Favours D1

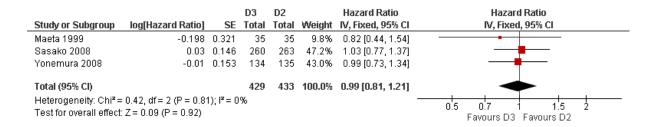
H.10.4 Adverse events following D2 versus D1 lymphadenectomy in patients with gastric cancer.

Figure 55: Adverse events

	D2		D1			Risk Ratio	Risk Ratio
Study or Subgroup		Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
1.5.1 Pancreatic leak							
Degiuli 2010	4	134	1	133	14.7%	3.97 [0.45, 35.06]	
Hartgrink 2004	10	331	3	380	41.0%	3.83 [1.06, 13.79]	
Li 2007	6	109	2	108	29.5%	2.97 [0.61, 14.40]	
Robertson 1994	0	29	0	25		Not estimable	
Wu 2006 Subtotal (95% CI)	1	111 714	1	111 757	14.7% 100.0%	1.00 [0.06, 15.79] 3.18 [1.36, 7.41]	
Total events	21	7.14	7	131	100.074	5.10[1.50, 1.41]	
Heterogeneity: Chi ² = (Test for overall effect: 2	D.80, df=		0.85); l ² =	:0%			
1.5.2 Reoperation rate	e						
Degiuli 2010	4	134	3	133	8.5%	1.32 [0.30, 5.80]	
Dent 1988	4	21	0	22	1.4%	9.41 [0.54, 164.74]	
Hartgrink 2004	59	331	30 3	380	78.8%	2.26 [1.49, 3.42]	
Li 2007 Robertson 1994	2 9	108 29	3 0	109 25	8.4% 1.5%	0.67 [0.11, 3.95] 16.47 [1.01, 269.41]	-
Wu 2006	1	111	0	110	1.4%	2.97 [0.12, 72.20]	·
Subtotal (95% CI)		734	Ŭ	779	100.0%	2.37 [1.63, 3.43]	•
Total events	79		36				
Heterogeneity: Chi ² = 5 Test for overall effect: 2	•			:7%			
1.5.3 Anastomotic lea	k						
Cuschieri 1999	26	200	11	200	33.9%	2.36 [1.20, 4.65]	■
Degiuli 2010	0	86	0	76		Not estimable	
Dent 1988	1	21	0	22	1.5%	3.14 [0.13, 72.96]	
Hartgrink 2004	30	331	16	380	46.0%	2.15 [1.19, 3.88]	
Li 2007 Deberteen 1994	3	108	5 0	109	15.4%	0.61 [0.15, 2.47]	
Robertson 1994 Wu 2006	5	29 111	0	25 110	1.7% 1.6%	6.07 [0.33, 112.07] 10.90 [0.61, 194.82]	
Subtotal (95% CI)	5	886	0		100.0%	2.20 [1.47, 3.29]	•
Total events	68		32				-
Heterogeneity: Chi ² = 4		5 (P =		:0%			
Test for overall effect: 2							
1.5.4 Haemorrhage							
Cuschieri 1999	4	200	6	200	23.0%	0.67 [0.19, 2.33]	
Degiuli 2010	2	134	3	133	11.5%	0.66 [0.11, 3.90]	
Hartgrink 2004	8	380	15	331	61.5%	0.46 [0.20, 1.08]	
Li 2007 Robertson 1994	0 3	109 29	0 0	108 25	2.1%	Not estimable 6.07 [0.33, 112.07]	
Wu 2006	1	111	0	110	1.9%	2.97 [0.12, 72.20]	
Subtotal (95% CI)		963	0		100.0%	0.70 [0.39, 1.26]	•
Total events	18		24				-
Heterogeneity: Chi² = 3 Test for overall effect: 2				0%			
1.5.5 Wound infection	1						
Cuschieri 1999	10	200	8	200	35.8%	1.25 [0.50, 3.10]	_
Dent 1988	0	200	Ő	200		Not estimable	
Hartgrink 2004	30	331	15	380	62.5%	2.30 [1.26, 4.19]	-∎-
Li 2007	0	1	0	108		Not estimable	
Wu 2006	5	11	2	110		25.00 [5.48, 114.10]	
Subtotal (95% CI)		564		820	100.0%	2.29 [1.45, 3.61]	
Total events Heterogeneity: Chi² = 1 Test for overall effect: 2				l² = 82°	%		
1.5.6 Pulmonary com	plication						
Cuschieri 1999	8	200	5	200	13.7%	1.60 [0.53, 4.81]	
Degiuli 2010	8	134	6	133	16.6%	1.32 [0.47, 3.71]	-
Dent 1988	3	21	3	22	8.1%	1.05 [0.24, 4.62]	
Hartgrink 2004	49	331	23	380	58.9%	2.45 [1.52, 3.92]	-■-
Li 2007	5	109	1	108	2.8%	4.95 [0.59, 41.71]	+
Subtotal (95% CI)		795		843	100.0%	2.10 [1.44, 3.06]	
Total events	73		38	0.07			
Heterogeneity: Chi ² = 3 Test for everall effect: 3				:0%			
Test for overall effect: 2	⊆= 3.87 (,r = 0.0	1001)				
							0.01 0.1 1 10 100
							Favours [D2] Favours [D1]

H.10.5 Overall survival following D3 versus D2 lymphadenectomy in patients with gastric cancer.

Figure 56: Overall survival



H.10.6 Disease (recurrence) free survival following D3 versus D2 lymphadenectomy in patients with gastric cancer.

Figure 57: Disease-free survival

	D3		D2					Hazard Ratio	Hazard Ratio
Study or Subgroup	Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% Cl	Exp[(O-E) / V], Fixed, 95% Cl
Sasako 2008	99	260	100	263	4.1	53.29	100.0%	1.08 [0.83, 1.41]	
Yonemura 2008 (1)	52	134	63	135	0	0		Not estimable	T
Total (95% Cl)		394		398			100.0%	1.08 [0.83, 1.41]	•
Total events	151		163						
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z=0.56 (P = 0.5	i7)						5 10 5 1 2 5 10 Favours [D3] Favours [D2]
<u>Footnotes</u>									
(1) Cannot calculate (D-E and v	ariance	1						

H.10.7 Post-operative mortality following D3 versus D2 lymphadenectomy in patients with gastric cancer

Figure 58: Post-operative mortality

	D3		D2			Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Fixed, 95% Cl		IV, Fixed, 95%	CI	
Kulig 2007	7	134	3	141	52.3%	2.46 [0.65, 9.30]				
Maeta 1999	1	35	1	35	12.4%	1.00 [0.07, 15.36]				
Sasako 2008	2	260	2	263	24.3%	1.01 [0.14, 7.13]		+		
Yonemura 2008	4	134	0	135	10.9%	9.07 [0.49, 166.77]				
Total (95% CI)		563		574	100.0%	2.04 [0.78, 5.35]				
Total events	14		6							
Heterogeneity: Chi ² =	1.84, df=	3 (P =	0.61); I ² =	= 0%						400
Test for overall effect	Z=1.45	(P = 0.1	5)				0.01	U.1 1 Favours D3 Favo	10 urs D2	100

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H.10.8 Adverse events following D3 versus D2 lymphadenectomy in patients with gastric cancer.

Figure 59: Adverse events

St	D3		D2	T-4-1	187-1-84	Risk Ratio	Risk Ratio
Study or Subgroup	Events	lotal	Events	lotal	weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
2.3.1 Pancreatic leak							
Kulig 2007	1	134	2	141	6.5%	0.53 [0.05, 5.73]	
Maeta 1999	2	35	3	35	10.0%	0.67 [0.12, 3.75]	
Sano 2004	16	260	14	263	46.6%	1.16 [0.58, 2.32]	
Yonemura 2006	15	128	11	128	36.8%	1.36 [0.65, 2.85]	
Subtotal (95% CI)		557		207	100.0%	1.14 [0.71, 1.83]	—
Total events	34		30				
Heterogeneity: Chi ² = 1		· ·		= 0%			
Test for overall effect: .	2 = 0.55	(P = 0.5	98)				
2.3.2 Anastomotic lea	k						
Kuliq 2007	9	134	9	141	26.8%	1.05 [0.43, 2.57]	_
Maeta 1999	2	35	3	35	9.2%	0.67 [0.12, 3.75]	
Sano 2004	5	260	6	263	18.2%	0.84 [0.26, 2.73]	
Yonemura 2006	11	128	15	128	45.8%	0.73 [0.35, 1.53]	_
Subtotal (95% CI)		557		567		0.83 [0.51, 1.36]	•
Total events	27		33				-
Heterogeneity: Chi² = I		3 (P =		= 0%			
Test for overall effect: .				•			
2.3.3 Wound infection	1						_
Kulig 2007	6	134	10	141	95.1%	0.63 [0.24, 1.69]	
Yonemura 2006	2	128	0	128		5.00 [0.24, 103.13]	
Subtotal (95% Cl)		262		269	100.0%	0.84 [0.35, 2.05]	-
Total events	8		10				
Heterogeneity: Chi ^z = 1	1.66, df=	: 1 (P =	0.20); l² =	= 40%			
Test for overall effect: .	Z = 0.37	(P = 0.7	71)				
2.3.4 Pulmonary com	nlication	\$					
Kuliq 2007	14	134	23	141	60.0%	0.64 [0.34, 1.19]	_ _
Sano 2004	10	260	13	263	34.6%	0.78 [0.35, 1.74]	
Yonemura 2006	4	128	2	128	5.4%	2.00 [0.37, 10.73]	
Subtotal (95% CI)	4	522	2		100.0%	0.76 [0.48, 1.21]	•
Total events	28	ULL	38	OOL	1001010		•
Heterogeneity: Chi² = 1		2 (P =		- 0%			
Test for overall effect: .				- 0 /0			
		¢	,				
2.3.5 Reoperation rat	в						
Maeta 1999	3	35	0	35	9.1%	7.00 [0.37, 130.69]	
Sano 2004	7	260	5	263	90.9%	1.42 [0.46, 4.40]	
Subtotal (95% CI)		295		298	100.0%	1.93 [0.69, 5.35]	
Total events	10		5				
Later and a star of the second star	1.03, df=	: 1 (P =	0.31); l² =	= 3%			
Heterogeneity: Chi ² = 1	7 - 1.26	(P = 0.2)	21)				
Heterogeneity: Chi+ = Test for overall effect: .	2 - 1.20	v 0	,				
	2 - 1.20		.,				
	2 - 1.20		.,				0.01 0.1 1 10 100

H.10.9 Overall survival following 3-field versus 2-field lymphadenectomy in patients with oesophageal cancer.

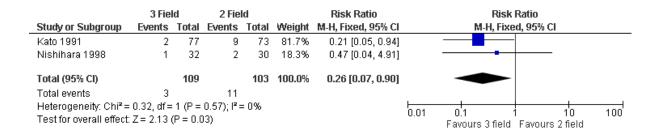
Figure 60: Overall survival

	3 Fie	ld	2 Fie	ld				Hazard Ratio		Hazard	Ratio	
Study or Subgroup	Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% CI		Exp[(0-E) /V],	Fixed, 95% Cl	
Kato 1991	27	77	42	73	-13.34	16.43	79.3%	0.44 [0.27, 0.72]				
Nishihara 1998	7	32	11	30	-2.7	4.28	20.7%	0.53 [0.21, 1.37]			_	
Total (95% CI)		109		103			100.0%	0.46 [0.30, 0.71]		•		
Total events	34		53									
Heterogeneity: Chi ² =	= 0.11, df =	: 1 (P =	0.74); l² :	= 0%					0.01	0.1 1	10	100
Test for overall effect	: Z = 3.52	(P = 0.0	0004)						0.01		Favours 2 field	100

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H.10.10 Post-operative mortality following 3-field versus 2-field lymphadenectomy in patients with oesophageal cancer.

Figure 61: Post-operative mortality



H.10.11 Adverse events following 3-field versus 2-field lymphadenectomy in patients with oesophageal cancer

Figure 62: Adverse events

	3 Field	I	2 Fiel	d		Risk Ratio	Risk Ratio
Study or Subgroup					Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
1.3.1 Any surgical con							
Kato 1991 Subtotal (95% CI)	29	77 77	18	73 73	100.0% 100.0 %	1.53 [0.93, 2.50] 1.53 [0.93, 2.50]	-
Total events	29		18				-
Heterogeneity: Not app Test for overall effect: 2		P = 0.0	9)				
1.3.2 Recurrent nerve	palsy						_
Kato 1991	11	77	15	73	74.9%	0.70 [0.34, 1.41]	
Nishihara 1998 Subtotal (95% CI)	18	32 109	5	30 103	25.1% 100.0 %	3.38 [1.43, 7.95] 1.37 [0.82, 2.27]	•
Total events	29		20				
Heterogeneity: Chi² = 7 Test for overall effect: 2	•			= 87%			
1.3.3 Anastomotic lea				70	70.00	4 45 10 00 0 11	_
Kato 1991 Nishihara 1998	26 2	77 32	17 6	73 30	73.8% 26.2%	1.45 [0.86, 2.44]	
Subtotal (95% CI)		32 109	-	30 103	26.2% 100.0%	0.31 [0.07, 1.43] 1.15 [0.71, 1.86]	*
Total events	28	=	23	300/			
Heterogeneity: Chi² = 3 Test for overall effect: 2	-			= 72%			
1.3.4 Pulmonary comp	olication						
Nishihara 1998 Subtotal (95% CI)	6	32 32	5	30 30	100.0% 100.0 %	1.13 [0.38, 3.30] 1.13 [0.38, 3.30]	
Total events	6		5				
Heterogeneity: Not app Test for overall effect: 2		P = 0.8	3)				
1.3.5 Chylothorax							
Kato 1991	0	77	3	73	100.0%	0.14 [0.01, 2.58]	←───
Nishihara 1998	0	0	0	0	100	Not estimable	
Subtotal (95% CI)		77		73	100.0%	0.14 [0.01, 2.58]	
Total events Listeregeneity: Notions	0 Nicoblo		3				
Heterogeneity: Not app Test for overall effect: 2		P = 0.1	8)				
1.3.6 Phrenic nerve pa	alsy						
Nishihara 1998 Subtotal (95% Cl)	4	32 32	0	30 30		8.45 [0.47, 150.66] 8.45 [0.47, 150.66]	
Total events	4		0				
Heterogeneity: Not app Test for overall effect: 2		P = 0.1	5)				
1.3.7 Tracheostomy							
Nishihara 1998 Subtotal (95% CI)	17	32 32	3	30 30	100.0% 100.0 %	5.31 [1.73, 16.31] 5.31 [1.73, 16.31]	
Total events	17	36	3	00			
Heterogeneity: Not app Test for overall effect: 2	licable	P = 0.0	-				
							0.01 0.1 1 10 10 Favours 3 Field Favours 2 Field

H.11 Localised oesophageal and gastro-oesophageal junctional adenocarcinoma

What is the optimal choice of chemotherapy or chemoradiotherapy in relation to surgical treatment for people with localised oesophageal and gastro-oesophageal junctional cancer?

H.11.1 Comparison 1: Preoperative chemotherapy versus postoperative chemotherapy

Figure 63: Overall survival

	Preoperati	ve CT	Postoperati	ve CT				Hazard Ratio		Hazar	d Ratio		
Study or Subgroup	Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% CI		Exp[(O-E) / V], Fixed, 95% CI		
Ando 2011 (1)	0	164	0	166	-13.16	41.82	100.0%	0.73 [0.54, 0.99]		-			
Total (95% CI)		164		166			100.0%	0.73 [0.54, 0.99]		•	•		
Total events	0		0										
Heterogeneity: Not app	plicable								0.01	0.1	1 1	0	100
Test for overall effect:	Z = 2.03 (P =	0.04)							0.01	Favours preoperative CT			100
Footnotes													
(1) number of event no	ot reported												

Figure 64: Progression free survival

	Preoperati	ve CT	Postoperat	ive CT				Hazard Ratio		Haza	rd Ratio		
Study or Subgroup	Events	Total	Events	Total	O-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% C	I	Exp[(O-E) / '	V], Fixed, 95% C	<u> </u>	
Ando 2011 (1)	0	164	0	166	-8.35	47.9	100.0%	0.84 [0.63, 1.12]					
Total (95% CI)		164		166			100.0%	0.84 [0.63, 1.12]		•			
Total events	0		0										
Heterogeneity: Not ap	plicable								H		+	+	
Test for overall effect:	Z = 1.21 (P =	0.23)							0.01	0.1 Favours preoperative CT		10 perative CT	100
Footnotes													
(1) number of events r	not reported												

Figure 65: Anastomotic leakage

	Preoperati	ve CT	Postoperat	ive CT		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	I	M-H, Fixed, 95%	CI	
Ando 2011	19	153	24	162	100.0%	0.84 [0.48, 1.47]			-		
Total (95% CI)		153		162	100.0%	0.84 [0.48, 1.47]			•		
Total events	19		24								
Heterogeneity: Not ap	plicable										100
Test for overall effect:	Z = 0.62 (P =	0.54)					0.01	0.1 Favours preopera	1 Itive CT Favour	10 s postoperative	100 CT

Figure 66: Wound infection

	Preoperati	ve CT	Postoperat	ive CT		Risk Ratio		Risk Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	N	I-H, Fixed, 95%	CI	
Ando 2011	16	153	20	162	100.0%	0.85 [0.46, 1.57]			-		
Total (95% CI)		153		162	100.0%	0.85 [0.46, 1.57]			•		
Total events	16		20								
Heterogeneity: Not ap	plicable						0.01		1	10	100
Test for overall effect:	Z = 0.53 (P =	0.60)					0.01	0.1 Favours preoperation	iive CT Favours	10 s postoperative	

Figure 67: Pulmonary complications

	Preoperati	ve CT	Postoperat	tive CT		Risk Ratio			Risk	Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl			M-H, Fixe	ed, 95% Cl		
Ando 2011	24	153	21	162	100.0%	1.21 [0.70, 2.08]			_			
Total (95% CI)		153		162	100.0%	1.21 [0.70, 2.08]						
Total events	24		21									
Heterogeneity: Not ap	plicable										10	100
Test for overall effect:	Z = 0.69 (P =	• 0.49)					0.01	0.1 Favours pre	operative CT	Favours posto	10 operative CT	100

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Figure 68: **Cardiovascular complications**

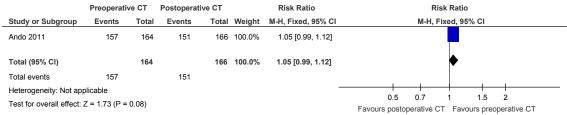
	Preoperati	ve CT	Postoperat	tive CT		Risk Ratio		Ri	sk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	М-Н, F	ixed, 95% Cl		
Ando 2011	4	153	3	162	100.0%	1.41 [0.32, 6.21]				-	
Total (95% CI)		153		162	100.0%	1.41 [0.32, 6.21]				-	
Total events	4		3								
Heterogeneity: Not ap	plicable						-		-		
Test for overall effect:	Z = 0.46 (P =	0.65)					0.01	0.1 Favours preoperative C	1 T Favours po	10 stoperative CT	100

Figure 69: **Treatment-related mortality**

	Preoperati	ve CT	Postoperat	ive CT		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M	H, Fixed, 95%	CI	
Ando 2011	1	153	2	162	100.0%	0.53 [0.05, 5.78]					
Total (95% CI)		153		162	100.0%	0.53 [0.05, 5.78]					
Total events	1		2								
Heterogeneity: Not ap	plicable										400
Test for overall effect:	Z = 0.52 (P =	0.60)					0.01 Fa	0.1 vours preoperati	1 ve CT Favou	10 s postoperative	100 CT

<Insert Note here>

Figure 70: **R0** tumour resection rate



H.11.2 Comparison 2: Preoperative chemotherapy versus surgery alone

Figure 71:

Overall survival (according to histology subtype) Hazard Ratio Hazard Ratio IV, Fixed, 95% CI Study or Subgroup Iog[Hazard Ratio] SE Weight IV, Fixed, 95% CI 10.1.1 SCC -0.163 0.256 6.4% 0.85 [0.51, 1.40] Ancona 2001 Law 1997 -0.46 0.167 15.1% 0.63 [0.46, 0.88] Nygaard 1992 0.077 0.206 10.0% 1.08 [0.72, 1.62] 0.174 0.321 4.1% 1.19 [0.63, 2.23] Schlag 1992a Subtotal (90% CI) 35.6% 0.83 [0.70, 1.00] Heterogeneity: Chi² = 5.59, df = 3 (P = 0.13); l² = 46% Test for overall effect: Z = 1.68 (P = 0.09) 10.1.2 Mixed MRC Allum 2009 -0.174 0.081 64.4% 0.84 [0.72, 0.98] Subtotal (90% CI) 64.4% 0.84 [0.74, 0.96] Heterogeneity: Not applicable Test for overall effect: Z = 2.15 (P = 0.03) Total (90% CI) 100.0% 0.84 [0.75, 0.93] Heterogeneity: Chi² = 5.59, df = 4 (P = 0.23); l² = 28% 0.01 0.1 10 100 Test for overall effect: Z = 2.73 (P = 0.006) Favours pre-op CT Favours surgery alone Test for subgroup differences: $Chi^2 = 0.00$, df = 1 (P = 0.94), l² = 0% <Insert Note here>

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Figure 72: Anastomotic leakage (according to histology subtype)

	Preoperati	VA CT	Surgery			Risk Ratio		Risk Ratio	
	•		0,						
Study or Subgroup	Events	Total	Events	lotal	Weight	M-H, Fixed, 95% C	I	M-H, Fixed, 95% Cl	
10.4.1 SCC									
Ancona 2001	2	48	1	48	2.8%	2.00 [0.19, 21.33]			
Baba 2000	5	21	6	21	16.9%	0.83 [0.30, 2.31]			
Law 1997	3	74	0	73	1.4%	6.91 [0.36, 131.40]			
Nygaard 1992	3	56	2	50	5.9%	1.34 [0.23, 7.69]			
Subtotal (95% CI)		199		192	27.0%	1.38 [0.64, 2.99]		-	
Total events	13		9						
Heterogeneity: Chi ² = 2	2.19, df = 3 (F	P = 0.53)	; I² = 0%						
Test for overall effect: 2	Z = 0.83 (P =	0.41)							
10.4.2 Mixed									
MRC Allum 2009	23	400	26	402	73.0%	0.89 [0.52, 1.53]			
Subtotal (95% CI)		400		402	73.0%	0.89 [0.52, 1.53]		•	
Total events	23		26						
Heterogeneity: Not app	licable								
Test for overall effect:	Z = 0.42 (P =	0.67)							
Total (95% CI)		599		594	100.0%	1.02 [0.66, 1.59]		•	
Total events	36		35						
Heterogeneity: Chi ² = 2	2.42, df = 4 (F	P = 0.66)	; I² = 0%						40
Test for overall effect: 2	Z = 0.10 (P =	0.92)					0.01	0.1 1 10	10
Test for subgroup diffe	rences: Chi ²	= 0.85, d	f = 1 (P = (0.36), I ²	= 0%			Favours pre-op CT Favours surgery alone	

<Insert Note here>

Figure 73: Cardiovascular complications (according to histology subtype)

	Preoperati	ve CT	Surgery	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	CI M-H, Fixed, 95% CI
10.6.1 SCC							
Ancona 2001	1	48	2	48	5.7%	0.50 [0.05, 5.33]	• • • • • • • • • • • • • • • • • • •
Law 1997	20	74	18	73	51.7%	1.10 [0.63, 1.90]	· • •
Subtotal (95% CI)		122		121	57.4%	1.04 [0.61, 1.77]	•
Total events	21		20				
Heterogeneity: Chi ² =	0.40, df = 1 (F	o = 0.52)	; l² = 0%				
Test for overall effect:	Z = 0.13 (P =	0.89)					
10.6.2 Mixed							
MRC Allum 2009	14	400	15	402	42.6%	0.94 [0.46, 1.92]	_ _
Subtotal (95% CI)		400		402	42.6%	0.94 [0.46, 1.92]	•
Total events	14		15				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 0.18 (P =	0.86)					
Total (95% CI)		522		523	100.0%	0.99 [0.65, 1.53]	•
Total events	35		35				
Heterogeneity: Chi ² =	0.47, df = 2 (F	P = 0.79)	; l² = 0%				
Test for overall effect:	Z = 0.02 (P =	0.98)					0.01 0.1 1 10 100 Favours pre-op CT Favours surgery alone
Test for subgroup diffe	erences: Chi ²	= 0.05, c	lf = 1 (P = (0.83), I²	= 0%		ravours pre-op or Favours surgery alone

Figure 74: Pulmonary complications (according to histology subtype)

	Preoperati	ve CT	Surgery	alone		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	M-H, Fixed, 95% Cl
10.8.1 SCC								
Ancona 2001	8	48	8	48	7.4%	1.00 [0.41, 2.45]		
Baba 2000	9	21	4	21	3.7%	2.25 [0.82, 6.18]		+
Law 1997	24	74	33	73	30.7%	0.72 [0.47, 1.09]		
Nygaard 1992	3	56	5	50	4.9%	0.54 [0.13, 2.13]		
Subtotal (95% CI)		199		192	46.6%	0.86 [0.62, 1.21]		•
Total events	44		50					
Heterogeneity: Chi ² = 4	4.78, df = 3 (F	o = 0.19)	; I² = 37%					
Test for overall effect: 2	Z = 0.84 (P =	0.40)						
10.8.2 MIxed								
MRC Allum 2009	56	400	58	402	53.4%	0.97 [0.69, 1.36]		
Subtotal (95% CI)		400		402	53.4%	0.97 [0.69, 1.36]		•
Total events	56		58					
Heterogeneity: Not app	licable							
Test for overall effect: 2	Z = 0.17 (P =	0.86)						
Total (95% CI)		599		594	100.0%	0.92 [0.72, 1.17]		•
Total events	100		108					
Heterogeneity: Chi ² = 5	5.11, df = 4 (ł	o = 0.28)	; I² = 22%					0.1 1 10 10
Test for overall effect: 2	Z = 0.67 (P =	0.50)					0.01	0.1 1 10 10 Favours pre-op CT Favours surgery alone
Test for subgroup differ	rences: Chi ²	= 0.22, d	lf = 1 (P = 0	0.64), l² :	= 0%			r avours pre-op Cr r avours surgery dione

<Insert Note here>

Infectious complications (according to histology subtype) Figure 75:

	Preoperati	ve CT	Surgery	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I M-H, Fixed, 95% CI
10.10.1 SCC							
Ancona 2001	3	48	3	48	7.1%	1.00 [0.21, 4.71]	
Law 1997	4	74	7	73	16.8%	0.56 [0.17, 1.84]	
Subtotal (95% CI)		122		121	23.9%	0.69 [0.27, 1.76]	
Total events	7		10				
Heterogeneity: Chi ² =	0.33, df = 1 (F	P = 0.56)	; I² = 0%				
Test for overall effect:	Z = 0.77 (P =	0.44)					
10.10.2 Mixed							
MRC Allum 2009	21	400	32	402	76.1%	0.66 [0.39, 1.12]	
Subtotal (95% CI)		400		402	76.1%	0.66 [0.39, 1.12]	\bullet
Total events	21		32				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 1.53 (P =	0.13)					
Total (95% CI)		522		523	100.0%	0.67 [0.42, 1.06]	•
Total events	28		42				
Heterogeneity: Chi ² =	0.34, df = 2 (F	P = 0.84)	; I² = 0%				
Test for overall effect:	Z = 1.71 (P =	0.09)					0.01 0.1 1 10 10 Favours pre-op CT Favours surgery alone
Test for subgroup diffe	erences: Chi ²	= 0.01, d	f = 1 (P = 0).93), I² :	= 0%		Favours pre-op CT Favours surgery alone
Insert Note hei	re>						

Figure 76: Postoperative mortality (according to histology subtype)

	Preoperati	ve CT	Surgery	alone		Risk Ratio		F	lisk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	М-Н,	Fixed, 95%	CI	
10.13.1 SCC											
Ancona 2001	1	48	2	48	3.8%	0.50 [0.05, 5.33]				_	
Law 1997	5	74	6	73	11.3%	0.82 [0.26, 2.58]			-		
Nygaard 1992	6	56	5	50	9.9%	1.07 [0.35, 3.30]		_	_		
Subtotal (95% CI)		178		171	25.0%	0.87 [0.41, 1.85]		•			
Total events	12		13								
Heterogeneity: Chi ² =	0.35, df = 2 (F	o = 0.84)	; I² = 0%								
Test for overall effect:	Z = 0.35 (P =	0.72)									
10.13.2 Mixed											
MRC Allum 2009	36	400	40	402	75.0%	0.90 [0.59, 1.39]			-		
Subtotal (95% CI)		400		402	75.0%	0.90 [0.59, 1.39]			•		
Total events	36		40								
Heterogeneity: Not ap	plicable										
Test for overall effect:	Z = 0.46 (P =	0.65)									
Total (95% CI)		578		573	100.0%	0.90 [0.62, 1.30]			•		
Total events	48		53								
Heterogeneity: Chi ² =	0.35, df = 3 (F	P = 0.95)	; I² = 0%				<u> </u>				
Test for overall effect:	Z = 0.57 (P =	0.57)					0.01	0.1 Favours pre-op	1 CT Fourieur	10	100
Test for subgroup diffe	erences: Chi ²	= 0.01. c	f = 1 (P = (0.94), l² :	= 0%			r avours pre-op	GI Favour	s surgery an	JIE

<Insert Note here>

Figure 77: R0 tumour resection rate (according to histology subtype)

0						•				
	Preoperati	ive CT	Surgery	alone		Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	M-H, Fixed, 95% CI		
10.15.1 SCC										
Ancona 2001	37	48	35	48	12.7%	1.06 [0.84, 1.33]		+		
Law 1997	4	74	0	73	0.2%	8.88 [0.49, 162.04]				
Nygaard 1992	22	56	15	50	5.8%	1.31 [0.77, 2.23]				
Schlag 1992a	7	22	10	24	3.5%	0.76 [0.35, 1.66]				
Subtotal (95% CI)		200		195	22.1%	1.14 [0.91, 1.44]		•		
Total events	70		60							
Heterogeneity: Chi ² =	3.63, df = 3 (l	P = 0.30)	; I² = 17%							
Test for overall effect:	Z = 1.13 (P =	0.26)								
10.15.2 Mixed										
MRC Allum 2009	233	400	215	402	77.9%	1.09 [0.96, 1.23]				
Subtotal (95% CI)		400		402	77.9%	1.09 [0.96, 1.23]		•		
Total events	233		215							
Heterogeneity: Not ap	plicable									
Test for overall effect:	Z = 1.36 (P =	= 0.17)								
Total (95% CI)		600		597	100.0%	1.10 [0.99, 1.23]		•		
Total events	303		275							
Heterogeneity: Chi ² =	3.40, df = 4 (l	P = 0.49)	; I² = 0%				0.01	0.1 1	10	10
Test for overall effect:	Z = 1.73 (P =	= 0.08)					0.01		oreoperative	
Test for subgroup diffe	erences: Chi2	= 0.12, d	lf = 1 (P = 0	0.72), l²	= 0%				coperative	01

Test for subgroup differences: Chi² = 0.12, df = 1 (P = 0.72 <Insert Note here>

H.11.3 Comparison 3: Postoperative chemotherapy versus surgery alone

Figure 78:	Dis	ease	e free	su	rviv	al							
	Postoperati	ive CT	Surgery	alone				Hazard Ratio		Hazar	d Ratio		
Study or Subgroup	Events	Total	Events	Total	O-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% C	I I	Exp[(O-E) / V]	, Fixed, 95% CI		
Ando 2003 (1)	0	120	0	122	-8.95	31.1	100.0%	0.75 [0.53, 1.07]		-			
Total (95% CI)		120		122			100.0%	0.75 [0.53, 1.07]		•	1		
Total events	0		0										
Heterogeneity: Not app	olicable												100
Test for overall effect: 2	Z = 1.60 (P = 0	0.11)							0.01 0.1 Favours poste	operative CT	1 10 Favours surgery		100
Footnotes													
(1) number of event no	t reported. Ha	zard ratio	o adjusted	for age,	sex, pe	erformance	status, tun	nour location, pathologic T-stage	e, intramural metas	tasis, patholog	gic N-stage, patho	ologic	

H.11.4 Comparison 4: Perioperative chemotherapy versus preoperative chemotherapy

Figure 79:	Ov	eral	l surv	vival									
	Perioperati	ve CT	Preoperati	ve CT				Hazard Ratio		Haza	ard Ratio		
Study or Subgroup	Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% C	CI	Exp[(O-E) /	V], Fixed, 95% (3	
Zhao 2015(i) (1)	146	173	158	170	-15.96	67.72	100.0%	0.79 [0.62, 1.00]			4		
Total (95% CI)		173		170			100.0%	0.79 [0.62, 1.00]		•	Þ		
Total events	146		158										
Heterogeneity: Not app	licable											10	
Test for overall effect: 2	Z = 1.94 (P =	0.05)							0.01	0.1 Favours perioperative C	Favours preo		100
Footnotes													
(1) number of death=nu	umber entere	d - numb	er survived a	at 5 years	6								

Figure 80: Relapse free survival

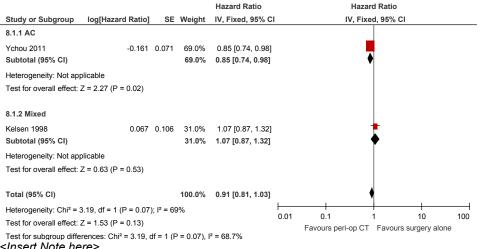
	Perioperativ	ve CT	Preoperativ	ve CT				Hazard Ratio			Hazar	d Ratio		
Study or Subgroup	Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% C	1		Exp[(O-E) / V], Fixed, 95% 0	:	
Zhao 2015(i) (1)	151	173	160	170	-46.22	96.69	100.0%	0.62 [0.51, 0.76]						
Total (95% CI)		173		170			100.0%	0.62 [0.51, 0.76]			•			
Total events	151		160											
Heterogeneity: Not app Test for overall effect: 2		0.00001))						0.01	0. Favours P	1 erioperative CT	1 Favours Preo	10 perative CT	100 Г

Footnotes

(1) number of patients free from relapse = number entered - number of patients with relapse

Comparison 5: Perioperative chemotherapy versus surgery alone H.11.5

Figure 81: **Overall survival**



<Insert Note here>

Figure 82: **Disease free survival**

•													
	Perioperati	ive CT	Surgery	alone				Hazard Ratio			Hazard Ratio	r	
Study or Subgroup	Events	Total	Events	Total	0-Е	Variance	Weight	Exp[(O-E) / V], Fixed, 95% C	:	Exp[(O	-E) / V], Fixed	i, 95% Cl	
8.3.1 AC													
Ychou 2011 (1)	0	113	0	111	-17.36	40.31	27.9%	0.65 [0.48, 0.89]					
Subtotal (95% CI)		113		111			27.9%	0.65 [0.48, 0.89]					
Total events	0		0										
Heterogeneity: Not ap	plicable												
Test for overall effect:	Z = 2.73 (P =	0.006)											
8.3.2 Mixed													
Kelsen 1998 (2)	11	213	11	227	-6.89	104.38	72.1%	0.94 [0.77, 1.13]					
Subtotal (95% CI)		213		227			72.1%	0.94 [0.77, 1.13]			•		
Total events	11		11										
Heterogeneity: Not ap	plicable												
Test for overall effect:	Z = 0.67 (P =	0.50)											
Total (95% CI)		326		338			100.0%	0.85 [0.72, 1.00]			•		
Fotal events	11		11										
Heterogeneity: Chi ² =	3.87, df = 1 (F	o = 0.05);	; l² = 74%						0.01	0.1			1(
Test for overall effect:	Z = 2.02 (P =	0.04)							0.01	U.1 Favours peri-o	n CT Favou	IU Irs surgery ald	
Test for subgroup diffe	erences: Chi2 :	= 3.87, d	f = 1 (P = 0	0.05), I² :	= 74.1%					. atoaio por c	, o. 1400	to cargory are	
Footnotes													
(1) number of disease	free patients	not repoi	rted										
(2) number of natients	with disease	free afte	r 5 vears										

(2) number of patients with disease free after 5 years

<Insert Note here>

Figure 83: Any treatment-related complications

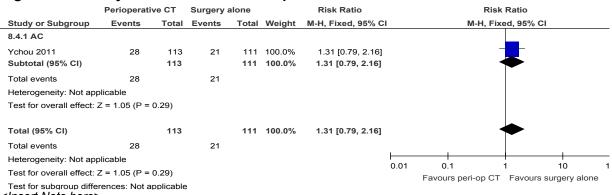


Figure 84: Treatment-related mortality

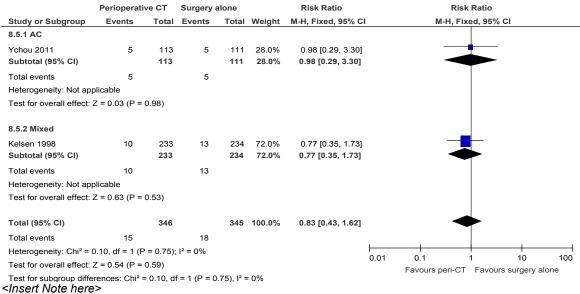
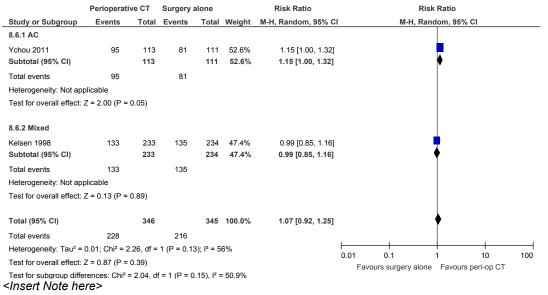


Figure 85: **R0** tumour resection rate



Comparison 6: Preoperative chemoradiotherapy versus preoperative H.11.6 chemotherapy

Figure 86: **Overall survival**

CRT f/by su	urgery	CT f/by su	urgery				Hazard Ratio			Hazard Ratio		
Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% C	1	Exp[(0	О-Е) / V], Fixed,	95% CI	
48	90	46	91	2.42	23.19	100.0%	1.11 [0.74, 1.67]			-		
	90		91			100.0%	1.11 [0.74, 1.67]			•		
48		46										
plicable								 				
Z = 0.50 (P =	0.62)									1 Surgery Favour		100 ery
	Events 48 48 olicable	48 90 90 48	Events Total Events 48 90 46 90 46 48 46 blicable 46	Events Total Events Total 48 90 46 91 90 91 90 91 48 46 91 viicable 90 91	Events Total Events Total O-E 48 90 46 91 2.42 90 91 48 46 48 46 46 46	Events Total Events Total O-E Variance 48 90 46 91 2.42 23.19 90 91 48 46 91 2.42 23.19 48 46 91 5.42 <td< td=""><td>Events Total Events Total O-E Variance Weight 48 90 46 91 2.42 23.19 100.0% 90 91 91 100.0% 100.0% 48 46 46 100.0% 100.0%</td><td>Events Total Events Total O-E Variance Weight Exp[(O-E) / V], Fixed, 95% C 48 90 46 91 2.42 23.19 100.0% 1.11 [0.74, 1.67] 90 91 100.0% 1.11 [0.74, 1.67] 48 46 48 46</td><td>Events Total Events Total O-E Variance Weight Exp[(O-E) / V], Fixed, 95% Cl 48 90 46 91 2.42 23.19 100.0% 1.11 [0.74, 1.67] 90 91 100.0% 1.11 [0.74, 1.67] 48 46 alicable 0.01 0.01 0.01 0.01</td><td>Events Total Events Total O-E Variance Weight Exp[(O-E) / V], Fixed, 95% Cl Exp[(I 48 90 46 91 2.42 23.19 100.0% 1.11 [0.74, 1.67] 90 91 100.0% 1.11 [0.74, 1.67] 48 46 alicable 7 = 0.50 (P = 0.62) 0.01 0.1</td><td>Events Total Events Total O-E Variance Weight Exp[(O-E) / V], Fixed, 95% Cl Exp[(O-E) / V], Fixed, 95% Cl Exp[(O-E) / V], Fixed, 95% Cl 48 90 46 91 2.42 23.19 100.0% 1.11 [0.74, 1.67] Image: Comparison of the system of the syste</td><td>Events Total Events Total O-E Variance Weight Exp[(O-E) / V], Fixed, 95% Cl Exp[(O-E) / V], Fixed, 95% Cl 48 90 46 91 2.42 23.19 100.0% 1.11 [0.74, 1.67] 90 91 100.0% 1.11 [0.74, 1.67] Image: Close of the second se</td></td<>	Events Total Events Total O-E Variance Weight 48 90 46 91 2.42 23.19 100.0% 90 91 91 100.0% 100.0% 48 46 46 100.0% 100.0%	Events Total Events Total O-E Variance Weight Exp[(O-E) / V], Fixed, 95% C 48 90 46 91 2.42 23.19 100.0% 1.11 [0.74, 1.67] 90 91 100.0% 1.11 [0.74, 1.67] 48 46 48 46	Events Total Events Total O-E Variance Weight Exp[(O-E) / V], Fixed, 95% Cl 48 90 46 91 2.42 23.19 100.0% 1.11 [0.74, 1.67] 90 91 100.0% 1.11 [0.74, 1.67] 48 46 alicable 0.01 0.01 0.01 0.01	Events Total Events Total O-E Variance Weight Exp[(O-E) / V], Fixed, 95% Cl Exp[(I 48 90 46 91 2.42 23.19 100.0% 1.11 [0.74, 1.67] 90 91 100.0% 1.11 [0.74, 1.67] 48 46 alicable 7 = 0.50 (P = 0.62) 0.01 0.1	Events Total Events Total O-E Variance Weight Exp[(O-E) / V], Fixed, 95% Cl Exp[(O-E) / V], Fixed, 95% Cl Exp[(O-E) / V], Fixed, 95% Cl 48 90 46 91 2.42 23.19 100.0% 1.11 [0.74, 1.67] Image: Comparison of the system of the syste	Events Total Events Total O-E Variance Weight Exp[(O-E) / V], Fixed, 95% Cl Exp[(O-E) / V], Fixed, 95% Cl 48 90 46 91 2.42 23.19 100.0% 1.11 [0.74, 1.67] 90 91 100.0% 1.11 [0.74, 1.67] Image: Close of the second se

Footnotes

(1) number of death at 3 year = number entered - number of overall survival at 3 years; OS from HR analysis

Figure 87: Any treatment-related complication

	CRT f/by surgery			urgery		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-	H, Fixed, 95%	CI	
Klevebro 2015	42	90	35	91	100.0%	1.21 [0.86, 1.71]					
Total (95% CI)		90		91	100.0%	1.21 [0.86, 1.71]			•		
Total events	42		35								
Heterogeneity: Not ap	plicable						H				
Test for overall effect:	Z = 1.11 (P =	0.27)					0.01 Fav	0.1 ours CRT f/by st	1 Jirgery Favour	10 s CT f/by surge	100 ery

<Insert Note here>

Figure 88: Anastomotic leakage

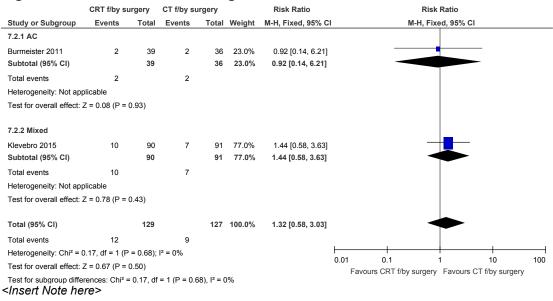


Figure 89: Cardiac complications

-	CRT f/by su	urgery	CT f/by su	urgery		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	1	M-H, Fixed, 95%	CI	
7.10.1 AC											
Burmeister 2011	7	39	6	36	61.1%	1.08 [0.40, 2.90]			_		
Subtotal (95% CI)		39		36	61.1%	1.08 [0.40, 2.90]			$ \rightarrow $		
Total events	7		6								
Heterogeneity: Not app	plicable										
Test for overall effect:	Z = 0.15 (P =	0.88)									
7.10.2 Mixed											
Klevebro 2015	7	90	4	91	38.9%	1.77 [0.54, 5.84]					
Subtotal (95% CI)		90		91	38.9%	1.77 [0.54, 5.84]					
Total events	7		4								
Heterogeneity: Not app	plicable										
Test for overall effect:	Z = 0.94 (P =	0.35)									
Total (95% CI)		129		127	100.0%	1.35 [0.63, 2.88]					
Total events	14		10								
Heterogeneity: Chi ² = (0.40, df = 1 (P	e = 0.53);	l² = 0%								
Test for overall effect:	Z = 0.77 (P =	0.44)					0.01 Fou	0.1	1 surgery Favour	10 CT f/by cura	100
Test for subgroup diffe <insert he<="" note="" td=""><td></td><td>= 0.39, df</td><td>= 1 (P = 0.5</td><td>53), I² = (</td><td>0%</td><td></td><td>Fav</td><td></td><td>Surgery Favour</td><td>s or inby surg</td><td>51 y</td></insert>		= 0.39, df	= 1 (P = 0.5	53), I² = (0%		Fav		Surgery Favour	s or inby surg	51 y

Figure 90: Wound infections

	CRT f/by su	urgery	CT f/by su	urgery		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		Ν	/I-H, Fixed, 95%	CI	
Burmeister 2011	5	39	1	36	100.0%	4.62 [0.57, 37.64]					_
Total (95% CI)		39		36	100.0%	4.62 [0.57, 37.64]					-
Total events	5		1								
Heterogeneity: Not ap	plicable						H		<u> </u>		
Test for overall effect:	Z = 1.43 (P =	0.15)					0.01 Fav	0.1 ours CRT f/by	1 Surgery Favour	10 s CT f/by Surge	100 ery

<Insert Note here>

Figure 91: Any treatment-related mortality

-	-						
(CRT f/by su	irgery	CT f/by su	irgery		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
7.3.1 AC							
Burmeister 2011 (1)	0	39	0	36		Not estimable	
Subtotal (95% CI)		39		36		Not estimable	
Total events	0		0				
Heterogeneity: Not applic	cable						
Test for overall effect: No	ot applicable						
7.3.2 Mixed							
Klevebro 2015 (2)	5	90	2	91	100.0%	2.53 [0.50, 12.69]	
Subtotal (95% CI)		90		91	100.0%	2.53 [0.50, 12.69]	
Total events	5		2				
Heterogeneity: Not applic	cable						
Test for overall effect: Z =	= 1.13 (P = 0	0.26)					
Total (95% CI)		129		127	100.0%	2.53 [0.50, 12.69]	
Total events	5		2				
Heterogeneity: Not applic	cable						0.01 0.1 1 10 1
Test for overall effect: Z =	= 1.13 (P = 0	0.26)					Favours CRT f/by surgery Favours CT f/by surgery
Test for subgroup differen	nces: Not ap	oplicable					
Footnotes							
(1) 30-days postoperative	e mortality						
(2) 90-day mortality							

<Insert Note here>

Figure 92: R0 tumour resection rate

	CRT f/by su	urgery	CT f/by su	urgery		Risk Ratio		F	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	1	М-Н,	Fixed, 95% CI		
7.6.1 AC											
Burmeister 2011	33	39	29	36	65.3%	1.05 [0.85, 1.29]			.		
Subtotal (95% CI)		39		36	65.3%	1.05 [0.85, 1.29]			•		
Total events	33		29								
Heterogeneity: Not app	plicable										
Test for overall effect:	Z = 0.46 (P =	0.64)									
7.6.2 Mixed											
Klevebro 2015	20	25	16	25	34.7%	1.25 [0.88, 1.78]			+		
Subtotal (95% CI)		25		25	34.7%	1.25 [0.88, 1.78]			•		
Total events	20		16								
Heterogeneity: Not app	plicable										
Test for overall effect:	Z = 1.24 (P =	0.22)									
Total (95% CI)		64		61	100.0%	1.12 [0.93, 1.35]			•		
Total events	53		45								
Heterogeneity: Chi ² = 0	0.73, df = 1 (P	e = 0.39);	l² = 0%								
Test for overall effect:	Z = 1.20 (P =	0.23)					0.01	0.1	I 	10 T f/bu auro	100
Test for subgroup diffe <i>Insert Note he</i>		= 0.69, df	= 1 (P = 0.4	41), l² = ()%			Favours CT f/by surg	Jely Favouis Cr	ti i/by suig	Jery

Figure 93: Poor Tumour Regression Grade (TRG >2)

	CRT f/by su	rgery	CT f/by su	rgery		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
7.4.1 AC							
Burmeister 2011 Subtotal (95% CI)	27	39 39	33	36 36	53.1% 53.1%	0.76 [0.60, 0.95] 0.76 [0.60, 0.95]	—
Total events Heterogeneity: Not a	27 pplicable		33				
Test for overall effect		0.02)					
7.4.2 Mixed							
Klevebro 2015 Subtotal (95% CI)	37	90 90	66	91 91	46.9% 46.9%	0.57 [0.43, 0.75] 0.57 [0.43, 0.75]	₩
Total events	37		66				
Heterogeneity: Not a Test for overall effect		0.0001))				
Total (95% CI)		129		127	100.0%	0.66 [0.49, 0.90]	•
Total events	64		99				
Heterogeneity: Tau ² =	= 0.03; Chi ² =	2.88, df	= 1 (P = 0.0	9); l ² = 6	5%	I	
Test for overall effect	: Z = 2.66 (P =	0.008)					0.01 0.1 1 10 10 Favours Preop CRT Favours Preop CT
To at fair and superior diff			-16 A (D	0.4.00.12	CO 70/		Favours Freup Ortin Favours Freup Or

Test for subgroup differences: $Chi^2 = 2.42$, df = 1 (P = 0.12), l² = 58.7%

Comparison 7: Preoperative chemoradiotherapy versus surgery alone H.11.7

Figure 94:	Ove	rall s	Surviv	al (a	acco	raing	to ni	stology subtyp	e)
	CRT f/by s	urgery	Surgery	alone				Hazard Ratio	Hazard Ratio
Study or Subgroup	Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% C	I Exp[(O-E) / V], Fixed, 95% CI
6.25.1 SCC									
Apinop 1994	27	35	31	34	-3.2	14.43	4.9%	0.80 [0.48, 1.34]	
Bass 2014	41	46	50	52	-9.98	22.66	7.7%	0.64 [0.43, 0.97]	
Bosset 1997	96	143	95	139	-1.93	47.75	16.3%	0.96 [0.72, 1.28]	+
Lee 2004	22	51	19	50	-1.31	10.2	3.5%	0.88 [0.48, 1.62]	
Lv 2010	60	80	70	80	-16	32.31	11.0%	0.61 [0.43, 0.86]	
Mariette 2014 (1)	61	98	64	96	-0.38	38.3	13.0%	0.99 [0.72, 1.36]	+
van Hagen 2012	33	41	39	43	-7.85	9.91	3.4%	0.45 [0.24, 0.84]	
Subtotal (95% CI)		494		494			59.8%	0.79 [0.68, 0.92]	♦
Total events	340		368						
Heterogeneity: Chi ² =	10.08, df = 6 ((P = 0.12); l² = 41%						
Test for overall effect:	Z = 3.07 (P =	0.002)							
6.25.2 AC									
Bass 2014	46	58	53	55	-16.33	24.63	8.4%	0.52 [0.35, 0.76]	
van Hagen 2012	116	134	131	141	-11.55	37.02	12.6%	0.73 [0.53, 1.01]	-
Subtotal (95% CI)		192		196			21.0%	0.64 [0.50, 0.82]	•
Total events	162		184						
Heterogeneity: Chi ² =	1.82, df = 1 (F	P = 0.18);	l² = 45%						
Test for overall effect:	Z = 3.55 (P =	0.0004)							
6.25.3 Mixed									
Burmeister 2005 (2)	113	128	118	128	-5.43	46.57	15.9%	0.89 [0.67, 1.19]	+
Tepper 2008 (3)	18	30	22	26	-9.75	9.95	3.4%	0.38 [0.20, 0.70]	_ _
Subtotal (95% CI)		158		154			19.2%	0.76 [0.59, 0.99]	•
Total events	131		140						
Heterogeneity: Chi ² =	6.11. df = 1 (F	P = 0.01);	² = 84%						
Test for overall effect:		-							
	- v	- /							
Total (95% CI)		844		844			100.0%	0.75 [0.67, 0.84]	♦
Total events	633		692						
Heterogeneity: Chi ² =	20.26, df = 10	(P = 0.0	3); I² = 51%	6					
Test for overall effect:	Z = 4.88 (P <	0.00001))						0.01 0.1 1 10 Favours CRT+S Favours S
Test for subgroup diffe	erences: Chi2 :	= 2.24, df	f = 2 (P = 0	.33), I² =	10.8%				

Overall survival (according to histology subtype) Figure 94:

Footnotes

(1) number of death not reported; calculated from survival rate; OS calculated from HR for death

(2) number of death calculated from overall survival rate

(3) number of death calcualted from overall survival rate

Figure 95: Overall survival (according to type of chemotherapy)

· ·gai e eei	••••								······································
	CRT f/by su	urgery	Surgery a	alone				Hazard Ratio	Hazard Ratio
Study or Subgroup	Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% CI	Exp[(O-E) / V], Fixed, 95% Cl
6.26.1 Single drug CT									
Bosset 1997	96	143	95	139	-1.93	47.75	16.2%	0.96 [0.72, 1.28]	
Subtotal (95% CI)		143		139			16.2%	0.96 [0.72, 1.28]	•
Total events	96		95						
Heterogeneity: Not app	licable								
Test for overall effect: 2	Z = 0.28 (P =	0.78)							
6.26.2 Double drug C	т								
Apinop 1994	27	35	31	34	-3.2	14.43	4.9%	0.80 [0.48, 1.34]	
Bass 2014	87	104	103	107	-22.6	47.16	16.0%	0.62 [0.47, 0.82]	
Burmeister 2005 (1)	113	128	118	128	-5.43	46.57	15.8%	0.89 [0.67, 1.19]	-
Lee 2004	22	51	19	50	-1.31	10.2	3.5%	0.88 [0.48, 1.62]	
Lv 2010	60	80	70	80	-16	32.31	11.0%	0.61 [0.43, 0.86]	
Mariette 2014 (2)	61	98	64	96	-0.38	38.3	13.0%	0.99 [0.72, 1.36]	+
Tepper 2008 (3)	18	30	22	26	-9.75	9.95	3.4%	0.38 [0.20, 0.70]	
van Hagen 2012 (4)	150	178	171	188	-33.71	48.12	16.3%	0.50 [0.37, 0.66]	
Subtotal (95% CI)		704		709			83.8%	0.69 [0.61, 0.78]	•
Total events	538		598						
Heterogeneity: Chi ² = 1	8.89, df = 7 (P = 0.00	9); l² = 63%	0					
Test for overall effect: 2	Z = 5.88 (P <	0.00001)							
Total (95% CI)		847		848			100.0%	0.73 [0.65, 0.81]	•
Total events	634		693						
Heterogeneity: Chi ² = 2	23.34, df = 8 (P = 0.00	3); I² = 66%						0.01 0.1 1 10 1
Test for overall effect: 2	Z = 5.49 (P <	0.00001)							Favours CRT+S Favours S
Test for subgroup differ	rences: Chi ² =	= 4.45, df	= 1 (P = 0.	03), I² =	77.5%				

Footnotes

(1) number of death calculated from overall survival rate

(2) number of death not reported; calculated from survival rate; OS calculated from HR for death

(3) number of death calcualted from overall survival rate

(4) calculated number of death

Figure 96: Overall survival (according to type of radiotherapy)

	••••	•		(-					~~J/
	CRT f/by si	urgery	Surgery a	alone				Hazard Ratio	Hazard Ratio
Study or Subgroup	Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% C	I Exp[(O-E) / V], Fixed, 95% CI
6.27.1 =40Gy RT</td <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>									
Apinop 1994	27	35	31	34	-3.2	14.43	4.9%	0.80 [0.48, 1.34]	
Bass 2014	87	104	103	107	-22.6	47.16	16.0%	0.62 [0.47, 0.82]	
Bosset 1997	96	143	95	139	-1.93	47.75	16.2%	0.96 [0.72, 1.28]	+
Burmeister 2005 (1)	113	128	118	128	-5.43	46.57	15.8%	0.89 [0.67, 1.19]	-
Lv 2010	60	80	70	80	-16	32.31	11.0%	0.61 [0.43, 0.86]	
Subtotal (95% CI)		490		488			63.8%	0.77 [0.67, 0.89]	•
Total events	383		417						
Heterogeneity: Chi ² =	7.33, df = 4 (P	e = 0.12);	l² = 45%						
Test for overall effect:	Z = 3.58 (P =	0.0003)							
6.27.2 >40Gy RT									
Lee 2004	22	51	19	50	-1.31	10.2	3.5%	0.88 [0.48, 1.62]	
Mariette 2014 (2)	61	98	64	96	-0.38	38.3	13.0%	0.99 [0.72, 1.36]	+
Tepper 2008 (3)	18	30	22	26	-9.75	9.95	3.4%	0.38 [0.20, 0.70]	
van Hagen 2012 (4)	150	178	171	188	-33.71	48.12	16.3%	0.50 [0.37, 0.66]	-
Subtotal (95% CI)		357		360			36.2%	0.65 [0.54, 0.79]	•
Total events	251		276						
Heterogeneity: Chi ² =	14.21, df = 3 (P = 0.00	3); l² = 79%	b					
Test for overall effect:	Z = 4.37 (P <	0.0001)							
Total (95% CI)		847		848			100.0%	0.73 [0.65, 0.81]	♦
Total events	634		693						
Heterogeneity: Chi ² = 2	23.34, df = 8 (P = 0.00	3); I² = 66%						
Test for overall effect:	Z = 5.49 (P <	0.00001)	1						0.01 0.1 1 10 10 Favours CRT+S Favours S
Test for subgroup diffe	rences: Chi ² =	= 1.80, df	= 1 (P = 0	.18), I² =	44.3%				Tavouis OKT+3 Favouis 3
Footpotes									

Footnotes

(1) number of death calculated from overall survival rate

(2) number of death not reported; calculated from survival rate; OS calculated from HR for death

(3) number of death calcualted from overall survival rate

(4) calculated number of death

Figure 97: Disease free survival (according to type of histology)

	CRT f/by su		Surgery a					Hazard Ratio	Hazard Ratio	
Study or Subgroup	Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% CI	Exp[(O-E) / V], Fixed, 95% Cl	
6.28.1 SCC										
Bosset 1997	80	143	97	139	-19.74	43.84	49.2%	0.64 [0.47, 0.86]		
Lee 2004	0	51	0	50	-0.24	11.82	13.3%	0.98 [0.55, 1.73]		
Mariette 2014 (1)	84	98	89	96	-2.79	33.44	37.5%	0.92 [0.66, 1.29]		
Subtotal (95% CI)		292		285			100.0%	0.77 [0.63, 0.95]	•	
Total events	164		186							
Heterogeneity: Chi ² =	3.31, df = 2 (l	P = 0.19)	; l² = 40%							
Test for overall effect:	Z = 2.41 (P =	0.02)								
Total (95% CI)		292		285			100.0%	0.77 [0.63, 0.95]	◆	
Total events	164		186							
Heterogeneity: Chi ² =	3.31, df = 2 (l	P = 0.19)	; l² = 40%							
Test for overall effect:	Z = 2.41 (P =	0.02)							0.01 0.1 1 10 Favours CRT f/by Sx Favours Sx alo	100
Test for subgroup diff	erences: Not	applicat	ole						Favours CRT I/by Sx Favours Sx alo	lie
Footnotes										

(1) number of death caculated from disease free survival rate; OS from reported HR

Figure 98: Disease free survival (according to type of chemotherapy)

			_							
	CRT f/by su	irgery	Surgery	alone				Hazard Ratio	Hazard Ratio	
Study or Subgroup	Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% CI	Exp[(O-E) / V], Fixed, 95% CI	
6.29.1 Single drug CT	Г									
Bosset 1997	80	143	97	139	-19.74	43.84	49.2%	0.64 [0.47, 0.86]	—	
Subtotal (95% CI)		143		139			49.2%	0.64 [0.47, 0.86]	•	
Total events	80		97							
Heterogeneity: Not ap	plicable									
Test for overall effect:	Z = 2.98 (P =	0.003)								
6.29.2 Double drug C	т									
Lee 2004	0	51	0	50	-0.24	11.82	13.3%	0.98 [0.55, 1.73]	_ _	
Mariette 2014 (1)	84	98	89	96	-2.79	33.44	37.5%	0.92 [0.66, 1.29]	-	
Subtotal (95% CI)		149		146			50.8%	0.94 [0.70, 1.25]		
Total events	84		89							
Heterogeneity: Chi ² =	0.03, df = 1 (l)	P = 0.85); I² = 0%							
Test for overall effect:	Z= 0.45 (P=	0.65)								
Total (95% CI)		292		285			100.0%	0.77 [0.63, 0.95]	◆	
Total events	164		186							
Heterogeneity: Chi ² =	3.31, df = 2 (P = 0.19); l² = 40%							1
Test for overall effect:	Z = 2.41 (P =	0.02)							Favours CRT f/by Sx Favours Sx alone	U
Test for subgroup diff	erences: Chi	r= 3.27,	df = 1 (P =	: 0.07), f	² = 69.49	6			ravours orci noy ox Favours ox alone	
Footnotes										
(1) number of death c	aculated from	n diseas	e free sur	vival rate	e; OS fro	m reported	HR			

<Insert Note here>

Figure 99: Disease free survival (according to type of radiotherapy)

6.30.1 >40Gy RT Bosset 1997 80 143 97 139 -19.74 43.84 49.2% 0.64 [0.47, 0.86] Subtotal (95% CI) 143 139 49.2% 0.64 [0.47, 0.86] • Total events 80 97 97 97 97 Heterogeneity: Not applicable Test for overall effect: Z = 2.98 (P = 0.003) • • 6.30.2 >40Gy RT Lee 2004 0 51 0 50 -0.24 11.82 13.3% 0.98 [0.55, 1.73] Mariette 2014 (1) 84 98 96 -2.79 33.44 37.5% 0.92 [0.66, 1.29] Subtotal (95% CI) 149 146 50.8% 0.94 [0.70, 1.25] • Total events 84 89 Heterogeneity: Chi ² = 0.03, df = 1 (P = 0.85); P = 0% 0% 0.77 [0.63, 0.95] • Total (95% CI) 292 285 100.0% 0.77 [0.63, 0.95] • Total events 164 186 100.0% 0.77 [0.63, 0.95] •	CRT	RT f/by surgery Surg	ery alone		Hazard Ratio	Hazard Ratio
Bosset 1997 80 143 97 139 -19.74 43.84 49.2% 0.64 [0.47, 0.86] Subtotal (95% CI) 143 139 49.2% 0.64 [0.47, 0.86] Total events 80 97 Heterogeneity: Not applicable Test for overall effect: Z = 2.98 (P = 0.003) 6.30.2 >406y RT Lee 2004 0 51 0 50 -0.24 11.82 13.3% 0.98 [0.55, 1.73] Mariette 2014 (1) 84 98 99 -2.79 33.44 37.5% 0.92 [0.66, 1.29] Subtotal (95% CI) 149 146 50.8% 0.94 [0.70, 1.25] • Total events 84 89 Heterogeneity: Chi² = 0.03, df = 1 (P = 0.85); P = 0% • • Total (95% CI) 292 285 100.0% 0.77 [0.63, 0.95] ● Total events 164 186 • • • •	r Subgroup Eve	Events Total Even	ts Total O-E	Variance Weight	Exp[(O-E) / V], Fixed, 95% CI	Exp[(O-E) / V], Fixed, 95% CI
Subtotal (95% CI) 143 139 49.2% 0.64 [0.47, 0.86] Total events 80 97 Heterogeneity: Not applicable Test for overall effect: Z = 2.98 (P = 0.003) 6.30.2 > 406y RT Lee 2004 0 51 0 50 -0.24 11.82 13.3% 0.98 [0.55, 1.73] Mariette 2014 (1) 84 98 96 -2.79 33.44 37.5% 0.92 [0.66, 1.29] Subtotal (95% CI) 149 146 50.8% 0.94 [0.70, 1.25] • Total events 84 89 + + + + Heterogeneity: Chi² = 0.03, df = 1 (P = 0.85); P = 0% Test for overall effect: Z = 0.45 (P = 0.65) • 0.77 [0.63, 0.95] • Total events 164 186 • • • • •	/=40Gy RT					
Heterogeneity: Not applicable Test for overall effect: Z = 2.98 (P = 0.003) 6.30.2 >40Gy RT Lee 2004 0 51 0 -0.24 11.82 13.3% 0.98 [0.55, 1.73] Mariette 2014 (1) 84 98 96 -2.79 33.44 37.5% 0.92 [0.66, 1.29] Subtotal (95% CI) 149 146 50.8% 0.94 [0.70, 1.25] Total events 84 89 Heterogeneity: Chi² = 0.03, df = 1 (P = 0.85); P = 0% 7 = 0.45 (P = 0.65) Total (95% CI) 292 285 100.0% 0.77 [0.63, 0.95] Total events 164 186						₩
Test for overall effect: Z = 2.98 (P = 0.003) 6.30.2 >40Gy RT Lee 2004 0 51 0 50 -0.24 11.82 13.3% 0.98 [0.55, 1.73] Mariette 2014 (1) 84 98 89 96 -2.79 33.44 37.5% 0.92 [0.66, 1.29] Subtotal (95% CI) 149 146 50.8% 0.94 [0.70, 1.25] Total events 84 89 Heterogeneity: Chi ^P = 0.03, df = 1 (P = 0.85); i ^P = 0% Test for overall effect: Z = 0.45 (P = 0.65) Total (95% CI) 292 285 100.0% 0.77 [0.63, 0.95] ● Total events 164 186 164 186 ●	ents	80	37			
6.30.2 >40Gy RT Lee 2004 0 51 0 50 -0.24 11.82 13.3% 0.98 [0.55, 1.73] Mariette 2014 (1) 84 98 89 96 -2.79 33.44 37.5% 0.92 [0.66, 1.29] Subtotal (95% CI) 149 146 50.8% 0.94 [0.70, 1.25] Total events 84 89 Heterogeneity: Chi ² = 0.03, df = 1 (P = 0.85); P = 0% Test for overall effect: Z = 0.45 (P = 0.66) Total events 164 186	eneity: Not applicabl	cable				
Lee 2004 0 51 0 50 -0.24 11.82 13.3% 0.98 [0.55, 1.73] Mariethe 2014 (1) 84 98 96 -2.79 33.44 37.5% 0.92 [0.66, 1.29] Subtotal (95% CI) 149 146 50.8% 0.94 [0.70, 1.25] Total events 84 89 Heterogeneity: Chi² = 0.03, df = 1 (P = 0.85); P = 0% Test for overall effect: Z = 0.45 (P = 0.65) Total events 164 164 186	overall effect: Z = 2.9	= 2.98 (P = 0.003)				
Mariette 2014 (1) 84 98 89 96 -2.79 33.44 37.5% 0.92 [0.66, 1.29] Subtotal (95% CI) 149 146 50.8% 0.94 [0.70, 1.25] Total events 84 89 Heterogeneity: Chi² = 0.03, df = 1 (P = 0.85); i² = 0% Test for overall effect: Z = 0.45 (P = 0.65) Total events 164 164	40Gy RT					
Subtotal (95% CI) 149 146 50.8% 0.94 [0.70, 1.25] Total events 84 89 Heterogeneity: Chi ² = 0.03, df = 1 (P = 0.85); P = 0% 7 Test for overall effect: Z = 0.45 (P = 0.65) 0.92 285 100.0% 0.77 [0.63, 0.95] ♦ Total events 164 186 0.94 0.77 <td>4</td> <td>0 51</td> <td>0 50 -0.24</td> <td>11.82 13.3%</td> <td>0.98 [0.55, 1.73]</td> <td>__</td>	4	0 51	0 50 -0.24	11.82 13.3%	0.98 [0.55, 1.73]	_ _
Total events 84 89 Heterogeneity: Chi² = 0.03, df = 1 (P = 0.85); P = 0% Test for overall effect: Z = 0.45 (P = 0.65) Total (95% Cl) 292 285 100.0% 0.77 [0.63, 0.95] Total events 164 186	2014 (1)	84 98	39 96 -2.79	33.44 37.5%	0.92 [0.66, 1.29]	- + -
Heterogeneity: Chi² = 0.03, df = 1 (P = 0.85); l² = 0% Test for overall effect: Z = 0.45 (P = 0.65) Total (95% Cl) 292 285 100.0% 0.77 [0.63, 0.95] ♦ Total events 164 186	l (95% CI)	149	146	50.8%	0.94 [0.70, 1.25]	+
Test for overall effect: Z = 0.45 (P = 0.65) Total (95% CI) 292 285 100.0% 0.77 [0.63, 0.95] ♦ Total events 164 186	ents	84	39			
Total (95% CI) 292 285 100.0% 0.77 [0.63, 0.95] ♦ Total events 164 186	eneity: Chi² = 0.03, c	03, df = 1 (P = 0.85); l ² = 0	1%			
Total events 164 186	overall effect: Z = 0.4	= 0.45 (P = 0.65)				
	5% CI)	292	285	100.0%	0.77 [0.63, 0.95]	•
	ents í	164 1	36			
Heterogeneity: Chi ² = 3.31, df = 2 (P = 0.19); l ² = 40%	eneity: Chi² = 3.31, c	31, df = 2 (P = 0.19); l ² = 4	0%			0.01 0.1 1 10 100
	overall effect: Z = 2.4	= 2.41 (P = 0.02)				Favours CRT f/by Sx Favours Sx alone
Test for subgroup differences: Chi ² = 3.27, df = 1 (P = 0.07), l ² = 69.4%	subgroup difference	ences: Chi ² = 3.27, df = 1	(P = 0.07), I ² = 69.4 ⁴	%		avours or they ox Tavours ox alone
Footnotes	es					

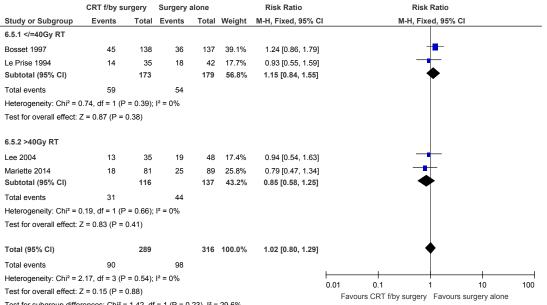
(1) number of death caculated from disease free survival rate; OS from reported HR

Figure 100: Any treatment-related complication (according to type of chemotherapy)

J	,						
	CRT f/by s	urgery	Surgery	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	CI M-H, Random, 95% CI
6.4.1 Single CT							
Bosset 1997	45	138	36	137	41.5%	1.24 [0.86, 1.79]	ı +∎-
Subtotal (95% CI)		138		137	41.5%	1.24 [0.86, 1.79]	i 🔶
Total events	45		36				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 1.15 (P =	0.25)					
6.4.2 Doublet CT							
Le Prise 1994	14	35	18	42	19.7%	0.93 [0.55, 1.59]	
Lee 2004	13	35	19	48	18.4%	0.94 [0.54, 1.63]	J — — — — — — — — — — — — — — — — — — —
Mariette 2014	18	81	25	89	20.4%	0.79 [0.47, 1.34]	
Subtotal (95% CI)		151		179	58.5%	0.88 [0.65, 1.20]	↓ ◆
Total events	45		62				
Heterogeneity: Tau ² =	0.00; Chi ² = 0).26, df =	2 (P = 0.88	3); I² = 0	%		
Test for overall effect:	Z = 0.79 (P =	0.43)					
Total (95% CI)		289		316	100.0%	1.02 [0.80, 1.29]	⊥ ♦
Total events	90		98				
Heterogeneity: Tau ² =	0.00; Chi ² = 2	2.17, df =	3 (P = 0.54	4); I² = 0	%		
Test for overall effect:	Z = 0.14 (P =	0.89)					0.01 0.1 1 10 1 Favours CRT f/by surgery Favours surgery alone
Test for subgroup diffe	erences: Chi ² :	= 1.92, df	= 1 (P = 0	.17), l² =	47.9%		r avours or ring surgery Favours surgery alone

<Insert Note here>

Figure 101: Any treatment-related complication (according to type of radiotherapy)



Test for subgroup differences: Chi² = 1.42, df = 1 (P = 0.23), I² = 29.6%

Figure 102: Treatment-related morbidity: Anastomotic leakage (according to type of histology)

	0,						
	CRT f/by su	urgery	Surgery	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	CI M-H, Fixed, 95% CI
6.1.1 SCC							
Apinop 1994	1	26	2	34	16.2%	0.65 [0.06, 6.83]	
Le Prise 1994	5	35	3	42	25.5%	2.00 [0.51, 7.79]	
Lv 2010	1	80	0	80	4.7%	3.00 [0.12, 72.56]	· · · · · · · · · · · · · · · · · · ·
Mashhadi 2015	0	50	1	50	14.0%	0.33 [0.01, 7.99]	• • • • • • • • • • • • • • • • • • •
Natsugo 2006	4	20	4	23	34.8%	1.15 [0.33, 4.01]	
Subtotal (95% CI)		211		229	95.3%	1.26 [0.58, 2.74]	•
Total events	11		10				
Heterogeneity: Chi ² = ²	1.72, df = 4 (P	= 0.79);	l² = 0%				
Test for overall effect:	Z = 0.59 (P =	0.55)					
6.1.2 Mixed							
Tepper 2008	2	26	0	26	4.7%	5.00 [0.25, 99.34]	
Subtotal (95% CI)		26		26	4.7%	5.00 [0.25, 99.34]	
Total events	2		0				
Heterogeneity: Not app	olicable						
Test for overall effect:	Z = 1.06 (P =	0.29)					
Total (95% CI)		237		255	100.0%	1.44 [0.69, 3.01]	-
Total events	13		10				
Heterogeneity: Chi ² = 2	2.47, df = 5 (P	= 0.78);	l² = 0%				
Test for overall effect:	Z = 0.97 (P =	0.33)					0.01 0.1 1 10 100
Test for subgroup diffe		= 0.76, df	= 1 (P = 0	.38), I² =	0%		Favours CRT f/by surgery Favours surgery alone

<Insert Note here>

Figure 103: Treatment-related morbidity: Anastomotic leakage (according to type of radiotherapy)

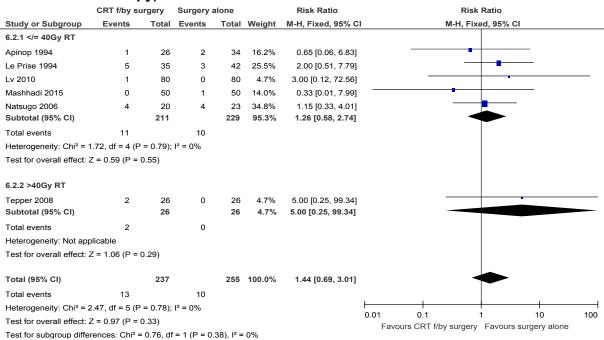


Figure 104: Treatment-related morbidity: Haemorrhage (>300 ml)

	CRT f/by su	rgery	Surgery	alone		Risk Ratio		Risk	Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fix	ed, 95% Cl		
Lv 2010	8	80	2	80	100.0%	4.00 [0.88, 18.26]					
Total (95% CI)		80		80	100.0%	4.00 [0.88, 18.26]					
Total events	8		2								
Heterogeneity: Not ap Test for overall effect:	•	0.07)					0.01	0.1 avours CT f/by surgery	1 Favours sur	10 gery alone	100

Figure 105: Treatment-related morbidity: Stenosis

	CRT f/by su	urgery	Surgery	alone		Risk Ratio			Risk Ratio)	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		1	VI-H, Fixed, 95	% CI	
Lv 2010	2	80	1	80	100.0%	2.00 [0.19, 21.62]		_			
Total (95% CI)		80		80	100.0%	2.00 [0.19, 21.62]		_			
Total events	2		1								
Heterogeneity: Not ap	plicable										
Test for overall effect:	Z = 0.57 (P =	0.57)					0.01 Fav	0.1 ours CRT f/by	surgery Favo	10 ours surgery alon	100 Ie

Figure 106: Treatment-related mortality

	CRT f/by su	urgery	Surgery	alone		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% Cl	
6.15.1 SCC								
Apinop 1994	5	35	5	34	29.7%	0.97 [0.31, 3.06]	_	
Bosset 1997	18	142	5	137	29.8%	3.47 [1.33, 9.09]		
Le Prise 1994	3	39	3	42	16.9%	1.08 [0.23, 5.02]		
Lee 2004	2	51	1	48	6.0%	1.88 [0.18, 20.09]		
Lv 2010	3	80	0	80	2.9%	7.00 [0.37, 133.36]		
Natsugo 2006	1	22	0	23	2.9%	3.13 [0.13, 72.99]	· · · · · · · · · · · · · · · · · · ·	—
Subtotal (95% CI)		369		364	88.1%	2.17 [1.20, 3.91]	•	
Total events	32		14					
Heterogeneity: Chi ² = 4	4.27, df = 5 (P	e = 0.51);	l² = 0%					
Test for overall effect:	Z = 2.57 (P =	0.01)						
6.15.2 Mixed								
Tepper 2008	1	28	1	26	6.1%	0.93 [0.06, 14.09]		
Subtotal (95% CI)		28		26	6.1%	0.93 [0.06, 14.09]		
Total events	1		1					
Heterogeneity: Not app	olicable							
Test for overall effect:	Z = 0.05 (P =	0.96)						
6.15.3 Unknown								
Bagheri 2012	1	20	1	20	5.8%	1.00 [0.07, 14.90]		
Subtotal (95% CI)		20		20	5.8%	1.00 [0.07, 14.90]		
Total events	1		1					
Heterogeneity: Not app	olicable							
Test for overall effect:	Z = 0.00 (P =	1.00)						
Total (95% CI)		417		410	100.0%	2.03 [1.16, 3.55]	◆	
Total events	34		16					
Heterogeneity: Chi ² = 4	4.77, df = 7 (P	e = 0.69);	l² = 0%				⊢ ⊢ ⊢ ⊢	
Test for overall effect:							0.01 0.1 1 10	100
Test for subgroup diffe	rences: Chi ² =	,	= 2 (P = 0	.73), I² =	0%		Favours CRT f/by surgery Favours surgery alone	

Figure 107: Treatment-related mortality (according to type of chemotherapy)

	CRT f/by su	urgery	Surgery a	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	M-H, Random, 95% Cl
6.16.1 Single drug CT							
Bosset 1997	18	142	5	137	36.9%	3.47 [1.33, 9.09]	
Subtotal (95% CI)		142		137	36.9%	3.47 [1.33, 9.09]	\bullet
Total events	18		5				
Heterogeneity: Not app	licable						
Test for overall effect: Z	2 = 2.54 (P =	0.01)					
6.16.2 Double drug C1	r						
Apinop 1994	5	35	5	34	26.0%	0.97 [0.31, 3.06]	
Bagheri 2012	1	20	1	20	4.7%	1.00 [0.07, 14.90]	
Le Prise 1994	3	39	3	42	14.4%	1.08 [0.23, 5.02]	
Lee 2004	2	51	1	48	6.1%	1.88 [0.18, 20.09]	
Lv 2010	3	80	0	80	3.9%	7.00 [0.37, 133.36]	
Natsugo 2006	1	22	0	23	3.4%	3.13 [0.13, 72.99]	
Tepper 2008	1	28	1	26	4.6%	0.93 [0.06, 14.09]	
Subtotal (95% CI)		275		273	63.1%	1.28 [0.61, 2.66]	\bullet
Total events	16		11				
Heterogeneity: Tau ² = 0	0.00; Chi² = 2	.12, df =	6 (P = 0.91); I² = 0°	%		
Test for overall effect: Z	2 = 0.65 (P =	0.52)					
Total (95% CI)		417		410	100.0%	1.85 [1.03, 3.31]	◆
Total events	34		16				
Heterogeneity: Tau ² = 0	0.00; Chi² = 4	.77, df =	7 (P = 0.69	9); l² = 09	%		
Test for overall effect: Z	z = 2.06 (P =	0.04)					0.01 0.1 1 10 10 Favours CRT f/by surgery Favours surgery alone
Test for subgroup differ	ences: Chi ² =	= 2.62, df	= 1 (P = 0	.11), l² =	61.9%		r avours on inby surgery Favours surgery alone

<Insert Note here>

Figure 108: Treatment-related mortality (according to type of radiotherapy)

	CRT f/by s	urgery	Surgery	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% Cl
6.17.1 =40Gy RT</td <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>							
Apinop 1994	5	35	5	34	29.7%	0.97 [0.31, 3.06]	+
Bagheri 2012	1	20	1	20	5.8%	1.00 [0.07, 14.90]	
Bosset 1997	18	142	5	137	29.8%	3.47 [1.33, 9.09]	
Le Prise 1994	3	39	3	42	16.9%	1.08 [0.23, 5.02]	_
Lv 2010	3	80	0	80	2.9%	7.00 [0.37, 133.36]	
Natsugo 2006	1	22	0	23	2.9%	3.13 [0.13, 72.99]	
Subtotal (95% CI)		338		336	87.9%	2.11 [1.17, 3.82]	•
Total events	31		14				
Heterogeneity: Chi ² = 4	4.51, df = 5 (F	= 0.48);	l² = 0%				
Test for overall effect: 2	Z = 2.47 (P =	0.01)					
6.17.2 >40Gy RT							
Lee 2004	2	51	1	48	6.0%	1.88 [0.18, 20.09]	
Tepper 2008	1	28	1	26	6.1%	0.93 [0.06, 14.09]	
Subtotal (95% CI)		79		74	12.1%	1.40 [0.24, 8.16]	
Total events	3		2				
Heterogeneity: Chi ² = 0).15, df = 1 (P	= 0.70);	l² = 0%				
Test for overall effect: 2	Z = 0.38 (P =	0.71)					
Total (95% CI)		417		410	100.0%	2.03 [1.16, 3.55]	◆
Total events	34		16				
Heterogeneity: Chi ² = 4	4.77, df = 7 (F	= 0.69);	l² = 0%				
Test for overall effect:	Z = 2.47 (P =	0.01)					0.01 0.1 1 10 1 Favours CRT f/by surgery Favours surgery alone
Test for subgroup diffe		= 0.19, df	= 1 (P = 0	.67), l² =	0%		r avours or r ing surgery if avours surgery alone

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	CRT f/by su	urgery	Surgery	alone		Risk Ratio		Risk	Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 90% Cl	1	M-H, Rano	dom, 90% Cl
6.12.1 SCC									
Bosset 1997	29	112	0	94	0.3%	49.60 [4.80, 512.16]			
Le Prise 1994	5	39	1	47	0.5%	6.03 [1.03, 35.24]			
Lee 2004	35	35	42	48	16.9%	1.14 [1.03, 1.25]			•
Lv 2010	76	80	64	80	16.8%	1.19 [1.07, 1.31]			
Mariette 2014	76	81	82	89	17.7%	1.02 [0.95, 1.09]			*
Subtotal (90% CI)		347		358	52.2%	1.18 [0.94, 1.48]			•
Total events	221		189						
Heterogeneity: Tau ² =	0.06; Chi² = 4	2.24, df =	= 4 (P < 0.0	00001); I	² = 91%				
Test for overall effect:	Z = 1.21 (P =	0.23)							
6.12.2 AC									
Zhao 2015(ii)	36	36	32	40	15.5%	1.24 [1.09, 1.42]			*
Subtotal (90% CI)		36		40	15.5%	1.24 [1.09, 1.42]			•
Total events	36		32						
Heterogeneity: Not app	olicable								
Test for overall effect:	Z = 2.66 (P =	0.008)							
6.12.3 Mixed									
Burmeister 2005	103	128	76	128	15.3%	1.36 [1.18, 1.56]			+
van Hagen 2012	148	161	111	161	17.0%	1.33 [1.21, 1.47]			
Subtotal (90% CI)		289		289	32.3%	1.34 [1.24, 1.45]			•
Total events	251		187						
Heterogeneity: Tau ² =	0.00; Chi² = 0	.03, df =	1 (P = 0.87	7); l² = 0	%				
Test for overall effect:	Z = 6.12 (P <	0.00001)							
Total (90% CI)		672		687	100.0%	1.23 [1.08, 1.40]			•
Total events	508		408						
Heterogeneity: Tau ² =	0.03; Chi² = 5	1.49, df =	= 7 (P < 0.0)0001); I	² = 86%			+	+ +
Test for overall effect:	Z = 2.60 (P =	0.009)					0.01	0.1	1 10 Favours CRT f/by surge
Test for subgroup diffe Insert Note here		= 1.17, df	= 2 (P = 0	.56), l² =	: 0%			r avours surgery alone	r avours or r indy surge

Figure 109: R0 tumour resection rate (according to type of histology)

Figure 110: R0 tumour resection rate (according to type of chemotherapy)

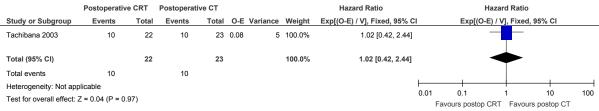
	CRT f/by su	urgery	Surgery	alone		Risk Ratio		Risk Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 90% Cl		М-Н,	Random, 90% Cl		
6.13.1 Single drug CT											
Bosset 1997	29	112	0	94	0.3%	49.60 [4.80, 512.16]					
Subtotal (90% CI)		112		94	0.3%	49.60 [4.80, 512.16]			-		
Total events	29		0								
Heterogeneity: Not app	licable										
Test for overall effect: 2	Z = 2.75 (P =	0.006)									
6.13.2 Double drug C	г										
Burmeister 2005	103	128	76	128	15.3%	1.36 [1.18, 1.56]			-		
Le Prise 1994	5	39	1	47	0.5%	6.03 [1.03, 35.24]					_
Lee 2004	35	35	42	48	16.9%	1.14 [1.03, 1.25]			•		
Lv 2010	76	80	64	80	16.8%	1.19 [1.07, 1.31]			•		
Mariette 2014	76	81	82	89	17.7%	1.02 [0.95, 1.09]			- †		
van Hagen 2012	148	161	111	161	17.0%	1.33 [1.21, 1.47]			•		
Zhao 2015(ii)	36	36	32	40	15.5%	1.24 [1.09, 1.42]			-		
Subtotal (90% CI)		560		593	99.7%	1.21 [1.09, 1.33]			♦		
Total events	479		408								
Heterogeneity: Tau ² = (0.02; Chi² = 2	9.01, df =	= 6 (P < 0.0	0001); l²	= 79%						
Test for overall effect: 2	Z = 3.14 (P =	0.002)									
Total (90% CI)		672		687	100.0%	1.23 [1.08, 1.40]			•		
Total events	508		408								
Heterogeneity: Tau ² = (0.03; Chi² = 5	1.49, df =	= 7 (P < 0.0	00001); I	l² = 86%						
Test for overall effect: 2	Z = 2.60 (P =	0.009)					0.01	0.1 Favours surgery a		10 2T f/by sure	1011/
Test for subaroun diffe	concoc: Chi2 -	- 6 95 df	- 1 (P - 0	0001 12	- 95 4%			avours surgery a	ione ravouis or	vi in by surg	JGI Y

Figure 111:	R0 resection rate (according to type of radiotherapy)
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	CRT f/by s	urgery	Surgery	alone		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 90% C	M-	H, Random, 90% Cl
6.14.1 =40Gy RT</td <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>								
Bosset 1997	29	112	0	94	0.3%	49.60 [4.80, 512.16]		
Burmeister 2005	103	128	76	128	15.3%	1.36 [1.18, 1.56]		-
Le Prise 1994	5	39	1	47	0.5%	6.03 [1.03, 35.24]		
Lv 2010	76	80	64	80	16.8%	1.19 [1.07, 1.31]		•
Subtotal (90% CI)		359		349	32.9%	1.49 [1.01, 2.17]		\blacklozenge
Total events	213		141					
Heterogeneity: Tau ² = 0	0.11; Chi² = 2	3.08, df =	= 3 (P < 0.0	0001); I²	= 87%			
Test for overall effect: 2	<u>z</u> = 1.71 (P =	0.09)						
6.14.2 >40Gy RT								
Lee 2004	35	35	42	48	16.9%	1.14 [1.03, 1.25]		•
Mariette 2014	76	81	82	89	17.7%	1.02 [0.95, 1.09]		•
van Hagen 2012	148	161	111	161	17.0%	1.33 [1.21, 1.47]		
Zhao 2015(ii)	36	36	32	40	15.5%	1.24 [1.09, 1.42]		*
Subtotal (90% CI)		313		338	67.1%	1.17 [1.04, 1.32]		•
Total events	295		267					
Heterogeneity: Tau ² = (0.02; Chi² = 1	9.42, df =	= 3 (P = 0.0	0002); I²	= 85%			
Test for overall effect: 2	Z = 2.14 (P =	0.03)						
Total (90% CI)		672		687	100.0%	1.23 [1.08, 1.40]		•
Total events	508		408					
Heterogeneity: Tau ² = (0.03; Chi² = 5	1.49, df =	= 7 (P < 0.0	00001); I	² = 86%			
Test for overall effect: 2	Z = 2.60 (P =	0.009)					0.01 0.1	1 10 alone Favours CRT f/by su
Test for subgroup differ		= 0.95, df	= 1 (P = 0	.33), l² =	: 0%		Favours surgery	aione Favouis CRT 1/Dy St

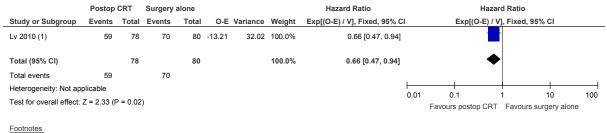
H.11.8 Comparison 8: Postoperative chemoradiotherapy versus postoperative chemotherapy

Figure 112: Overall survival



H.11.9 Comparison 9: Postoperative chemoradiotherapy versus surgery alone

Figure 113: Overall survival



(1) number of death = number entered - number survived

Figure 114: Treatment-related mortality

	Surgery followed	Surgery alone			Risk Ratio	Risk Ratio						
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		N	I-H, Fix	ed, 95% Cl		
Lv 2010 (1)	0	78	0	80		Not estimable						
Total (95% CI)		78		80		Not estimable						
Total events	0		0									
Heterogeneity: Not appl	cable						H			+		
Test for overall effect: N	ot applicable						0.01	0.1 Favours posto	p CRT	1 Favours s	10 urgery ald	100 ne
Footnotes												
(1) no death in either an	n											

Figure 115: Radical resection rate

	Surgery followed	by CRT	Surgery	alone		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-	-H, Fixed, 95% (CI	
Lv 2010	61	78	64	80	100.0%	0.98 [0.83, 1.15]					
Total (95% CI)		78		80	100.0%	0.98 [0.83, 1.15]			•		
Total events	61		64								
Heterogeneity: Not ap	plicable										100
Test for overall effect:	Z = 0.28 (P = 0.78)						0.01 Fav	0.1 ours surgery f/b	y CRT Favours	10 s surgery alone	100 e

H.12 Gastric Cancer

What is the optimal choice of chemotherapy of chemoradiotherapy in relation to surgical treatment for gastric cancer?

H.12.1 Post-operative chemoradiotherapy versus post-operative chemotherapy

Figure 116: Overall survival

				Hazard Ratio			Hazaro	l Ratio	
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Fixed, 95% C			IV, Fixed	l, 95% Cl	
Bamias 2010	0.18	0.23	15.8%	1.20 [0.76, 1.88]			_	-	
Kim 2012	-0.14	0.33	7.7%	0.87 [0.46, 1.66]					
Kwon 2010	-0.11	0.43	4.5%	0.90 [0.39, 2.08]					
Lee 2012	0.12	0.19	23.2%	1.13 [0.78, 1.64]			_	-	
Yu 2012	-0.76	0.37	6.1%	0.47 [0.23, 0.97]					
Zhu 2012	-0.21	0.14	42.7%	0.81 [0.62, 1.07]			-		
Total (95% CI)			100.0%	0.91 [0.76, 1.09]			•	,	
Heterogeneity: Chi ² =	6.63, df = 5 (P = 0.25)	; ² = 2	25%		 				<u> </u>
Test for overall effect:	7 = 1.04 (P = 0.20)				0.01	0.1	1	10	100
	$z = 1.04 (r^2 = 0.30)$				Fa	avours [pos	st-op CRT]	Favours [post-op C	T]

Figure 117: Disease-free survival

				Hazard Ratio		Hazard	d Ratio	
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Fixed, 95% CI Year	r	IV, Fixed	d, 95% Cl	
Bamias 2010	0.04	0.22	14.0%	1.04 [0.68, 1.60] 2010)		-	
Kwon 2010	-0.56	0.46	3.2%	0.57 [0.23, 1.41] 2010)		<u> </u>	
Zhu 2012	-0.3	0.14	34.6%	0.74 [0.56, 0.97] 2012	2	+		
Yu 2012	-0.74	0.32	6.6%	0.48 [0.25, 0.89] 2012	2	_ 		
Kim 2012	-0.36	0.31	7.1%	0.70 [0.38, 1.28] 2012	2		_	
Lee 2012	-0.3	0.14	34.6%	0.74 [0.56, 0.97] 2012	2	-		
Total (95% CI)			100.0%	0.75 [0.63, 0.88]		•		
Heterogeneity: Chi ² = 4	4.63, df = 5 (P = 0.46)); l² = (0%		<u>⊢</u>			
Test for overall effect:	Z = 3.57 (P = 0.0004))			0.01	0.1 Favours [post-op CRT]	1 10 Favours [post-op CT]	100

Figure 118: Treatment-related morbidity: grade 3-4 neutropenia

	Post-op	CRT	Post-op	р СТ		Risk Ratio		Ri	sk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	M-H, F	ixed, 95% (CI	
Bamias 2010	17	71	14	70	10.8%	1.20 [0.64, 2.24]					
Kwon 2010	15	31	5	30	3.9%	2.90 [1.21, 6.99]					
Lee 2012	110	230	92	228	70.9%	1.19 [0.96, 1.46]					
Yu 2012	9	34	6	34	4.6%	1.50 [0.60, 3.75]		-			
Zhu 2012	14	186	12	165	9.8%	1.03 [0.49, 2.17]		_	-		
Total (95% CI)		552		527	100.0%	1.25 [1.04, 1.51]			•		
Total events	165		129								
Heterogeneity: Chi ² =	4.21, df = 4	+ (P = 0.	38); l² = 5	%			—				
Test for overall effect:	Z = 2.40 (F	P = 0.02	1				0.01 Fav	0.1 ours [post-op CR	1 T] Favours	10 post-op CT [100 []

H.12.2 Post-operative chemotherapy versus surgery alone

Figure 119: Overall survival

				Hazard Ratio			Haz	ard Rat	io	
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Random, 95% CI	Year		IV, Ran	dom, 9	5% CI	
Neri 2001	-0.42	0.14	21.1%	0.66 [0.50, 0.86]	2001		-	-		
Chipponi 2004	-0.01	0.17	17.6%	0.99 [0.71, 1.38]	2004			+		
Bouche 2005	-0.3	0.16	18.7%	0.74 [0.54, 1.01]	2005		-	•		
Di Constanzo 2008	-0.11	0.17	17.6%	0.90 [0.64, 1.25]	2008		-	-		
Bang 2012	-0.54	0.11	25.0%	0.58 [0.47, 0.72]	2012		-			
Total (95% CI)			100.0%	0.74 [0.61, 0.90]			•			
Heterogeneity: Tau ² =	0.03; Chi ² = 9.29, df =	= 4 (P	= 0.05); l ²	= 57%		H		<u> </u>		
Test for overall effect:	Z = 2.99 (P = 0.003)					0.01	0.1 Favours [Post-op C]	1] Favo	10 ours [surgery alone]	100

Figure 120: Disease-free survival

				Hazard Ratio				Hazard	Ratio		
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Fixed, 95% Cl	Year			IV, Fixed	, 95% CI		
Neri 2001	0	0		Not estimable	2001						
Chipponi 2004	0	0		Not estimable	2004						
Bouche 2005	-0.36	0.16	29.4%	0.70 [0.51, 0.95]	2005						
Di Constanzo 2008	-0.08	0.17	26.0%	0.92 [0.66, 1.29]	2008			-	_		
Bang 2012	-0.42	0.13	44.5%	0.66 [0.51, 0.85]	2012			-			
Total (95% CI)			100.0%	0.73 [0.62, 0.87]				•			
Heterogeneity: Chi ² =	2.64, df = 2 (P = 0.27)); I ² = 2	24%			H				+	
Test for overall effect:	Z = 3.62 (P = 0.0003))				0.01 Fav	0.1 vours [post-op	1 chemo]	Favours [su	10 rgery alone	100]

Figure 121: Treatment-related morbidity: any grade 3-4 toxicity

	Post-op	o CT	Surgery	alone		Risk Ratio			Risk	Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl			M-H, Fix	ed, 95% CI		
Bang 2012	279	496	30	478	100.0%	8.96 [6.28, 12.78]				-	-	
Total (95% CI)		496		478	100.0%	8.96 [6.28, 12.78]					•	
Total events	279		30									
Heterogeneity: Not ap	olicable						0.01	0	1	1	10	100
Test for overall effect:	Z = 12.11	(P < 0.0	00001)				0.01		oost-op chemo]	Favours [surg		100

Figure 122: Treatment-related morbidity: grade 3-4 neutropenia

			Surgery alone			Risk Ratio	Risk Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fix	ed, 95% Cl		
Bang 2012	107	496	1	478	100.0%	103.12 [14.45, 735.80]					
Total (95% CI)		496		478	100.0%	103.12 [14.45, 735.80]					
Total events	107		1								
Heterogeneity: Not ap	plicable										4000
Test for overall effect:	Z = 4.62 (I	⊃ < 0.00	0001)				0.001 Favours	0.1 [post-op chemo]	1 10 Favours [su	urgery alone]	1000

Figure 123: Treatment-related mortality

	Post-op	о СТ	Surgery a	alone		Risk Ratio		Risk	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	M-H, Fixe	ed, 95% Cl	
Bouche 2005	2	127	1	133	50.0%	2.09 [0.19, 22.81]				
Chipponi 2004	4	93	0	103	24.3%	9.96 [0.54, 182.49]				
Di Constanzo 2008	1	130	0	128	25.8%	2.95 [0.12, 71.85]				
Total (95% CI)		350		364	100.0%	4.22 [0.91, 19.59]				
Total events	7		1							
Heterogeneity: Chi ² =	0.71, df = 2	2 (P = 0	.70); l² = 09	%			H			
Test for overall effect:	Z = 1.84 (I	P = 0.07	7)				0.01	0.1 Favours post-op CT	1 10 Favours surge	

H.12.3 Pre-operative chemotherapy versus surgery alone

Figure 124: Overall survival

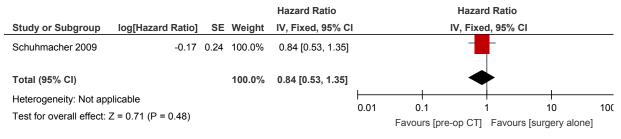


Figure 125: Disease-free survival

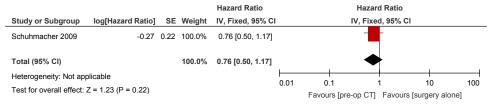


Figure 126: Death at the end of follow-up

	Pre-op cl	nemo	Surgery a	alone		Risk Ratio			Ris	k Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year		M-H, Fi	xed, 95% C	I	
Wang 2000	18	30	23	30	25.9%	0.78 [0.55, 1.11]	2000		-	₽┤		
Kobayashi 2000	34	91	29	80	34.7%	1.03 [0.70, 1.53]	2000		-	• -		
Schuhmacher 2009	32	72	35	72	39.4%	0.91 [0.64, 1.30]	2009		-	•		
Total (95% CI)		193		182	100.0%	0.92 [0.74, 1.14]				•		
Total events	84		87									
Heterogeneity: Chi ² =	1.13, df = 2	(P = 0.5	57); I ² = 0%							+		
Test for overall effect:	Z = 0.75 (P	= 0.45)						0.01	0.1 Favours [pre-op chemo	Favours	10 [surgery alone]	100 e]

Figure 127: Treatment-related mortality: operative mortality

	Pre-op cl	hemo	Surgery	alone		Risk Ratio	Ris	k Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fi	xed, 95% Cl	
Schuhmacher 2009	3	70	1	68	100.0%	2.91 [0.31, 27.33]			-
Total (95% CI)		70		68	100.0%	2.91 [0.31, 27.33]			-
Total events	3		1						
Heterogeneity: Not ap	plicable					F	.01 0.1	+ +	100
Test for overall effect:	Z = 0.94 (P	= 0.35)				0.	.01 0.1 Favours [pre-op CT	1 10] Favours [surgery ale	100 one]

Figure 128: Treatment-related morbidity: anastomotic leakage

	Pre-op ch	nemo	Surgery	alone	Risk Ratio			Risk Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	Year			M-H, Fixed, 95	% CI	
Schuhmacher 2009	3	70	2	68	100.0%	1.46 [0.25, 8.45]	2009					
Imano 2010	0	47	0	16		Not estimable	2010					
Total (95% CI)		117		84	100.0%	1.46 [0.25, 8.45]						
Total events	3		2									
Heterogeneity: Not ap	plicable							H				
Test for overall effect:	Z = 0.42 (P	= 0.67)						0.01	0.1 Favours [pre-op	1 chemo] Favo	10 urs [surgery alo	100 ne]

Figure 129: Treatment-related morbidity: surgical site infection

	Pre-op ch	nemo	Surgery	alone		Risk Ratio			Ris	k Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	Year		M-H, F	xed, 95%	CI	
Schuhmacher 2009	2	70	1	68	57.9%	1.94 [0.18, 20.93]	2009					
Imano 2010	1	47	0	16	42.1%	1.06 [0.05, 24.86]	2010			•		
Total (95% CI)		117		84	100.0%	1.57 [0.24, 10.29]						
Total events	3		1									
Heterogeneity: Chi ² =	0.09, df = 1	(P = 0.7	'6); l² = 0%							+		
Test for overall effect:	Z = 0.47 (P	= 0.64)						0.01	0.1 Favours [pre-op chemo	1] Favou	10 Irs [surgery alon	100 ne]

Figure 130: Treatment-related morbidity: any operative complication

	Pre-op ch	nemo	Surgery	alone		Risk Ratio			Risk	Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl			M-H, Fixe	ed, 95% Cl		
Schuhmacher 2009	19	70	11	68	100.0%	1.68 [0.86, 3.26]			-			
Total (95% CI)		70		68	100.0%	1.68 [0.86, 3.26]						
Total events	19		11									
Heterogeneity: Not ap	plicable						H					<u> </u>
Test for overall effect:	Z = 1.53 (P	= 0.13)					0.01	0.1 Favours	[pre-op CT]	1 Favours [s	10 urgery alc	100 one]

Figure 131: Treatment-related morbidity: transfusion-related complication

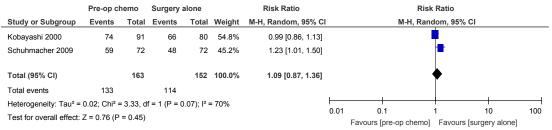
	Pre-op cl	nemo	Surgery	alone		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H	l, Fixed, 95% C	1	
Schuhmacher 2009	10	70	4	68	100.0%	2.43 [0.80, 7.37]			╡		
Total (95% CI)		70		68	100.0%	2.43 [0.80, 7.37]				►	
Total events	10		4								
Heterogeneity: Not app	plicable						0.01	0.1	1	10	100

Figure 132: Treatment-related morbidity: post-operative pneumonia

	Pre-op ch	nemo	Surgery	alone	Risk Ratio			Risk Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI Yea	ar	M-H, Fix	ced, 95% Cl			
Imano 2010	0	47	1	16	100.0%	0.12 [0.01, 2.76] 201	₀ ←					
Total (95% CI)		47		16	100.0%	0.12 [0.01, 2.76]						
Total events	0		1									
Heterogeneity: Not ap	plicable								+ +			
Test for overall effect:	Z = 1.33 (P	= 0.18)					0.01	0.1 Favours [pre-op chemo]	1 10 Favours [surgery	100 alone]		

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Figure 133: Complete resection (R0) at surgery



H.12.4 Post-operative chemoradiotherapy versus surgery alone

Figure 134: Overall survival

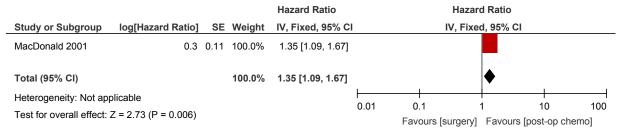


Figure 135: Relapse-free survival

				Hazard Ratio		I	Hazard Ratio		
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Fixed, 95% C	I	IV	, Fixed, 95%	CI	
MacDonald 2001	0.42	0.11	100.0%	1.52 [1.23, 1.89]					
Total (95% CI)			100.0%	1.52 [1.23, 1.89]			•		
Heterogeneity: Not ap	plicable							10	100
Test for overall effect:	Z = 3.82 (P = 0.0001)				0.01	0.1 Favours [su	rgery] Favou	10 s [post-op ch	100 emo]

H.12.5 Peri-operative chemoradiotherapy versus peri-operative chemotherapy alone

Figure 136: Surgical complications: anastamotic leak

	Pre-op chemorad	iation	Perioperative chem	no alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Leong 2017	4	51	3	54	100.0%	1.41 [0.33, 6.00]	
Total (95% CI)		51		54	100.0%	1.41 [0.33, 6.00]	
Total events	4		3				
Heterogeneity: Not a							
Test for overall effect	CZ = 0.47 (P = 0.64)						Favours pre-op CRT + CT Favours peri-op CT alone

Figure 137: Surgical complications: chest infection

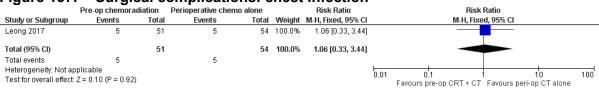


Figure 138: Surgical complications: overall

	Pre-op chemora	diation	Perioperative cher	mo alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Leong 2017	11	51	12	54	100.0%	0.97 [0.47, 2.00]	
Total (95% CI)		51		54	100.0%	0.97 [0.47, 2.00]	-
Total events	11		12				
Heterogeneity: Not ap Test for overall effect:)					0.01 0.1 10 100 Favours pre-op CRT + CT Favours peri-op CT alone

Figure 139: Haematological complications: neutropenia

-	Pre-op chemora	diation	Perioperative che	mo alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Leong 2017	27	60	24	60	100.0%	1.13 [0.74, 1.71]	
Total (95% CI)		60		60	100.0%	1.13 [0.74, 1.71]	•
Total events	27		24				
Heterogeneity: Not ap	oplicable						0.01 0.1 1 10 100
Test for overall effect	Z = 0.55 (P = 0.58))					0.01 0.1 1 10 100 Favours pre-op CRT + CT Favours peri-op CT alone

Figure 140: Haematological complications: overall

-	Pre-op chemora	diation	Perioperative cher	no alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Leong 2017	31	60	30	60	100.0%	1.03 [0.73, 1.47]	
Total (95% CI)		60		60	100.0%	1.03 [0.73, 1.47]	. ◆
Total events	31		30				
Heterogeneity: Not ap Test for overall effect:		I					0.01 0.1 10 100 Favours pre-op CRT + CT Favours peri-op CT alone

Figure 141: Gastrointestinal complications: overall

	Pre-op chemora	diation	Perioperative chem	no alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Leong 2017	18	60	19	60	100.0%	0.95 [0.55, 1.62]	
Total (95% CI)		60		60	100.0%	0.95 [0.55, 1.62]	+
Total events	18		19				
Heterogeneity: Not a	pplicable						
Test for overall effect	: Z = 0.20 (P = 0.84)						Favours pre-op CRT + CT Favours peri-op CT alone

H.12.6 Peri-operative chemotherapy versus surgery alone

Figure 142: Overall survival

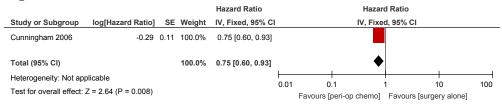
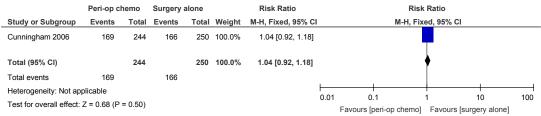


Figure 143: Disease-free survival

				Hazard Ratio			Hazar	d Ratio		
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Fixed, 95% CI			IV, Fixe	d, 95% Cl		
Cunningham 2006	-0.42	0.11	100.0%	0.66 [0.53, 0.82]						
Total (95% CI)			100.0%	0.66 [0.53, 0.82]			•			
Heterogeneity: Not applicable				H			1	+		
				0.01	0	.1	1	10	100	
Test for overall effect: Z = 3.82 (P = 0.0001)						Favours [p	peri-op chemo]	Favours [surg	gery alone]	

Figure 144: Curative resection



H.12.7 Intraperitoneal chemotherapy versus surgery alone

Figure 145: Overall survival rate

	IP chemoth	erapy	Surgery	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
9.6.1 Normothermic	intraperative	e IPC					
Fujimura 1994 (1)	9	18	2	9	6.8%	2.25 [0.61, 8.31]	
Takahashi 1995 (2)	37	56	11	57	19.3%	3.42 [1.95, 6.01]	
Yonemura 2001 (3) Subtotal (95% Cl)	29	44 118	10	24 90	20.6% 46.8%		•
Total events	75		23				
Heterogeneity: Tau ² = Test for overall effect:				= 0.13);	l ² = 50%		
9.6.2 Hyperthermic in	ntraoperative	e IPC					
Fujimura 1994 (4)	15	22	2	9	7.3%	3.07 [0.87, 10.76]	
Hamazoe 1994 (5)	27	42	21	40	25.3%	1.22 [0.84, 1.77]	- -
Yonemura 2001 (6) Subtotal (95% CI)	29	48 112	10	23 72	20.6% 53.2%		•
Total events	71		33				
Heterogeneity: Tau ² = Test for overall effect:			lf = 2 (P =	= 0.35);	l ² = 3%		
Total (95% CI)		230		162	100.0%	1.80 [1.23, 2.65]	•
Total events	146		56				-
Heterogeneity: Tau ² =	0.12; Chi ² =	11.36,	df = 5 (P	= 0.04)	$ ^2 = 56$	%	0.01 0.1 1 10 100
Test for overall effect:	Z = 3.01 (P	= 0.003	0				Favours Surgery alone Favours IPC+Sx
Test for subgroup diff	erences: Chi ²	= 2.59,	df = 1 (P	= 0.11), $ ^2 = 61$	3%	Favours surgery alone Favours in C+3X
Footnotes							
(1) 3 year OS							
(2) 3-year OS							
(3) 5-year OS							
(4) 3 year OS							
(5) 5 year OS							
(6) 5 year							

H.12.8 Intraperitoneal chemotherapy versus systemic chemotherapy

Figure 146: Perioperative mortality

	IP chemoth	erapy	IV chemoth	nerapy		Risk Ratio		Ris	sk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		<u>М-Н</u> , F	ixed, 95% Cl	
Kodera 2016	0	39	1	44	100.0%	0.38 [0.02, 8.95]	_			
Total (95% CI)		39		44	100.0%	0.38 [0.02, 8.95]	_			
Total events	0		1							
Heterogeneity: Not ap	plicable									2 400
Test for overall effect:	Z = 0.61 (P =	0.54)					0.01	0.1 Favours IP chemotherap	1 10 y Favours IV chen	

Figure 147: Treatment-related morbidity: grade 3-4 neutropenia

	IP chemoth	erapy	IV chemot	herapy		Risk Ratio		Ris	k Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	M-H, F	xed, 95% CI		
Kodera 2016	1	39	2	44	100.0%	0.56 [0.05, 5.98]					
Total (95% CI)		39		44	100.0%	0.56 [0.05, 5.98]					
Total events	1		2								
Heterogeneity: Not ap	plicable								+		
Test for overall effect:	Z = 0.48 (P =	0.63)					0.01	0.1 Favours IP chemotherap	T Y Favours IV cl	10 nemotherapy	100

Figure 148: Overall survival rate

8.7.1 Normothermic intraoperative IPC Kang 2014 (1) 155 263 129 258 41.7% 1.18 [1.01, 1.38] Shimoyama 1999 (2) 22 30 11 33 10.8% 2.20 [1.30, 3.73] Subtotal (95% CI) 293 291 52.6% 1.53 [0.83, 2.79] Total events 177 140 Heterogeneity: Tau ² = 0.16; Chi ² = 4.93, df = 1 (P = 0.03); l ² = 80% Test for overall effect: Z = 1.37 (P = 0.17) 8.7.2 Hyperthermic intraoperative IPC Fujinoto 1999 (3) 44 71 34 70 23.9% 1.28 [0.94, 1.73] Ikeguchi 1999 (3) 44 71 34 70 23.9% 1.28 [0.94, 1.73] Ikeguchi 1999 (3) 44 71 34 70 23.9% 1.28 [0.94, 1.73] Ikeguchi 1999 (3) 44 78 1.20 [0.36, 1.48] 1.20 [0.36, 1.48] 1.20 [0.36, 1.48] Total events 84 78 Heterogeneity: Tau ² = 0.02; Chi ² = 5.36, df = 3 (P = 0.15); l ² = 44% 1.27 [1.05, 1.54] 1.01 1.0 1.0 Total (95% CI) 442 457 100.0% 1.	0							
8.7.1 Normothermic intraoperative IPC Kang 2014 (1) 155 263 129 258 41.7% 1.18 [1.01, 1.38] Shimoyama 1999 (2) 22 30 11 33 10.8% 2.20 [1.30, 3.73] Subtotal (95% CI) 293 291 52.6% 1.53 [0.83, 2.79] Total events 177 140 Heterogeneity: Tau ² = 0.16; Chi ² = 4.93, df = 1 (P = 0.03); l ² = 80% Test for overall effect: Z = 1.37 (P = 0.17) 8.7.2 Hyperthermic intraoperative IPC Fujinoto 1999 (3) 44 71 34 70 23.9% 1.28 [0.94, 1.73] Ikeguchi 1999 (3) 44 71 34 70 23.9% 1.28 [0.94, 1.73] Ikeguchi 1999 (3) 44 71 34 70 23.9% 1.28 [0.94, 1.73] Ikeguchi 1999 (3) 44 78 1.20 [0.36, 1.48] 1.20 [0.36, 1.48] 1.20 [0.36, 1.48] Total events 84 78 Heterogeneity: Tau ² = 0.02; Chi ² = 5.36, df = 3 (P = 0.15); l ² = 44% 1.27 [1.05, 1.54] 1.01 1.0 1.0 Total (95% CI) 442 457 100.0% 1.		IP chemo+S	urgery	IV chemo+S	urgery		Risk Ratio	Risk Ratio
Kang 2014 (1) 155 263 129 258 41.7% 1.18 [1.01, 1.38] Shimoyama 1999 (2) 22 30 11 33 10.8% 2.20 [1.30, 3.73] Subtotal (95% CI) 293 291 52.6% 1.53 [0.83, 2.79] Total events 177 140 Heterogeneity: Tau ² = 0.16; Ch ² = 4.93, df = 1 (P = 0.03); l ² = 80% Test for overall effect: $Z = 1.37$ (P = 0.17) 8.7.2 Hyperthermic intraoperative IPC Fujimoto 1999 (3) 44 71 34 70 23.9% 1.28 [0.94, 1.73] Ikeguchi 1995 (4) 40 78 44 96 23.5% 1.12 [0.82, 1.52] Subtotal (95% CI) 149 166 47.4% 1.20 [0.96, 1.48] Total events 84 78 Heterogeneity: Tau ² = 0.00; Ch ² = 0.36, df = 1 (P = 0.55); l ² = 0% Test for overall effect: $Z = 1.63$ (P = 0.10) Total (95% CI) 442 457 100.0% 1.27 [1.05, 1.54] Total events 261 218 Heterogeneity: Tau ² = 0.02; Ch ² = 5.36, df = 3 (P = 0.15); l ² = 0% Test for overall effect: $Z = 2.43$ (P = 0.02) Test for overall effect: $Z = 2.43$ (P = 0.02) Test for overall effect: $Z = 2.43$ (P = 0.02) Test for subgroup differences: Chi ² = 0.56, df = 1 (P = 0.45), l ² = 0% Footnotes (1) 5 year OS (2) 4 year OS (3) 8-year	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Shimoyana 1999 (2) 22 30 11 33 10.8% 2.20 [1.30, 3.73] Subtotal (95% CI) 293 291 52.6% 1.53 [0.83, 2.79] Total events 177 140 Heterogeneity: Tau ² = 0.16; Chi ² = 4.93, df = 1 (P = 0.03); I ² = 80% Test for overall effect: Z = 1.37 (P = 0.17) 8.7.2 Hyperthermic intraoperative IPC Fujimoto 1999 (3) 44 71 34 70 23.9% 1.28 [0.94, 1.73] Ikeguchi 1995 (4) 40 78 44 96 23.5% 1.12 [0.82, 1.52] Subtotal (95% CI) 149 166 47.4% 1.20 [0.96, 1.48] Total events 84 78 Heterogeneity: Tau ² = 0.00; Chi ² = 0.36, df = 1 (P = 0.55); I ² = 0% Test for overall effect: Z = 1.63 (P = 0.10) Total (95% CI) 442 457 100.0% 1.27 [1.05, 1.54] Total events 261 218 Heterogeneity: Tau ² = 0.02; Chi ² = 5.36, df = 3 (P = 0.15); I ² = 44% Test for overall effect: Z = 2.43 (P = 0.02) Test for subgroup differences: Chi ² = 0.56, df = 1 (P = 0.45), I ² = 0% <u>Footnotes</u> (2) 4 year OS (3) 8-year	8.7.1 Normothermic in	ntraoperative I	PC					
Subtotal (95% CI) 293 291 52.6% 1.53 [0.83, 2.79] Total events 177 140 Heterogeneity: Tau ² = 0.16; Chi ² = 4.93, df = 1 (P = 0.03); l ² = 80% Test for overall effect: Z = 1.37 (P = 0.17) 8.7.2 Hyperthermic intraoperative IPC Fujimoto 1999 (3) 44 71 34 70 23.9% 1.28 [0.94, 1.73] Ikeguchi 1995 (4) 0 78 44 96 23.5% 1.12 [0.82, 1.52] Subtotal (95% CI) 149 166 47.4% 1.20 [0.96, 1.48] Total events 84 78 Heterogeneity: Tau ² = 0.00; Chi ² = 0.36, df = 1 (P = 0.55); l ² = 0% Test for overall effect: Z = 1.63 (P = 0.10) Total (95% CI) 442 457 100.0% 1.27 [1.05, 1.54] Heterogeneity: Tau ² = 0.02; Chi ² = 5.36, df = 3 (P = 0.15); l ² = 44% Test for overall effect: Z = 2.43 (P = 0.02) Test for subgroup differences: Chi ² = 0.56, df = 1 (P = 0.45), l ² = 0% Footnotes (1) 5 year OS (2) 4 year OS (3) 8-year	Kang 2014 (1)	155	263	129	258	41.7%	1.18 [1.01, 1.38]	•
Total events 177 140 Heterogeneity: Tau ² = 0.16; Chi ² = 4.93, df = 1 (P = 0.03); l ² = 80% Test for overall effect: Z = 1.37 (P = 0.17) 8.7.2 Hyperthermic intraoperative IPC Fujimoto 1999 (3) 44 71 34 70 23.9% 1.28 [0.94, 1.73] Ikeguchi 1995 (4) 40 78 44 96 23.5% 1.12 [0.82, 1.52] Subtotal (95% Cl) 149 166 47.4% 1.20 [0.96, 1.48] Total events 84 78 Heterogeneity: Tau ² = 0.00; Chi ² = 0.36, df = 1 (P = 0.55); l ² = 0% Test for overall effect: Z = 1.63 (P = 0.10) Total (95% Cl) 442 457 100.0% 1.27 [1.05, 1.54] Total events 261 218 Heterogeneity: Tau ² = 0.02; Chi ² = 5.36, df = 3 (P = 0.15); l ² = 44% Test for overall effect: Z = 2.43 (P = 0.02) Test for overall effect: Z = 2.43 (P = 0.02) Test for subgroup differences: Chi ² = 0.56, df = 1 (P = 0.45), l ² = 0% <u>Footnotes</u> (1) 5 year OS (2) 4 year OS (3) 8-year	Shimoyama 1999 (2)	22	30	11	33	10.8%	2.20 [1.30, 3.73]	
Heterogeneity: Tau ² = 0.16; Chi ² = 4.93, df = 1 (P = 0.03); l ² = 80% Test for overall effect: Z = 1.37 (P = 0.17) 8.7.2 Hyperthermic intraoperative IPC Fujimoto 1999 (3) 44 71 34 70 23.9% 1.28 [0.94, 1.73] Ikeguchi 1995 (4) 40 78 44 96 23.5% 1.12 [0.82, 1.52] Subtotal (95% Cl) 149 166 47.4% 1.20 [0.96, 1.48] Total events 84 78 Heterogeneity: Tau ² = 0.00; Chi ² = 0.36, df = 1 (P = 0.55); l ² = 0% Test for overall effect: Z = 1.63 (P = 0.10) Total (95% Cl) 442 457 100.0% 1.27 [1.05, 1.54] Total events 261 218 Heterogeneity: Tau ² = 0.02; Chi ² = 5.36, df = 3 (P = 0.15); l ² = 44% Test for subgroup differences: Chi ² = 0.56, df = 1 (P = 0.45), l ² = 0% Eootnotes (1) 5 year OS (2) 4 year OS (3) 8-year	Subtotal (95% CI)		293		291	52.6%	1.53 [0.83, 2.79]	◆
Test for overall effect: $Z = 1.37 (P = 0.17)$ 8.7.2 Hyperthermic intraoperative IPC Fujimoto 1999 (3) 44 71 34 70 23.9% 1.28 [0.94, 1.73] Ikeguchi 1995 (4) 40 78 44 96 23.5% 1.12 [0.82, 1.52] Subtotal (95% Cl) 149 166 47.4% 1.20 [0.96, 1.48] Total events 84 78 Heterogeneity: Tau ² = 0.00; Chi ² = 0.36, df = 1 (P = 0.55); l ² = 0% Test for overall effect: $Z = 1.63 (P = 0.10)$ Total (95% Cl) 442 457 100.0% 1.27 [1.05, 1.54] Total events 261 218 Heterogeneity: Tau ² = 0.02; Chi ² = 5.36, df = 3 (P = 0.15); l ² = 44% Test for subgroup differences: Chi ² = 0.56, df = 1 (P = 0.45), l ² = 0% Eootnotes (1) 5 year OS (2) 4 year OS (3) 8-year	Total events	177		140				
8.7.2 Hyperthermic intraoperative IPC Fujimoto 1999 (3) 44 71 34 70 23.9% $1.28 [0.94, 1.73]$ Ikeguchi 1995 (4) 40 78 44 96 23.5% $1.12 [0.82, 1.52]$ Subtotal (95% CI) 149 166 47.4% $1.20 [0.96, 1.48]$ Total events 84 78 Heterogeneity: Tau ² = 0.00; Chi ² = 0.36, df = 1 (P = 0.55); I ² = 0% Test for overall effect: Z = 1.63 (P = 0.10) Total (95% CI) 442 457 100.0% $1.27 [1.05, 1.54]$ Total (95% CI) 442 457 100.0% $1.27 [1.05, 1.54]$ Total events 261 218 Heterogeneity: Tau ² = 0.02; Chi ² = 5.36, df = 3 (P = 0.15); I ² = 44% 0.01 0.1 10 10 Test for overall effect: Z = 2.43 (P = 0.02) Test for subgroup differences: Chi ² = 0.56, df = 1 (P = 0.45), I ² = 0% Favours IV chemo+Sx Favours IP chemo+Sx Footnotes (1) 5 year OS (2) 4 year OS (3) 8-year (3) 8-year	Heterogeneity: Tau ² = 0).16; Chi² = 4.9	3, df = 1 (l	P = 0.03); l ² =	= 80%			
Fujinot 1999 (3) 44 71 34 70 23.9% 1.28 [0.94, 1.73] lkeguchi 1995 (4) 40 78 44 96 23.5% 1.12 [0.82, 1.52] Subtotal (95% Cl) 149 166 47.4% 1.20 [0.96, 1.48] Total events 84 78 Heterogeneity: Tau ² = 0.00; Chi ² = 0.36, df = 1 (P = 0.55); l ² = 0% Test for overall effect: Z = 1.63 (P = 0.10) Total (95% Cl) 442 457 100.0% 1.27 [1.05, 1.54] Total events 261 218 Heterogeneity: Tau ² = 0.02; Chi ² = 5.36, df = 3 (P = 0.15); l ² = 44% Test for overall effect: Z = 2.43 (P = 0.02) Test for subgroup differences: Chi ² = 0.56, df = 1 (P = 0.45), l ² = 0% <u>Footnotes</u> (1) 5 year OS (2) 4 year OS (3) 8-year	Test for overall effect: Z	z = 1.37 (P = 0.	17)					
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	8.7.2 Hyperthermic int	traoperative IF	РС					
Subtotal (95% Cl) 149 166 47.4% 1.20 [0.96, 1.48] Total events 84 78 Heterogeneity: Tau ² = 0.00; Chi ² = 0.36, df = 1 (P = 0.55); l ² = 0% Test for overall effect: Z = 1.63 (P = 0.10) Total events 261 218 Heterogeneity: Tau ² = 0.02; Chi ² = 5.36, df = 3 (P = 0.15); l ² = 44% 0.01 0.1 1 10 10 Test for overall effect: Z = 2.43 (P = 0.02) Test for subgroup differences: Chi ² = 0.56, df = 1 (P = 0.45), l ² = 0% Favours IV chemo+Sx Favours IP chemo+Sx Footnotes (1) 5 year OS (2) 4 year OS (3) 8-year (3) 8-year (3) 8-year	Fujimoto 1999 (3)	44	71	34	70	23.9%	1.28 [0.94, 1.73]	+ - -
Total events 84 78 Heterogeneity: Tau ² = 0.00; Chi ² = 0.36, df = 1 (P = 0.55); l ² = 0% Test for overall effect: Z = 1.63 (P = 0.10) Total (95% Cl) 442 457 100.0% 1.27 [1.05, 1.54] Total events 261 218 Heterogeneity: Tau ² = 0.02; Chi ² = 5.36, df = 3 (P = 0.15); l ² = 44% Test for overall effect: Z = 2.43 (P = 0.02) Test for subgroup differences: Chi ² = 0.56, df = 1 (P = 0.45), l ² = 0% Footnotes (1) 5 year OS (2) 4 year OS (3) 8-year	Ikeguchi 1995 (4)	40	78	44	96	23.5%	1.12 [0.82, 1.52]	
Heterogeneity: Tau ² = 0.00; Chi ² = 0.36, df = 1 (P = 0.55); l ² = 0% Test for overall effect: Z = 1.63 (P = 0.10) Total (95% Cl) 442 457 100.0% 1.27 [1.05, 1.54] Total events 261 218 Heterogeneity: Tau ² = 0.02; Chi ² = 5.36, df = 3 (P = 0.15); l ² = 44% Test for overall effect: Z = 2.43 (P = 0.02) Test for subgroup differences: Chi ² = 0.56, df = 1 (P = 0.45), l ² = 0% <u>Footnotes</u> (1) 5 year OS (2) 4 year OS (3) 8-year	Subtotal (95% CI)		149		166	47.4%	1.20 [0.96, 1.48]	•
Test for overall effect: $Z = 1.63$ (P = 0.10) Total (95% CI) 442 457 100.0% 1.27 [1.05, 1.54] Total events 261 218 Heterogeneity: Tau ² = 0.02; Chi ² = 5.36, df = 3 (P = 0.15); l ² = 44% 0.01 0.1 1 10 10 Test for overall effect: Z = 2.43 (P = 0.02) Test for subgroup differences: Chi ² = 0.56, df = 1 (P = 0.45), l ² = 0% Favours IV chemo+Sx Favours IV chemo+Sx Favours IP chemo+Sx Footnotes (1) 5 year OS (2) 4 year OS (3) 8-year (3) 8-year (3) 8-year	Total events	84		78				
Total (95% Cl) 442 457 100.0% 1.27 [1.05, 1.54] Total events 261 218 Heterogeneity: Tau ² = 0.02; Chi ² = 5.36, df = 3 (P = 0.15); l ² = 44% 0.01 0.1 1 10 10 Test for overall effect: Z = 2.43 (P = 0.02) Test for subgroup differences: Chi ² = 0.56, df = 1 (P = 0.45), l ² = 0% Favours IV chemo+Sx Favours IV chemo+Sx Favours IP chemo+Sx Footnotes (1) 5 year OS (2) 4 year OS (3) 8-year (3) 8-year (3) 8-year	Heterogeneity: Tau ² = 0	0.00; Chi² = 0.3	6, df = 1 (l	P = 0.55); l² =	= 0%			
Total events 261 218 Heterogeneity: Tau ² = 0.02; Chi ² = 5.36, df = 3 (P = 0.15); l ² = 44% 0.01 0.1 1 Test for overall effect: Z = 2.43 (P = 0.02) Favours IV chemo+Sx Favours IV chemo+Sx Footnotes (1) 5 year OS (2) 4 year OS (3) 8-year	Test for overall effect: Z	z = 1.63 (P = 0.	10)					
Heterogeneity: Tau ² = 0.02; Chi ² = 5.36, df = 3 (P = 0.15); l ² = 44% 0.01 0.1 1 10 10 Test for overall effect: Z = 2.43 (P = 0.02) Favours IV chemo+Sx Favours IV chemo+Sx Favours IP chemo+Sx Footnotes (1) 5 year OS (2) 4 year OS (3) 8-year (3) 8-year (4) 4 year OS	Total (95% CI)		442		457	100.0%	1.27 [1.05, 1.54]	◆
0.01 0.1 1 10 10 Test for overall effect: Z = 2.43 (P = 0.02) Favours IV chemo+Sx Favours IV chemo+Sx Favours IV chemo+Sx Test for subgroup differences: Chi ² = 0.56, df = 1 (P = 0.45), I ² = 0% 60 Favours IV chemo+Sx Favours IV chemo+Sx Footnotes (1) 5 year OS (2) 4 year OS (3) 8-year (3) Sector	Total events	261		218				
Test for overall effect: Z = 2.43 (P = 0.02) Favours IV chemo+Sx Test for subgroup differences: Chi ² = 0.56, df = 1 (P = 0.45), l ² = 0% Favours IV chemo+Sx Footnotes (1) 5 year OS (2) 4 year OS (3) 8-year	Heterogeneity: Tau ² = 0).02; Chi² = 5.3	6, df = 3 (l	P = 0.15); l² =	= 44%			
Test for subgroup differences: Chi ² = 0.56, df = 1 (P = 0.45), l ² = 0% Footnotes (1) 5 year OS (2) 4 year OS (3) 8-year	Test for overall effect: Z	Z = 2.43 (P = 0.	02)					
(1) 5 year OS (2) 4 year OS (3) 8-year	Test for subgroup differ	ences: Chi ² = (0.56, df = ⁻	1 (P = 0.45), I	² = 0%			
(2) 4 year OS (3) 8-year	Footnotes							
(3) 8-year	(1) 5 year OS							
	(2) 4 year OS							
(4) 5 year OS	(3) 8-year							
	(4) 5 year OS							

H.13 Squamous cell carcinoma of the oesophagus

What is the most effective curative treatment of squamous cell carcinoma of the oesophagus?

H.13.1 Chemoradiotherapy followed by surgery versus surgery alone

Figure 149:	Overa	li su	rvivai	rate	(acc	oraing to ty	pe of surgical approach)
	CRT f/by su	rgery	Surgery	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
6.24.1 2-stage appro	ach						
Apinop 1994 Subtotal (95% Cl)	8	35 35	3	34 34	4.5% <mark>4.5%</mark>	2.59 [0.75, 8.95] 2.59 [0.75, 8.95]	
Total events	8		3				
Heterogeneity: Not ap	oplicable						
Test for overall effect:	Z = 1.50 (P =	0.13)					
6.24.2 2-stage or tra	nshiatal appr	oach					
van Hagen 2012 Subtotal (95% CI)	8	41 41	4	43 43	5.8% 5.8%	2.10 [0.68, 6.44] 2.10 [0.68, 6.44]	
Total events	8	41	4		5.0%	2.10 [0.00, 0.44]	
Heterogeneity: Not as			4				
Test for overall effect:		0.20)					
6.24.3 2 or 3 stage a	pproach						
Lee 2004	28	51	29	50	43.4%	0.95 [0.67, 1.33]	
Mariette 2014	15	98	11	96	16.5%	1.34 [0.65, 2.76]	
Subtotal (95% CI)		149		146	59.9%	1.05 [0.76, 1.46]	•
Total events	43		40				
Heterogeneity: Chi² = Test for overall effect:); *= 0%				
6.24.4 Left or right th	oracotomy						
Lv 2010	20	80	10	80	14.8%	2.00 [1.00, 4.00]	_
Subtotal (95% CI)		80		80	14.8%	2.00 [1.00, 4.00]	◆
Total events	20		10				
Heterogeneity: Not ap	oplicable						
Test for overall effect:	Z=1.96 (P=	0.05)					
6.24.5 Not reported							
Burmeister 2005	8	45	4	50	5.6%	2.22 [0.72, 6.88]	
Le Prise 1994	8	39	7	47	9.4%	1.38 [0.55, 3.46]	
Subtotal (95% CI)		84		97	15.0%	1.69 [0.83, 3.45]	
Total events	16		11				
Heterogeneity: Chi² = Test for overall effect:); 1* = 0%				
Total (95% CI)		389		400	100.0%	1.42 [1.09, 1.84]	◆
Total events	95		68				
Heterogeneity: Chi ² =	8.31, df = 6 (F	P = 0.22)); I² = 28%				0.01 0.1 1 10 100
Test for overall effect:							Favours surgery alone Favours CRT f/by surgery
Test for subgroup dif	ferences: Chi ^a	² = 5.48,	df = 4 (P =	: 0.24), I	²= 27.1%		a croate bargery alone in avoire or they bargery

Figure 149: Overall survival rate (according to type of surgical approach)

Figure 150: Disease free survival rate (according to type of surgical approach)

	CRT f/by su	rgery	Surgery	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
6.10.1 2 or 3 stage a	pproach						
Bosset 1997	106	112	49	94	31.7%	1.82 [1.49, 2.21]	+
Lee 2004	25	51	26	50	24.8%	0.94 [0.64, 1.39]	
Mariette 2014	14	98	7	96	11.4%	1.96 [0.83, 4.64]	+
Subtotal (95% CI)		261		240	67.9%	1.45 [0.87, 2.41]	◆
Total events	145		82				
Heterogeneity: Tau ² =	= 0.14; Chi ² = !	9.03, df=	= 2 (P = 0.0	01); I² = 1	78%		
Test for overall effect:	Z=1.44 (P=	0.15)					
6.10.2 Left or right th	noracotomy						
Lv 2010	15	80	5	80	9.8%	3.00 [1.14, 7.86]	
Subtotal (95% CI)		80		80	9.8%	3.00 [1.14, 7.86]	
Total events	15		5				
Heterogeneity: Not ap	pplicable						
Test for overall effect:	Z = 2.23 (P =	0.03)					
6.10.3 Not reported							
Burmeister 2005	30	45	16	50	22.3%	2.08 [1.32, 3.28]	_
Subtotal (95% CI)		45		50	22.3%	2.08 [1.32, 3.28]	•
Total events	30		16				
Heterogeneity: Not ap	pplicable						
Test for overall effect:	Z = 3.17 (P =	0.002)					
Total (95% CI)		386		370	100.0%	1.69 [1.18, 2.40]	◆
Total events	190		103				-
Heterogeneity: Tau ² =	= 0.09; Chi ² = 1	11.59, di	f = 4 (P = 0	.02); I ² =	= 65%		
Test for overall effect:			¢. –	21.5	-		0.01 0.1 1 10 10
Test for subaroup dif			df = 2 (P =	0.35) B	² = 5.3%		Favours surgery alone Favours CRT f/by surgery

Figure 151: Postoperative mortality (Concomitant or sequential)

	CRT f/by su	irgery	Surgery	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% Cl
6.18.1 Concomitant							
Bosset 1997	17	138	5	137	21.4%	3.38 [1.28, 8.89]	
Cao 2009	0	118	0	118		Not estimable	
Lee 2004	1	35	1	48	3.6%	1.37 [0.09, 21.18]	
Mariette 2014	9	81	3	89	12.2%	3.30 [0.92, 11.76]	
Mashhadi 2015	5	50	6	50	25.6%	0.83 [0.27, 2.55]	
Natsugo 2006	1	20	0	23	2.0%	3.43 [0.15, 79.74]	
Subtotal (95% CI)		442		465	64.8%	2.25 [1.26, 4.02]	◆
Total events	33		15				
Heterogeneity: Chi ² = 4	4.23, df = 4 (P	= 0.38);	l² = 5%				
Test for overall effect:	Z = 2.72 (P = 0	0.006)					
6.18.2 Sequential							
Le Prise 1994	3	35	3	42	11.6%	1.20 [0.26, 5.58]	
Nygaard 1992	8	47	5	38	23.6%	1.29 [0.46, 3.63]	
Subtotal (95% CI)		82		80	35.2%	1.26 [0.54, 2.97]	
Total events	11		8				
Heterogeneity: Chi ² = 0	0.01, df = 1 (P	= 0.94);	l² = 0%				
Test for overall effect:	Z = 0.53 (P = 0	0.59)					
Total (95% CI)		524		545	100.0%	1.90 [1.18, 3.07]	•
Total events	44		23				
Heterogeneity: Chi ² = \$	5.22, df = 6 (P	= 0.52);	l² = 0%				
Test for overall effect:	Z = 2.63 (P =)	0.009)					0.01 0.1 1 10 10 Favours CRT f/by surgery Favours surgery alone

Figure 152: Postoperative mortality (Different type of surgical approach)

	CRT f/by su	rgery	Surgery	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events				Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
6.20.1 Transhiatal							
Mashhadi 2015 Subtotal (95% CI)	5	50 50	6	50 <mark>50</mark>	25.6% <mark>25.6%</mark>	0.83 [0.27, 2.55] 0.83 [0.27, 2.55]	
Total events	5		6				
Heterogeneity: Not ap							
Test for overall effect: .	Z = 0.32 (P =	0.75)					
6.20.2 2-stage approa	ach						
Nygaard 1992	8	47	5	38	23.6%	1.29 [0.46, 3.63]	
Subtotal (95% CI)		47		38	23.6%	1.29 [0.46, 3.63]	
Total events	8		5				
Heterogeneity: Not ap							
Test for overall effect: .	Z = 0.49 (P =	0.62)					
6.20.3 2 or 3 stage ap	proach						
Bosset 1997	17	138	5	137	21.4%	3.38 [1.28, 8.89]	
Lee 2004	1	35	1	48	3.6%	1.37 [0.09, 21.18]	
Mariette 2014 Subtotal (95% CI)	9	81 254	3	89 274	12.2% 37.2%	3.30 [0.92, 11.76] 3.16 [1.51, 6.60]	
Total events	27	2.54	9	214	J1.2/0	5.10[1.51, 0.00]	
Heterogeneity: Chi ² = 1		P = 0.831	-				
Test for overall effect: .			,,, = 0,0				
6.20.4 Left thoracotor	my						
Cao 2009	0	118	0	118		Not estimable	
Subtotal (95% CI)		118		118		Not estimable	
Total events	0		0				
Heterogeneity: Not ap	•						
Test for overall effect:	Not applicabl	le					
6.20.5 Not reported							
Le Prise 1994	3	35	3	42	11.6%	1.20 [0.26, 5.58]	
Natsugo 2006	1	20	0	23	2.0%	3.43 [0.15, 79.74]	
Subtotal (95% CI)		55		65	13.6%	1.53 [0.39, 5.90]	
Total events	4		3				
Heterogeneity: Chi ² = I); I* = 0%				
Test for overall effect: .	∠ = 0.61 (P =	0.54)					
Total (95% CI)		524		545	100.0%	1.90 [1.18, 3.07]	◆
Total events	44		23				
Heterogeneity: Chi ² =); I² = 0%				
Test for overall effect: .							Favours CRT f/by surgery Favours surgery alone
Test for subgroup diffe	erences: Chiª	°= 4.49,	dt = 3 (P =	0.21), I	*= 33.2%		

Figure 153: 30-day mortality (Concomitant or sequential)

	0.07.64					B 1 B <i>C</i>	51 L 5 /
	CRT f/by su	irgery	Surgery a	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
6.5.1 Concomitant							
Cao 2009	0	118	0	118		Not estimable	
Mariette 2014	6	81	1	89	14.7%	6.59 [0.81, 53.59]	
Subtotal (95% CI)		199		207	14.7%	6.59 [0.81, 53.59]	
Total events	6		1				
Heterogeneity: Not ap	oplicable						
Test for overall effect:	Z=1.76 (P=	0.08)					
6.5.2 Sequential							
Nygaard 1992	8	47	5	38	85.3%	1.29 [0.46, 3.63]	
Subtotal (95% CI)		47		38	85.3%	1.29 [0.46, 3.63]	-
Total events	8		5				
Heterogeneity: Not ap	oplicable						
Test for overall effect:	Z=0.49 (P=	0.62)					
Total (95% CI)		246		245	100.0%	2.07 [0.85, 5.03]	-
Total events	14		6				
Heterogeneity: Chi ² =	1.97, df = 1 (P = 0.16); l² = 49%				
Test for overall effect:	Z = 1.61 (P =	0.11)					0.01 0.1 1 10 100 Equation CRT f/by our gapy Equation of the surgery closes
Test for subgroup diff	ferences: Chi	r= 1.87,	df = 1 (P =	0.17), I	² = 46.4%		Favours CRT f/by surgery Favours surgery alone

Figure 154: 30-day mortality (Different type of surgical approach)

CRT f/by su	rgery	Surgery a	alone		Risk Ratio	Risk Ratio
Events				Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
h						
8	47	5	38	85.3%	1.29 [0.46, 3.63]	
	47		38	85.3%	1.29 [0.46, 3.63]	
8		5				
licable						
:= 0.49 (P =	0.62)					
oach						
6	81	1	89	14.7%	6.59 (0.81, 53,59)	
-	81		89	14.7%	6.59 [0.81, 53.59]	
6		1				
licable						
= 1.76 (P =	0.08)					
roach						
0	118	0	118		Not estimable	
	118		118		Not estimable	
0		0				
licable						
lot applicabl	e					
	246		245	100.0%	2.07 [0.85, 5.03]	
14		6				
.97, df = 1 (F	P = 0.16); l² = 49%				
= 1.61 (P =	0.11)					Favours CRT f/by surgery Favours surgery alone
rences: Chiª	² = 1.87,	df = 1 (P =	0.17), P	² = 46.4%		rations of they surgery rations surgery alone
	h 8 8 1icable = 0.49 (P = 0 6 1icable = 1.76 (P = 0 1icable 1ot applicabl 14 .97, df = 1 (f = 1.61 (P =	h 8 47 8 licable = 0.49 (P = 0.62) oach 6 81 6 licable = 1.76 (P = 0.08) roach 0 118 118 0 licable 0 118 118 0 licable 246 14 .97, df = 1 (P = 0.16) = 1.61 (P = 0.11)	h 8 47 5 47 5 1 1 1 1 1 1 1 1 1 1 1 1 1	h 8 47 5 38 47 38 8 5 licable = 0.49 (P = 0.62) oach 6 81 1 89 6 1 89 6 1 licable = 1.76 (P = 0.08) roach 0 118 0 118 118 118 0 0 licable lot applicable 246 245 14 6 .97, df = 1 (P = 0.16); I ² = 49% = 1.61 (P = 0.11)	h 8 47 5 38 85.3% 47 38 85.3% 8 5 licable = $0.49 (P = 0.62)$ oach 6 81 1 89 14.7% 6 1 89 14.7% 6 1 1 89 14.7% 6 2 1 89 14.7% 6 2 1 89 14.7% 8 2 1 8 1 89 14.7% 8 2 1 8 1 8 18 18 18 18 18 18 18 18 18 18 1	$\begin{array}{cccccccccccccccccccccccccccccccccccc$

Figure 155: Treatment-related mortality (Concomitant or sequential)

	CRT f/by su	irgery	Surgery	alone		Risk Ratio		Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	M-H, Fixed, 95% Cl	
6.15.1 Concomitant									
Apinop 1994	5	35	5	34	33.7%	0.97 [0.31, 3.06]		_	
Bosset 1997	18	142	5	137	33.8%	3.47 [1.33, 9.09]			
Cao 2009	0	118	0	118		Not estimable			
Lee 2004	2	51	1	48	6.8%	1.88 [0.18, 20.09]			
Lv 2010	3	80	0	80	3.3%	7.00 [0.37, 133.36]			
Natsugo 2006	1	22	0	23	3.2%	3.13 [0.13, 72.99]	-		
Subtotal (95% CI)		448		440	80.8%	2.43 [1.27, 4.63]		\bullet	
Total events	29		11						
Heterogeneity: Chi ² =	3.55, df = 4 (P	= 0.47);	l² = 0%						
Test for overall effect:	Z = 2.69 (P =	0.007)							
6.15.2 Sequential									
Le Prise 1994	3	39	3	42	19.2%	1.08 [0.23, 5.02]			
Subtotal (95% CI)		39		42	19.2%	4 00 00 00 000			
				42	19.2 /0	1.08 [0.23, 5.02]			
Total events	3		3	42	13.2 /0	1.08 [0.23, 5.02]			
			3	42	13.2 /0	1.08 [0.23, 5.02]			
Heterogeneity: Not ap	plicable		3	42	13.2 /0	1.08 [0.23, 5.02]			
Total events Heterogeneity: Not ap Test for overall effect: Total (95% CI)	plicable		3		19.2 %	1.08 [0.23, 5.02] 2.17 [1.20, 3.91]		•	
Heterogeneity: Not ap Test for overall effect:	plicable	0.92)	3					•	
Heterogeneity: Not ap Test for overall effect: Total (95% CI)	2 = 0.09 (P = 1	0.92) 487	14				L		
Heterogeneity: Not ap Test for overall effect: Total (95% CI) Total events	2 = 0.09 (P = 1 32 4.27, df = 5 (P	0.92) 487 = 0.51);	14				0.01 0.1	1 10 /by surgery Favours surgery alone	10

Figure 156: Treatment-related mortality (Different type of surgical approach)

C	CRT f/by sur	gery	Surgery a	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% Cl
i.16.1 2-stage approac							
pinop 1994 Subtotal (95% CI)	5	35 35	5	34 34	33.7% 33.7%	0.97 [0.31, 3.06] 0.97 [0.31, 3.06]	
iotal events leterogeneity: Not appli	5 icable		5				
est for overall effect: Z:		0.96)					
.16.2 2 or 3-stage app	roach						
losset 1997	18	142	5	137	33.8%	3.47 [1.33, 9.09]	
.ee 2004 Subtotal (95% CI)	2	51 193	1	48 185	6.8% 40.6%	1.88 [0.18, 20.09] 3.21 [1.32, 7.79]	
otal events	20		6			. / .	
leterogeneity: Chi² = 0.1	22, df = 1 (P	= 0.64)	; I² = 0%				
est for overall effect: Z	= 2.57 (P = 0	0.01)					
.16.3 Left thoracotom							
ao 2009 Subtotal (05% CI)	0	118 118	0	118 118		Not estimable Not estimable	
Subtotal (95% CI) Total events	0	118	0	118		Notestimable	
leterogeneity: Not appli	-		0				
est for overall effect: N		e					
.16.4 Left or right thor	acotomy						
v 2010	3	80	0	80		7.00 [0.37, 133.36]	
Subtotal (95% CI)		80		80	3.3%	7.00 [0.37, 133.36]	
otal events	3		0				
leterogeneity: Not appli est for overall effect: Z :		0 201					
est for overall effect. Z :	= 1.29 (P = 1	0.20)					
.16.5 Not reported							
e Prise 1994	3	39	3	42	19.2%	1.08 [0.23, 5.02]	
latsugo 2006 Subtotal (95% CI)	1	22 61	0	23 65	3.2% 22.4%	3.13 [0.13, 72.99] 1.37 [0.35, 5.32]	
otal events	4		3		22.470	101 [0.00, 0.02]	
leterogeneity: Chi² = 0.1	•	= 0.55)	-				
est for overall effect: Z							
otal (95% CI)		487		482	100.0%	2.17 [1.20, 3.91]	◆
otal events	32		14				
leterogeneity: Chi ² = 4.1			; I² = 0%				0.01 0.1 1 10
est for overall effect: Z:							

Figure 157: Overall survival (According to type of surgical approach)

	CRT f/by su		Surgery a					Hazard Ratio	Hazard Ratio
Study or Subgroup	Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% CI	Exp[(O-E) / V], Fixed, 95% CI
6.27.1 2 stage appro									
Apinop 1994 Subtotal (95% CI)	27	35 35	31	34 34	-3.2	14.43	8.6% <mark>8.6%</mark>	0.80 [0.48, 1.34] 0.80 [0.48, 1.34]	•
Total events Heterogeneity: Not ap Test for overall effect:		0.40)	31						
6.27.2 2 or 3 stage aj	pproach								
Bosset 1997	96	143	95	139	-1.93	47.75	28.6%	0.96 [0.72, 1.28]	+
Lee 2004	22	51	19		-1.31	10.2	6.1%	0.88 [0.48, 1.62]	
Mariette 2014 (1)	61	98	64		-0.38	38.3		0.99 [0.72, 1.36]	-
Subtotal (95% CI)		292		285			57.6%	0.96 [0.79, 1.18]	+
Total events	179		178						
Heterogeneity: Chi² =			I ² = 0%						
Test for overall effect:	Z = 0.37 (P =	0.71)							
6.27.3 2 stage or trar	nshiatal appro	bach							
/an Hagen 2012 (2)	0	41	0		-7.85	9.91	5.9%	0.45 [0.24, 0.84]	
Subtotal (95% CI)		41		43			5.9%	0.45 [0.24, 0.84]	◆
Total events	0		0						
Heterogeneity: Not ap									
Test for overall effect:	Z = 2.49 (P =	0.01)							
6.27.4 Not reported									
Burmeister 2005 (3)	0	128	0	128	-5.43	46.57	27.9%	0.89 [0.67, 1.19]	
Subtotal (95% CI)		128		128			27.9%	0.89 [0.67, 1.19]	•
Total events	0		0						
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z = 0.80 (P =	0.43)							
Total (95% CI)		496		490			100.0%	0.89 [0.76, 1.03]	•
Total events	206		209						
Heterogeneity: Chi² =	5.39, df = 5 (F	P = 0.37);	I² = 7%					H	0.01 0.1 1 10
Test for overall effect:	Z = 1.55 (P =	0.12)						l	Favours CRT+S Favours S
Test for subgroup diff	erences: Chiª	= 5.28, 0	#f = 3 (P = 1	0.15), I [≥]	= 43.2	%			
Footnotes									
(1) number of death n	ot reported;								
(2) number of death n	orreponeu								

Figure 158: Disease-free survival (Concomitant; 2- or 3-stage open oesophagectomy)

	CRT f/by su	irgery	Surgery	alone				Hazard Ratio	Hazard Ratio	
Study or Subgroup	Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% CI	Exp[(O-E) / V], Fixed, 95% CI	
Bosset 1997	80	143	97	139	-19.74	43.84	49.2%	0.64 [0.47, 0.86]		
Lee 2004	0	51	0	50	-0.24	11.82	13.3%	0.98 [0.55, 1.73]	_ + _	
Mariette 2014	0	98	0	96	-2.79	33.44	37.5%	0.92 [0.66, 1.29]		
Total (95% CI)		292		285			100.0%	0.77 [0.63, 0.95]	•	
Total events	80		97							
Heterogeneity: Chi ² =	3.31, df = 2 (P = 0.19); I ^z = 40%						0.01 0.1 1 10	100
Test for overall effect	Z= 2.41 (P=	0.02)							Favours CRT f/by Sx Favours Sx alon	

Figure 159: Any postoperative complication (Concomitant or sequential)

	CRT f/by su	urgery	Surgery	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I M-H, Fixed, 95% CI
6.3.1 Concomitant							
Bosset 1997	45	138	36	137	33.9%	1.24 [0.86, 1.79]	- -
Lee 2004	13	35	19	48	15.0%	0.94 [0.54, 1.63]	
Mariette 2014	18	81	25	89	22.3%	0.79 [0.47, 1.34]	
Subtotal (95% CI)		254		274	71.2%	1.04 [0.80, 1.35]	•
Total events	76		80				
Heterogeneity: Chi ² = 2	2.05, df = 2 (P	= 0.36);	l² = 3%				
Test for overall effect:	Z = 0.26 (P =	0.79)					
6.3.2 Sequential							
_e Prise 1994	14	35	18	42	15.3%	0.93 [0.55, 1.59]	
Nygaard 1992	16	47	13	38	13.5%	1.00 [0.55, 1.80]	
Subtotal (95% CI)		82		80	28.8%	0.96 [0.65, 1.43]	•
Total events	30		31				
Heterogeneity: Chi ² = (0.02, df = 1 (P	= 0.88);	I² = 0%				
Test for overall effect:	Z = 0.19 (P =	0.85)					
Total (95% CI)		336		354	100.0%	1.01 [0.81, 1.27]	•
Total events	106		111				
Heterogeneity: Chi ² = 2	2.18, df = 4 (P	= 0.70);	l² = 0%				0.01 0.1 1 10 100
Test for overall effect:	Z = 0.13 (P =	0.90)					Favours CRT f/by surgery Favours surgery alone
Test for subgroup diffe	rences: Chi ² =	= 0.09, df	= 1 (P = 0	.76), l² =	: 0%		r avours orch inby surgery Favours surgery alone

Figure 160: Any postoperative complication (Different type of surgical approach)

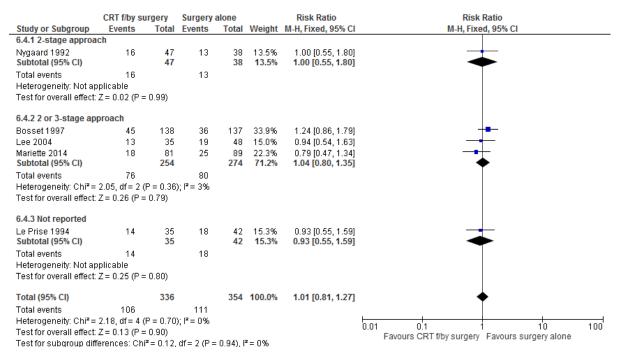


Figure 161: Treatment-related morbidity: anastomotic leak (Concomitant or sequential)

	CRT f/by su	irgery	Surgery	alone		Risk Ratio		R	isk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C		M-H, I	Fixed, 95% CI		
6.1.1 Concomitant											
Apinop 1994	1	26	2	34	12.9%	0.65 [0.06, 6.83]			•	_	
Cao 2009	3	118	1	118	7.5%	3.00 [0.32, 28.43]					-
Lv 2010	1	80	0	80	3.7%	3.00 [0.12, 72.56]					
Mashhadi 2015	0	50	1	50	11.2%	0.33 [0.01, 7.99]				_	
Natsugo 2006	4	20	4	23	27.8%	1.15 [0.33, 4.01]					
Subtotal (95% CI)		294		305	63.1%	1.23 [0.52, 2.93]		-			
Total events	9		8								
Heterogeneity: Chi ² =	1.84, df = 4 (P	= 0.76);	l² = 0%								
Test for overall effect:	Z = 0.47 (P =	0.64)									
6.1.2 Sequential											
6.1.2 Sequential	5	35	3	42	20.4%	2 00 [0 51 7 79]		-			
Le Prise 1994	5	35	3	42	20.4%	2.00 [0.51, 7.79]					
Le Prise 1994 Nygaard 1992	5 2	47	3 2	38	16.5%	0.81 [0.12, 5.48]					
Le Prise 1994 Nygaard 1992 Subtotal (95% CI)	2		2						•		
Le Prise 1994 Nygaard 1992 Subtotal (95% CI) Total events	2 7	47 82	2	38	16.5%	0.81 [0.12, 5.48]			-		
Le Prise 1994 Nygaard 1992 Subtotal (95% CI) Total events Heterogeneity: Chi ² = (2 7 0.57, df = 1 (P	47 82 = 0.45);	2	38	16.5%	0.81 [0.12, 5.48]			-		
Le Prise 1994 Nygaard 1992 Subtotal (95% CI) Total events	2 7 0.57, df = 1 (P	47 82 = 0.45);	2	38	16.5%	0.81 [0.12, 5.48]			•		
Le Prise 1994 Nygaard 1992 Subtotal (95% CI) Total events Heterogeneity: Chi ² = (2 7 0.57, df = 1 (P	47 82 = 0.45);	2	38 80	16.5%	0.81 [0.12, 5.48]			•		
Le Prise 1994 Nygaard 1992 Subtotal (95% CI) Total events Heterogeneity: Chi ² = (Test for overall effect:	2 7 0.57, df = 1 (P	47 82 = 0.45); 0.49)	2	38 80	16.5% 36.9%	0.81 [0.12, 5.48] 1.47 [0.50, 4.33]			•		
Le Prise 1994 Nygaard 1992 Subtotal (95% CI) Total events Heterogeneity: Chi ² = (Test for overall effect: . Total (95% CI)	2 7 0.57, df = 1 (P Z = 0.69 (P = 16	47 82 = 0.45); 0.49) 376	2 5 1² = 0%	38 80	16.5% 36.9%	0.81 [0.12, 5.48] 1.47 [0.50, 4.33]			•		
Le Prise 1994 Nygaard 1992 Subtotal (95% CI) Total events Heterogeneity: Chi ² = (Test for overall effect: . Total (95% CI) Total events	2 7 0.57, df = 1 (P Z = 0.69 (P = 16 2.49, df = 6 (P	47 82 = 0.45); 0.49) 376 = 0.87);	2 5 1² = 0%	38 80	16.5% 36.9%	0.81 [0.12, 5.48] 1.47 [0.50, 4.33]	0.01				10

Figure 162: Treatment-related morbidity: anastomotic leak (Different type of surgical approach)

	CRT f/by su		Surgery			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
5.2.1 Transhiatal app							
Mashhadi 2015 Subtotal (95% CI)	0	50 <mark>50</mark>	1	50 <mark>50</mark>	11.2% 11.2%	0.33 [0.01, 7.99] 0.33 [0.01, 7.99]	
Fotal events	0		1				
Heterogeneity: Not ap							
Fest for overall effect:	: Z = 0.68 (P =	0.50)					
5.2.2 2-stage approa	ich						
Apinop 1994	1	26	2	34	12.9%	0.65 [0.06, 6.83]	
Nygaard 1992	2	47	2	38	16.5%	0.81 [0.12, 5.48]	
Subtotal (95% CI)		73		72	29.5%	0.74 [0.17, 3.26]	
Fotal events	3		4				
Heterogeneity: Chi² =	0.02, df = 1 (F	P = 0.89); I² = 0%				
Fest for overall effect	Z = 0.40 (P =	0.69)					
5.2.3 Left thoracotor	ny						
Cao 2009	3	118	1	118	7.5%	3.00 [0.32, 28.43]	
Subtotal (95% CI)		118		118	7.5%	3.00 [0.32, 28.43]	
Fotal events	3		1				
Heterogeneity: Not ap	oplicable						
Fest for overall effect:		0.34)					
6.2.4 Left or right the	oracotomy						
_v 2010	1	80	0	80	3.7%	3.00 [0.12, 72.56]	
Subtotal (95% CI)		80		80	3.7%	3.00 [0.12, 72.56]	
Fotal events	1		0				
Heterogeneity: Not ap	oplicable						
Fest for overall effect:	Z = 0.68 (P =	0.50)					
6.2.5 Not reported							
_e Prise 1994	5	35	3	42	20.4%	2.00 [0.51, 7.79]	
Vatsugo 2006	4	20	4	23	27.8%	1.15 [0.33, 4.01]	
Subtotal (95% CI)	-	55		65	48.1%	1.51 [0.61, 3.76]	
Total events	9		7				_
Heterogeneity: Chi ² =	0.35, df = 1 (F	P = 0.56); I² = 0%				
Fest for overall effect:	Z = 0.88 (P =	0.38)	-				
Fotal (95% CI)		376		385	100.0%	1.32 [0.67, 2.59]	-
Total events	16		13				-
Heterogeneity: Chi² =		P = 0.87					F
Fest for overall effect:			0 /0				
	· 0.00 (i =	w. 7 4/					Favours CRT f/by surgery Favours surgery alone

Figure 163: Treatment-related morbidity: infection (Concomitant or sequential)

	CRT f/by su	irgery	Surgery	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
6.17.1 Concomitant							
Mariette 2014 Subtotal (90% CI)	8	81 81	5	89 <mark>89</mark>	22.9% <mark>22.9%</mark>	1.76 [0.60, 5.16] 1.76 [0.71, 4.34]	
Total events	8		5				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 1.03 (P =	0.30)					
6.17.2 Sequential							
Nygaard 1992	26	47	15	41	77.1%	1.51 [0.94, 2.44]	- -
Subtotal (90% CI)		47		41	77.1%	1.51 [1.01, 2.26]	◆
Total events	26		15				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 1.70 (P =	0.09)					
Total (90% CI)		128		130	100.0%	1.57 [1.08, 2.28]	•
Total events	34		20				
Heterogeneity: Chi ² =	0.07, df = 1 (P = 0.80); I² = 0%				
Test for overall effect:	Z = 1.98 (P =	0.05)					Favours CRT f/by surgery Favours surgery alone
Test for subgroup diff	erences: Chi	= 0.06,	df=1 (P=	: 0.80), I	z =0%		r avours orch noy surgery in avours surgery alone

Figure 164: Treatment-related morbidity: infection (Different type of surgical approach)

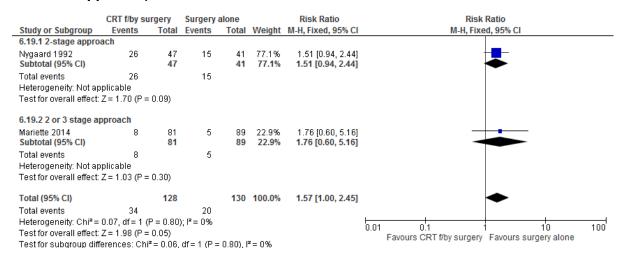


Figure 165: Treatment-related morbidity: stenosis

CRT f/by su	rgery	Surgery	alone		Risk Ratio	Risk Ratio
Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% Cl
2	80	1	80	100.0%	2.00 [0.19, 21.62]	
	80		80	100.0%	2.00 [0.19, 21.62]	
2 plicable Z = 0.57 (P =	0.57)	1				0.01 0.1 1 10 100 Favours CRT f/by surgery Favours surgery alone
	Events 2 2 plicable	2 80 80 2	Events Total Events 2 80 1 80 2 1 plicable	Events Total Events Total 2 80 1 80 80 80 80 80 2 1 1 1 plicable 1 1 1	Events Total Events Total Weight 2 80 1 80 100.0% 80 80 100.0% 2 1 100.0% 2 1 100.0% 2 1 100.0% 2 1 100.0%	Events Total Events Total Weight M-H, Fixed, 95% CI 2 80 1 80 100.0% 2.00 [0.19, 21.62] 80 80 100.0% 2.00 [0.19, 21.62] 2 1 9 100.0% 2.00 [0.19, 21.62] 2 1 9 100.0% 100.0% 100.0%

Figure 166: Treatment-related morbidity: blood loss (mL)

	CRT f/b	y surg	jery	Surge	ry ald	one		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Mashhadi 2015	400	25	50	390	15	50	100.0%	10.00 [1.92, 18.08]	
Total (95% CI)			50			50	100.0%	10.00 [1.92, 18.08]	
Heterogeneity: Not ap Test for overall effect:		P = 0.0	02)						-100 -50 0 50 100 Favours CRT f/by surgery Favours surgery alone

Figure 167: Treatment-related morbidity: haemorrhage (>300 mL)

	CRT f/by su	irgery	Surgery alone			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Lv 2010	8	80	2	80	100.0%	4.00 [0.88, 18.26]	
Total (95% CI)		80		80	100.0%	4.00 [0.88, 18.26]	
Total events	8		2				
Heterogeneity: Not a Test for overall effect		: 0.07)					0.01 0.1 1 10 100 Favours CT f/by surgery Favours surgery alone

H.13.2 Chemoradiotherapy (concomitant) followed by surgery versus chemoradiotherapy (concomitant) alone

Figure 168: Overall mortality estimates (2-stage approach)

	CRT f/b	y Sx	CRT al	one		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
Stahl 2005/2008	69	86	75	86	100.0%	0.92 [0.81, 1.05]	•
Total (95% CI)		86		86	100.0%	0.92 [0.81, 1.05]	•
Total events	69		75				
Heterogeneity: Not ap Test for overall effect:		P = 0.2	2)				L L L L L L L L L L L L L L L L L L L

Figure 169: Treatment-related mortality (2-stage approach)

	CRT f/b	y Sx	CRT al	Talone Risk Ratio		Risk Ratio	Risk	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fix	ed, 95% Cl	
Stahl 2005/2008	11	86	3	86	100.0%	3.67 [1.06, 12.68]			
Total (95% CI)		86		86	100.0%	3.67 [1.06, 12.68]			
Total events	11		3						
Heterogeneity: Not ap Test for overall effect:		P = 0.0	4)				0.01 0.1 Favours CRT f/by Surgery	1 10 Favours CRT alone	100

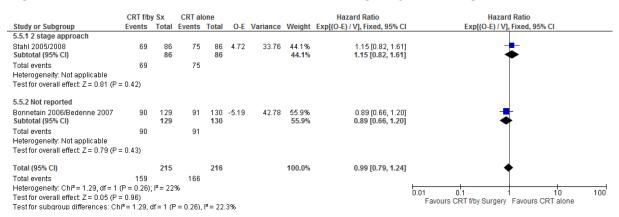
Figure 170: 3-year overall survival rate (Surgical approach – unspecified)

	CRT f/b	y Sx	CRT al	one		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
Bonnetain 2006/Bedenne 2007	23	129	25	130	100.0%	0.93 [0.56, 1.55]	
Total (95% CI)		129		130	100.0%	0.93 [0.56, 1.55]	+
Total events Heterogeneity: Not applicable Test for overall effect: Z = 0.29 (P =	23 = 0.77)		25				0.01 0.1 1 10 100 Favours CRT alone Favours CRT f/by surgery

Figure 171: Quality of life (Spitzer) at 5-year follow-up (5 to 25 months) (Surgical approach – unspecified)

	CRT	f/by S	x	CR	T alon	е		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Bonnetain 2006/Bedenne 2007	8.76	2.02	25	7.81	2.57	37	100.0%	0.95 [-0.20, 2.10]	+
Total (95% CI)			25			37	100.0%	0.95 [-0.20, 2.10]	◆
Heterogeneity: Not applicable Test for overall effect: Z = 1.63 (P =	= 0.10)								-10 -5 0 5 10 Favours CRT f/by Sx Favours CRT alone

Figure 172 Overall survival (Concomitant; according to type of surgical approach)



H.13.3 Chemoradiotherapy followed by surgery versus chemotherapy followed by surgery alone

Figure 173: Mortality (Concomitant or sequential)

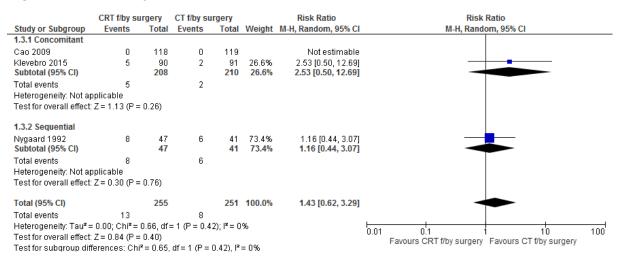


Figure 174: Mortality (Different type of surgical approach)

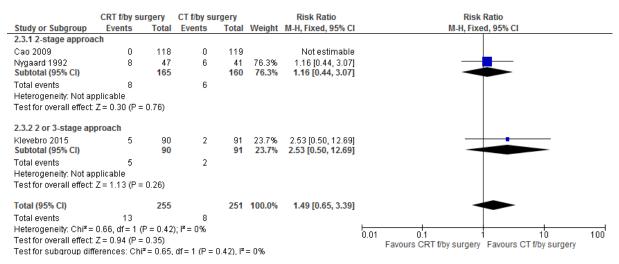


Figure 175: Any postoperative mortality (Concomitant or sequential)

	CRT f/by su		CT f/by su			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
1.4.1 Concomitant							
Cao 2009	0	118	0	119		Not estimable	
Subtotal (95% CI)		118		119		Not estimable	
Total events	0		0				
Heterogeneity: Not a	pplicable						
Test for overall effect	: Not applicab	le					
1.4.2 Sequential							
Nygaard 1992	8	47	6	41	100.0%	1.16 [0.44, 3.07]	
Subtotal (95% CI)		47		41	100.0%	1.16 [0.44, 3.07]	
Total events	8		6				
Heterogeneity: Not a	pplicable						
Test for overall effect	• •	0.76)					
Total (95% CI)		165		160	100.0%	1.16 [0.44, 3.07]	
Total events	8		6				
Heterogeneity: Not a	pplicable						t
Test for overall effect	• •	0.76)					
Test for subgroup dif			ble				Favours CRT f/by surgery Favours CT f/by surgery

Figure 176: Any postoperative mortality (2-stage approach)

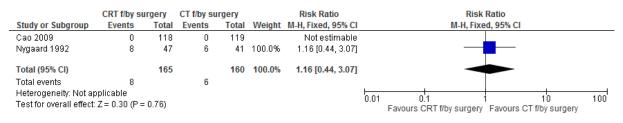


Figure 177: 3-year overall survival rate (Concomitant)

	CRT f/by su	irgery	CT f/by su	irgery		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI	
Cao 2009	87	118	68	119	83.9%	1.29 [1.07, 1.56]		
Klevebro 2015	14	25	13	25	16.1%	1.08 [0.65, 1.80]		
Total (95% CI)		143		144	100.0%	1.26 [1.05, 1.50]	•	
Total events	101		81					
Heterogeneity: Chi ² =	0.42, df = 1 (P = 0.51)	; I² = 0%					00
Test for overall effect	: Z = 2.51 (P =	0.01)					Favours CT f/by surgery Favours CRT f/by surgery	00

Figure 178: 3-year overall survival rate (Different type of surgical approach)

	CRT f/by su	rgery	CT f/by su	irgery		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% Cl
2.7.1 2-stage approa	ch						
Cao 2009	87	118	68	119		1.29 [1.07, 1.56]	
Subtotal (95% CI)		118		119	83.9%	1.29 [1.07, 1.56]	◆
Total events	87		68				
Heterogeneity: Not ap	oplicable						
Test for overall effect:	Z=2.64 (P=	0.008)					
2.7.2 2 or 3-stage ap	proach						
Klevebro 2015	14	25	13	25	16.1%	1.08 [0.65, 1.80]	
Subtotal (95% CI)		25		25	16.1%	1.08 [0.65, 1.80]	•
Total events	14		13				
Heterogeneity: Not ap	oplicable						
Test for overall effect:	Z = 0.28 (P =	0.78)					
Total (95% CI)		143		144	100.0%	1.26 [1.05, 1.50]	•
Total events	101		81				
Heterogeneity: Chi ² =	0.42, df = 1 (F	^o = 0.51)); I ² = 0%				
Test for overall effect:	Z = 2.51 (P =	0.01)					0.01 0.1 1 10 100 Favours CT f/by surgery Favours CRT f/by surgery
Test for subgroup diff	ferences: Chi ^a	² = 0.42.	df = 1 (P =	0.52), l ^z	= 0%		Tavours of insystingery Pavours Ort insystingery

Figure 179 Overall survival (Concomitant; 2- or 3-stage approach)

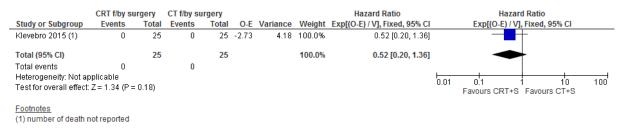


Figure 180: Progression-free survival rate (Concomitant; 2- or 3-stage approach)

	CRT f/by su	urgery	CT f/by su	irgery		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% Cl
Klevebro 2015	14	25	13	25	100.0%	1.08 [0.65, 1.80]	
Total (95% CI)		25		25	100.0%	1.08 [0.65, 1.80]	+
Total events	14		13				
Heterogeneity: Not ap	oplicable						0.01 0.1 1 10 100
Test for overall effect:	Z = 0.28 (P =	= 0.78)					Favours CT f/by surgery Favours CRT f/by surgery

Figure 181: Treatment-related morbidity: anastomotic leak (Concomitant or sequential)

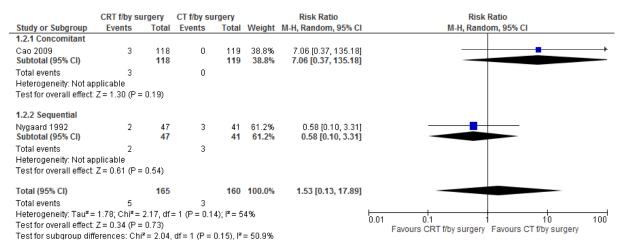


Figure 182: Treatment-related morbidity: anastomotic leak (2-stage appraoch)

	CRT f/by su	rgery	CT f/by su	rgery		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	I M-H, Random, 95% CI
Cao 2009	3	118	0	119	38.8%	7.06 [0.37, 135.18]]
Nygaard 1992	2	47	3	41	61.2%	0.58 [0.10, 3.31]]
Total (95% CI)		165		160	100.0%	1.53 [0.13, 17.89]	
Total events	5		3				
Heterogeneity: Tau ² =	= 1.78; Chi ² =	2.17, df=	= 1 (P = 0.1	4); I ² = 5	4%		
Test for overall effect:	Z = 0.34 (P =	0.73)					0.01 0.1 1 10 100 Favours CRT f/by surgery Favours CT f/by surgery

Figure 183: Treatment-related morbidity: stenosis (Concomitant; 2-stage approach)

	CRT f/by su	irgery	CT f/by su	irgery		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
Cao 2009	2	118	0	119	100.0%	5.04 [0.24, 103.91]	
Total (95% CI)		118		119	100.0%	5.04 [0.24, 103.91]	
Total events	2		0				
Heterogeneity: Not ap Test for overall effect:		: 0.29)					0.01 0.1 1 10 100 Favours CRT f/by surgery Favours CT f/by surgery

H.13.4 Surgery (left or right open oesophagectomy) followed by (concomitant) chemoradiotherapy versus surgery (left or right open oesophagectomy) alone

Figure 184: 10-year overall survival rate

	Surgery followed b	y CRT	Surgery	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Lv 2010	19	78	10	80	100.0%	1.95 [0.97, 3.92]	
Total (95% CI)		78		80	100.0%	1.95 [0.97, 3.92]	◆
Total events	19		10				
Heterogeneity: Not ap	oplicable						0.01 0.1 1 10 100
Test for overall effect:	Z = 1.87 (P = 0.06)						Favours surgery f/by CRT Favours surgery alone

Figure 185: 10-year progression free survival rate

	Surgery followed b	y CRT	Surgery	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
Lv 2010	14	78	5	80	100.0%	2.87 [1.09, 7.59]	
Total (95% CI)		78		80	100.0%	2.87 [1.09, 7.59]	
Total events	14		5				
Heterogeneity: Not ap Test for overall effect:							0.01 0.1 1 10 100 Favours surgery fby CRT Favours surgery alone

H.13.5 Surgery alone versus radiotherapy alone

Figure 186: Overall survival rate (Different type of surgical approach)

	Surge	erv	Radiothe	erapy		Risk Ratio	Risk Ratio
Study or Subgroup	-	-	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
9.1.1 2-stage approa	ch						
Badwe 1998 Subtotal (95% CI)	24	44 <mark>44</mark>	14	43 43	81.7% 81.7%	1.68 [1.01, 2.78] 1.68 [1.01, 2.78]	
Total events	24		14				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 1.99 ((P = 0.0	15)				
9.1.2 3-stage approa	ch						
Fok 1994 Subtotal (95% CI)	6	39 39	3	35 35	18.3% 18.3%	1.79 [0.48, 6.64] 1.79 [0.48, 6.64]	
		29		30	10.3%	1.79 [0.46, 0.04]	
Total events	6 Nicoblo		3				
Heterogeneity: Not ap	•	- 0 -	0				
Test for overall effect:	Z = 0.88 ((P = 0.3	(8)				
Total (95% CI)		83		78	100.0%	1.70 [1.05, 2.74]	◆
Total events Heterogeneity: Chi² =	30 0.01, df=	1 (P =	17 0.92); l ² =	0%			
Test for overall effect: Test for subgroup diff		`	·	1 (P = 0	.92), I² = 0	1%	0.01 0.1 1 10 100 Favours radiotherapy Favours surgery

Figure 187 Overall survival (3-stage approach)

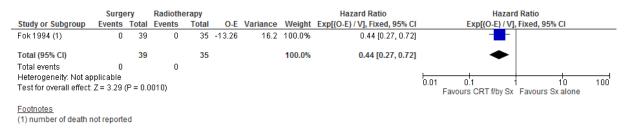


Figure 188: Treatment-related mortality (Different type of surgical approach)

	Surge	rv	Radiothe	rapy		Risk Ratio	Risk Ratio
Study or Subgroup	-		Events		Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
9.2.1 2-stage approa		- o cui	2101110			in the function of the function	
Badwe 1998 Subtotal (95% CI)	3	44 44	0	43 43	39.3% 39.3%	6.84 [0.36, 128.68] 6.84 [0.36, 128.68]	
Total events	3		0				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z=1.28 ((P = 0.2	!0)				
9.2.2 3-stage approa	ch						
Fok 1994 Subtotal (95% Cl)	3	39 39	7	37 37	60.7% 60.7%	0.41 [0.11, 1.46] 0.41 [0.11, 1.46]	
Total events	3		7				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 1.38 ((P = 0.1	7)				
Total (95% CI)		83		80	100.0%	1.23 [0.08, 20.09]	
Total events Heterogeneity: Tau ² = Test for overall effect: Test for subgroup diffe	Z = 0.15 ((P = 0.8	18)				0.01 0.1 1 10 100 Favours surgery Favours radiotherapy

H.13.6 Chemotherapy followed by surgery versus surgery alone

Figure 189: 30-day mortality

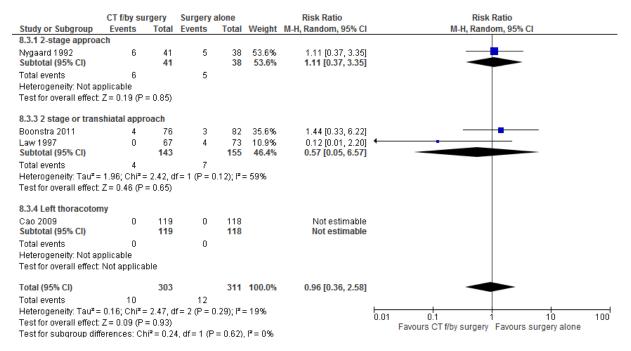


Figure 190: Treatment-related mortality

	CT f/by su	irgery	Surgery a	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% Cl
3.5.1 3 stage approa	ch						
Ancona 2001	2	47	2	47	16.6%	1.00 [0.15, 6.81]	
3aba 2000	1	21	0	21	4.2%	3.00 [0.13, 69.70]	
Subtotal (95% CI)		68		68	20.8%	1.40 [0.29, 6.87]	
Fotal events	3		2				
Heterogeneity: Chi ² =	0.34, df = 1	(P = 0.5)	6); I ^z = 0%				
Fest for overall effect	Z = 0.41 (P	= 0.68)					
3.5.2 2 or 3 stage ap	proach						
Maipang 1994	4	24	0	22		8.28 [0.47, 145.50]	
Subtotal (95% CI)		24		22	4.3%	8.28 [0.47, 145.50]	
Fotal events	4		0				
Heterogeneity: Not a	oplicable						
Fest for overall effect	: Z = 1.45 (P	= 0.15)					
3.5.3 2-stage or tran	shiatal appi	roach					
3oonstra 2011	5	80	3	82	24.6%	1.71 [0.42, 6.91]	_
_aw 1997	5	74	6	73	50.2%	0.82 [0.26, 2.58]	
Subtotal (95% CI)		154		155	74.9%	1.11 [0.47, 2.66]	
Fotal events	10		9				
Heterogeneity: Chi ² =	0.63, df = 1	(P = 0.4)	3); I ² = 0%				
Fest for overall effect	Z = 0.24 (P	= 0.81)					
3.5.4 Left thoracotor	ny						
Cao 2009	0	119	0	118		Not estimable	
Subtotal (95% CI)		119		118		Not estimable	
Fotal events	0		0				
Heterogeneity: Not a	oplicable						
Fest for overall effect	: Not applica	ıble					
Total (95% CI)		365		363	100.0%	1.48 [0.73, 3.03]	-
Fotal events	17		11				
Heterogeneity: Chi ² =	2.80, df = 4	(P = 0.5	9); I ² = 0%				
Fest for overall effect							0.01 0.1 1 10 1 Favours CT f/by surgery Favours surgery alone
		ni² = 1.70					

Figure 191: Postoperative mortality

	CT f/by su		Surgery a			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% Cl
8.4.1 2-stage approa							
Nygaard 1992	6	41	5	38	32.1%	1.11 [0.37, 3.35]	
Subtotal (95% CI)		41	-	38	32.1%	1.11 [0.37, 3.35]	
Total events	6		5				
Heterogeneity: Not ap		- 0.05					
Test for overall effect:	Z=0.19(P	= 0.85)					
8.4.2 3-stage approa	ch						
Ancona 2001	1	40	2	47	11.4%	0.59 [0.06, 6.24]	
Baba 2000	1	21	0	21	3.1%	3.00 [0.13, 69.70]	
Subtotal (95% CI)		61		68	14.5%	1.10 [0.19, 6.36]	
Total events	2		2				
Heterogeneity: Chi² =			2); I² = 0%				
Test for overall effect:	Z=0.11 (P	= 0.91)					
8.4.3 2 stage or trans	shiatal appr	roach					
Boonstra 2011	4	76	3	82	17.9%	1.44 [0.33, 6.22]	
Law 1997	5	67	6	73	35.5%	0.91 [0.29, 2.84]	_
Subtotal (95% CI)		143		155	53.4%	1.09 [0.44, 2.65]	-
Total events	9		9				
Heterogeneity: Chi ^z =			3); I² = 0%				
Test for overall effect:	Z = 0.18 (P	= 0.86)					
8.4.4 Left thoracoton	ny						
Cao 2009	0	119	0	118		Not estimable	
Subtotal (95% CI)		119		118		Not estimable	
Total events	0		0				
Heterogeneity: Not ap	•						
Test for overall effect:	Not applica	ble					
Total (95% CI)		364		379	100.0%	1.10 [0.57, 2.09]	-
Total events	17		16				
Heterogeneity: Chi ^z =	0.90, df = 4	(P = 0.9	2); I ² = 0%				0.01 0.1 1 10 11
Test for overall effect:							U.U1 U.1 1 1U 11 Favours CT f/by surgery Favours surgery alone
Test for subgroup diff	erences: Cl	hi² = 0.01), df = 2 (P	= 1.00).	l² = 0%		r avours or noy surgery Favours surgery alone

Figure 192: Overall survival rate

	CT f/by su	rgery	Surgery a	alone		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
8.8.1 3 stage approa	ch						
Ancona 2001	7	47	3	47	18.4%	2.33 [0.64, 8.48]	
Subtotal (95% CI)		47		47	18.4%	2.33 [0.64, 8.48]	
Total events	7		3				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 1.29 (P	= 0.20)					
8.8.2 2 or 3 stage ap	-						_
Maipang 1994	7	24	8	22	51.1%	0.80 [0.35, 1.85]	
Subtotal (95% CI)		24		22	51.1%	0.80 [0.35, 1.85]	
Total events	7		8				
Heterogeneity: Not ap	•						
Test for overall effect:	Z = 0.52 (P	= 0.60)					
8.8.3 Not reported							
MRC 2002	9	123	5	124	30.5%	1.81 [0.63, 5.26]	
Subtotal (95% CI)		123		124	30.5%	1.81 [0.63, 5.26]	
Total events	9		5				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z=1.10 (P	= 0.27)					
Total (95% CI)		194		193	100.0%	1.39 [0.78, 2.49]	-
Total events	23		16				-
Heterogeneity: Chi ² =		(P = 0.2		6			
Test for overall effect:			-71	-			
Test for subaroup diff			5. df = 2 (P	= 0.29).	. I ² = 18.5	%	Favours surgery alone Favours CT f/by surgery

Figure 193 Overall survival (According to type of surgical approach)

	CT f/by su	rgery	Surgery	alone				Hazard Ratio	Hazard Ratio
Study or Subgroup	Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% CI	Exp[(O-E) / V], Fixed, 95% CI
8.13.1 2-stage or tran	shiatal app	proach							
Boonstra 2011 (1) Subtotal (95% CI)	0	85 <mark>85</mark>	0	84 <mark>84</mark>	-12.34	36.02	43.8% 43.8%	0.71 [0.51, 0.98] 0.71 [0.51, 0.98]	→
Total events	0		0						
Heterogeneity: Not app	plicable								
Test for overall effect: 2	Z = 2.06 (P	= 0.04)							
8.13.2 Not reported									
MRC 2002 Subtotal (95% CI)	87	123 123	97	124 124	-11.49	46.25	56.2% 56.2%	0.78 [0.58, 1.04] 0.78 [0.58, 1.04]	₩
Total events	87		97						
Heterogeneity: Not app	plicable								
Test for overall effect: 2	Z = 1.69 (P	= 0.09)							
Total (95% CI)		208		208			100.0%	0.75 [0.60, 0.93]	•
Total events	87		97						
Heterogeneity: Chi ² = I	0.18, df = 1	(P = 0.6	7); I ² = 0%						
Test for overall effect: 3	Z = 2.63 (P	= 0.009)							Favours CT f/by surgery Favours surgery alone
Test for subgroup diffe	erences: Ch	ni² = 0.18	8, df = 1 (P	= 0.67),	$ ^{2} = 0\%$				Tavours of they surgery Tavours surgery alone
Footnotes									
(1) number of death n	ot reported								

Figure 194: Disease-free survival (2-stage or transhiatal)

	CT f/by su	rgery	Surgery	alone				Hazard Ratio	Hazard Ratio
Study or Subgroup	Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% Cl	Exp[(O-E) / V], Fixed, 95% CI
Boonstra 2011 (1)	0	85	0	84	-11.8	35.93	100.0%	0.72 [0.52, 1.00]	
Total (95% CI)		85		84			100.0%	0.72 [0.52, 1.00]	•
Total events Heterogeneity: Not a Test for overall effect		= 0.05)	0						0.01 0.1 10 100 Favours CT f/by surgery Favours surgery alone
<u>Footnotes</u> (1) number of event r	not reported								

Figure 195: Treatment-related morbidity: anastomotic leak

	CT f/by su		Surgery a			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% Cl
3.2.1 2-stage approa							
Vygaard 1992	3	41	2	38	10.6%	1.39 [0.25, 7.87]	
Subtotal (95% CI)		41	_	38	10.6%	1.39 [0.25, 7.87]	
Total events	3		2				
Heterogeneity: Not ap	•	- 0.74)					
Fest for overall effect:	Z=0.37 (P	= 0.71)					
3.2.2 3-stage approa	ich						
Ancona 2001	2	40	1	47	4.7%	2.35 [0.22, 24.97]	
3aba 2000	5	21	6	21	30.6%	0.83 [0.30, 2.31]	
Subtotal (95% CI)		61		68	35.2%	1.03 [0.41, 2.61]	-
otal events	7		7				
leterogeneity: Chi² =			3); I^z = 0%				
Test for overall effect:	Z = 0.07 (P	= 0.94)					
3.2.3 2-stage or tran	shiatal app	raoch					
Boonstra 2011	8	76	9	82	44.1%	0.96 [0.39, 2.36]	_
.aw 1997	3	67	0	73	2.4%	7.62 [0.40, 144.79]	
Subtotal (95% CI)		143		155	46.5%	1.31 [0.58, 2.97]	-
"otal events	11		9				
Heterogeneity: Chi² =			8); I² = 459	6			
Fest for overall effect:	Z=0.64 (P	= 0.52)					
3.2.4 Left thoracic							
Cao 2009	0	119	1	118	7.7%	0.33 [0.01, 8.03]	
Subtotal (95% CI)		119		118	7.7%	0.33 [0.01, 8.03]	
Fotal events	0		1				
Heterogeneity: Not ap	•						
Fest for overall effect:	Z = 0.68 (P	= 0.50)					
Fotal (95% CI)		364		379	100.0%	1.15 [0.65, 2.02]	-
Fotal events	21		19				
Heterogeneity: Chi² =	3.10, df = 5	(P = 0.6	8); I ² = 0%				0.01 0.1 1 10 1
Test for overall effect:							U.U1 U.1 1 1U 1 Favours CT f/by surgery Favours surgery alone
est for subaroup dif	, ferences: Cl	hi² = 0.71	df = 3 (P	= 0.85)	I ² = 0%		r avours of inby surgery in avours surgery alone

Figure 196: Treatment-related morbidity: bleeding

	CT f/by	surg	егу	Surge	ery alo	ne		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Law 1997	795	58	60	733	30	69	100.0%	62.00 [45.71, 78.29]	
Total (95% CI)			60			69	100.0%	62.00 [45.71, 78.29]	•
Heterogeneity: Not ap Test for overall effect:		P < 0	.00001)					-100 -50 0 50 100 Favours CT f/by surgery Favours surgery alone

Figure 197: Treatment related morbidity: wound infection

	CT f/by su	irgery	Surgery	alone		Risk Ratio		Risl	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fix	ed, 95% Cl	
Law 1997	4	60	7	69	100.0%	0.66 [0.20, 2.14]				
Total (95% CI)		60		69	100.0%	0.66 [0.20, 2.14]		$ \rightarrow $		
Total events	4		7							
Heterogeneity: Not ap Test for overall effect:		= 0.49)					0.01	0.1 Favours CT f/by surgery	1 10 Favours surgery :	100 alone

H.13.7 Chemoradiotherapy versus radiotherapy alone

Figure 198: Treatment-related mortality (Concomitant)

	Chemoradioth	егару	Radiothe	erapy		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Araujo1991	0	28	1	31	17.2%	0.37 [0.02, 8.68]	
Cooper 1999	1	61	0	60	6.1%	2.95 [0.12, 71.05]	
Gao 2002	0	40	0	41		Not estimable	
Kaneta 1997	0	13	0	12		Not estimable	
Slabber 1998	2	34	2	36	23.4%	1.06 [0.16, 7.10]	
Smith 1998	0	59	2	60	29.9%	0.20 [0.01, 4.15]	←
Zhao 2005	5	54	2	57	23.4%	2.64 [0.53, 13.03]	
Zhu 2000	0	33	0	33		Not estimable	
Total (95% CI)		322		330	100.0%	1.17 [0.47, 2.90]	
Total events	8		7				
Heterogeneity: Chi ² =	3.14, df = 4 (P =	0.53); I ^z	= 0%				
Test for overall effect:	Z = 0.34 (P = 0.7	'3)					0.01 0.1 1 1 10 100 Favours chemoradiotherapy Favours radiotherapy

Figure 199: Overall survival (According to type of chemoradiotherapy)

	Treatm	nent	Contr	ol				Hazard Ratio	Hazard Ratio
Study or Subgroup	Events	Total	Events	Total	O-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% CI	Exp[(O-E) / V], Fixed, 95% CI
1.1.1 Concomitant									
Araujo1991	25	28	30	31	-5.22	11.84	10.8%	0.64 [0.36, 1.14]	
Cooper 1999	48	61	62	62	-28.24	53.46	48.6%	0.59 [0.45, 0.77]	
Gao 2002	24	40	27	41	-3.02	12.75	11.6%	0.79 [0.46, 1.37]	
Zhu 2000	23	33	29	33	-6.27	13	11.8%	0.62 [0.36, 1.06]	
Subtotal (95% CI)		162		167			82.8%	0.63 [0.51, 0.77]	•
Total events	120		148						
Heterogeneity: Chi² =	0.89, df=	3 (P =	0.83); I² =	:0%					
Test for overall effect:	Z = 4.48 ((P ≺ 0.0	0001)						
4.4.2 Convention									
1.1.2 Sequential			_						
Hatlevoll 1992	0	46 46	5	51 51	3.6	18.92		1.21 [0.77, 1.90]	
Subtotal (95% CI)		40	-	2.1			17.2%	1.21 [0.77, 1.90]	
Total events			5						
Heterogeneity: Not ap									
Test for overall effect:	Z = 0.83 ((P = 0.4)	1)						
Total (95% CI)		208		218			100.0%	0.70 [0.58, 0.84]	◆
Total events	120		153						
Heterogeneity: Chi² =	7.71, df=	4 (P =	0.10); I 2 =	= 48%				H	
Test for overall effect:	Z = 3.73 ((P = 0.0	002)					l	Favours treatment Favours control
Test for subgroup diff	erences:	Chi² = 6	6.82,df=	1 (P =	0.009), P	²= 85.3%			avous a cament - i avous control

Figure 200: Overall survival rate at 1 year

	Chemoradioth	егару	Radiothe	rapy		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
7.1.1 Concomitant							
Araujo1991	17	28	17	31	10.4%	1.11 [0.72, 1.71]	_ -
Cooper 1999	32	61	21	62	10.8%	1.55 [1.02, 2.36]	
Gao 2002	32	40	30	41	16.0%	1.09 [0.86, 1.39]	+
Han 2012	46	65	48	65	16.8%	0.96 [0.77, 1.19]	+
Herskovic 1992/Al-Sarraf 1997	28	61	17	60	9.3%	1.62 [1.00, 2.63]	
Kumar 2007	33	65	18	60	10.0%	1.69 [1.07, 2.67]	
Smith 1998	32	59	20	60	10.6%	1.63 [1.06, 2.50]	
Zhao 2005	36	54	44	57	16.1%	0.86 [0.68, 1.09]	
Subtotal (95% CI)		433		436	100.0%	1.21 [0.99, 1.48]	◆
Total events	256		215				
Heterogeneity: Tau ² = 0.05; Chi ²	= 19.81, df = 7 (F	P = 0.006); I ^z = 65%				
Test for overall effect: Z = 1.87 (F	° = 0.06)						
Total (95% CI)		433		436	100.0%	1.21 [0.99, 1.48]	•
Total events	256		215				
Heterogeneity: Tau ² = 0.05; Chi ²	= 19.81, df = 7 (F	° = 0.006); I ^z = 65%	ŀ			
Test for overall effect: Z = 1.87 (F	P = 0.06)				0.01 0.1 1 10 100 Favours radiotherapy Favours chemoradiotherapy		
Test for subaroup differences: N	lot applicable						Favours radiomerapy Favours chemoladiomerapy

Figure 201: Overall survival rate at 3 years (Concomitant)

	Chemoradiotherapy Ra		Radiothe	erapy		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
Araujo1991	6	28	5	31	7.3%	1.33 [0.46, 3.88]	+
Cooper 1999	18	61	0	62	0.8%	37.60 [2.32, 610.31]	│
Gao 2002	16	40	14	41	21.2%	1.17 [0.66, 2.07]	
Han 2012	26	65	12	65	18.4%	2.17 [1.20, 3.91]	_
Herskovic 1992/Al-Sarraf 1997	7	61	0	60	0.8%	14.76 [0.86, 252.80]	· · · · · · · · · · · · · · · · · · ·
Kumar 2007	12	65	7	60	11.2%	1.58 [0.67, 3.75]	- +
Smith 1998	8	59	5	60	7.6%	1.63 [0.56, 4.69]	
Zhao 2005	24	54	22	57	32.8%	1.15 [0.74, 1.79]	
Total (95% CI)		433		436	100.0%	1.82 [1.40, 2.37]	•
Total events	117		65				
Heterogeneity: Chi ² = 13.86, df =	7 (P = 0.05); I ² =	49%					
Test for overall effect: Z = 4.50 (P	< 0.00001)						0.01 0.1 1 1 10 100 Favours radiotherapy Favours chemoradiotherapy

Figure 202: Overall survival rate at 5 years

	Chemoradioth	егару	Radiothe	егару		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
Araujo1991	4	28	2	31	7.5%	2.21 [0.44, 11.17]	
Cooper 1999	14	61	0	62	2.0%	29.47 [1.80, 483.28]	│→
Gao 2002	8	65	3	60	12.4%	2.46 [0.68, 8.85]	
Kumar 2007	8	65	3	60	12.4%	2.46 [0.68, 8.85]	
Smith 1998	5	59	4	60	15.7%	1.27 [0.36, 4.50]	
Zhao 2005	19	54	13	57	50.1%	1.54 [0.85, 2.81]	+■
Total (95% CI)		332		330	100.0%	2.33 [1.51, 3.58]	◆
Total events	58		25				
Heterogeneity: Chi ² =	5.86, df = 5 (P =	0.32); l²	= 15%				0.01 0.1 1 10 100
Test for overall effect:	Z = 3.83 (P = 0.0	0001)					Favours radiotherapy Favours chemoradiotherapy

Figure 203: Disease-free survival

	Treatm	ent	Contr	rol				Hazard Ratio	Hazard Ratio
Study or Subgroup	Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% Cl	CI Exp[(O-E) / V], Fixed, 95% CI
Cooper 1999	35	57	54	61	-16.66	21.24	62.5%	0.46 [0.30, 0.70]	n — — — — — — — — — — — — — — — — — — —
Gao 2002	16	40	13	41	-3.02	12.75	37.5%	0.79 [0.46, 1.37]	r] — – –
Total (95% CI)		97		102			100.0%	0.56 [0.40, 0.78]	
Total events	51		67						
Heterogeneity: Chi ² =	2.39, df=	1 (P =	0.12); l² =	= 58%					
Test for overall effect:	Z = 3.38 (P = 0.0	007)						Favours treatment Favours control

Figure 204: Any treatment-related morbidity

	Chemoradioth	егару	Radiothe	erapy		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
Araujo1991	26	28	25	31	27.2%	1.15 [0.94, 1.41]	- <mark>-</mark> -
Cooper 1999	12	61	15	60	17.4%	0.79 [0.40, 1.54]	
Han 2012	12	65	10	65	11.5%	1.20 [0.56, 2.58]	-
Kumar 2007	31	65	18	60	21.5%	1.59 [1.00, 2.53]	
Zhao 2005	10	54	17	57	19.0%	0.62 [0.31, 1.23]	
Zhu 2000	4	33	3	33	3.4%	1.33 [0.32, 5.50]	
Total (95% CI)		306		306	100.0%	1.09 [0.88, 1.36]	
Total events	95		88				
Heterogeneity: Chi ² =	6.43, df = 5 (P =	0.27); l²	= 22%				0.01 0.1 1 10 100
Test for overall effect	Z = 0.80 (P = 0.4	43)					Favours chemoradiotherapy Favours radiotherapy

H.13.8 Chemoradiotherapy (concomitant) alone versus surgery (2-stage or 3-stage oesophagectomy) alone

Figure 205: Overall mortality estimate

	Chemoradioth	erapy	Surge	ery		Risk Ratio	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% (1	
Chiu 2005/Teoh 2012	15	36	20	44	100.0%	0.92 [0.55, 1.52]			
Total (95% CI)		36		44	100.0%	0.92 [0.55, 1.52]	+		
Total events	15		20						
Heterogeneity: Not applic Test for overall effect: Z =							0.01 0.1 1 Favours chemoradiotherapy Favour	10 s surgery	100

Figure 206: 30-day mortality rate

	Chemoradiothe	erapy	Surge	ery		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
Chiu 2005/Teoh 2012	0	36	3	44	100.0%	0.17 [0.01, 3.26]	
Total (95% CI)		36		44	100.0%	0.17 [0.01, 3.26]	
Total events	0		3				
Heterogeneity: Not app Test for overall effect: Z							I I I I 0.002 0.1 1 10 500 Favours chemoradiotherapy Favours surgery

Figure 207 Overall survival (Concomitant; 2- or 3-stage approach)

	Chemoradioth	erapy	Surge	ery	Hazard Ratio			Hazard Ratio				
Study or Subgroup	Events	Total	Events	Total	O-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% CI		Exp[(O-E) / V], Fixed	l, 95% CI	
Chiu 2005/Teoh 2012	15	36	20	44	-0.72	8.59	100.0%	0.92 [0.47, 1.79]				
Total (95% CI)		36		44			100.0%	0.92 [0.47, 1.79]		•		
Total events	15		20									
Heterogeneity: Not appl Test for overall effect: Z									0.01	0.1 1 Favours CRT Favo	10 urs S	100

Figure 208: Overall survival rate at 2 years

	Chemoradiotherapy		Surgery			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Chiu 2005/Teoh 2012	21	36	24	44	100.0%	1.07 [0.73, 1.57]	
Total (95% CI)		36		44	100.0%	1.07 [0.73, 1.57]	★
Total events	21		24				
Heterogeneity: Not appl	licable						0.01 0.1 1 10 100
Test for overall effect: Z	= 0.34 (P = 0.73)						Favours surgery Favours chemoradiotherapy

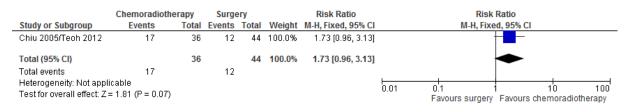
Figure 209: Overall survival rate at 5 years

	Chemoradiothe	erapy	Surge	ery		Risk Ratio	Risk Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixe	ed, 95% Cl		
Chiu 2005/Teoh 2012	17	36	10	44	100.0%	2.08 [1.09, 3.96]					
Total (95% CI)		36		44	100.0%	2.08 [1.09, 3.96]			-		
Total events	17		10								
Heterogeneity: Not appl Test for overall effect: Z							0.01	0.1 Favours surgery	Favours che	10 moradio	100 therapy

Figure 210: Disease-free survival rate at 2 years

	Chemoradiothe	erapy	Surge	ery		Risk Ratio		Risk F	latio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixed	I, 95% CI	
Chiu 2005/Teoh 2012	20	36	24	44	100.0%	1.02 [0.68, 1.52]			-	
Total (95% CI)		36		44	100.0%	1.02 [0.68, 1.52]			•	
Total events	20		24							
Heterogeneity: Not appl Test for overall effect: Z							L 0.01	0.1 1 Favours surgery	10 Favours chemorad	100 diotherapy

Figure 211: Disease-free survival rate at 5 years



H.14 Non-metastatic oesophageal cancer not suitable for surgery

What is the optimal treatment for adults with non-metastatic disease in the oesophagus who are not suitable for surgery?

H.14.1 Comparison 1: Chemotherapy versus radiotherapy in inoperable oesophageal cancer

Figure 212: Overall Survival

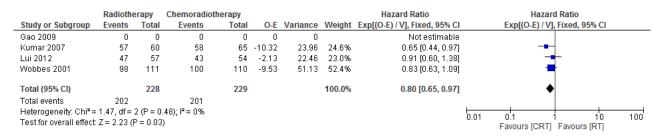


Figure 213: One Year Overall Survival

	Radiothe	erapy	Chemoradioth	nerapy		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
1.2.1 5FU-based che	motherapy	1					
Lui 2012	13	57	18	54	13.0%	0.68 [0.37, 1.26]	
Subtotal (95% CI)		57		54	13.0%	0.68 [0.37, 1.26]	-
Total events	13		18				
Heterogeneity: Not ap	oplicable						
Test for overall effect:	Z=1.22 (F	° = 0.22)					
1.2.2 Non-5FU based	chemothe	егару					
Gao 2009	10	33	10	35	9.5%	1.06 [0.51, 2.21]	_ _
Kumar 2007	42	60	32	65	33.2%	1.42 [1.06, 1.91]	
Wobbes 2001	79	111	60	110	44.2%	1.30 [1.06, 1.61]	
Subtotal (95% CI)		204		210	87.0%	1.33 [1.12, 1.57]	•
Fotal events	131		102				
Heterogeneity: Tau² =	= 0.00; Chi ^a	'= 0.60, i	df = 2 (P = 0.74); I² = 0%			
Test for overall effect:	Z = 3.34 (F	P = 0.000	39)				
Total (95% CI)		261		264	100.0%	1.21 [0.95, 1.55]	◆
Fotal events	144		120				
Heterogeneity: Tau ² =	= 0.02; Chi ²	= 5.04, i	df = 3 (P = 0.17); l² = 409	6		
Test for overall effect:	Z = 1.52 (F	^o = 0.13)					Favours [RT] Favours [Chemo + RT]
Fest for subgroup dif	ferences: C	⊳hi² = 4.2	23, df = 1 (P = 0	.04), I ^z = 1	76.3%		r avouro [ref] i r avouro [offenno - ref]

Figure 214: Two Year Overall Survival

	Radiothe	erapy	Chemoradioth	erapy		Risk Ratio	I		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, F	Random, 95% C	I
Gao 2009	16	35	23	33	16.5%	0.66 [0.43, 1.00]			
Kumar 2007	51	60	48	65	38.2%	1.15 [0.96, 1.38]		+	
Lui 2012	0	0	0	0		Not estimable			
Wobbes 2001	95	111	88	110	45.3%	1.07 [0.95, 1.21]		•	
Total (95% CI)		206		208	100.0%	1.01 [0.82, 1.25]		•	
Total events	162		159						
Heterogeneity: Tau ² =	= 0.02; Chi ⁼	² = 6.14,	df = 2 (P = 0.05)); l ² = 679	%				10 100
Test for overall effect	: Z = 0.14 (F	P = 0.89)				0.01 0.1 Favours	(RT) Favours (10 100 Chemo + RT]

Figure 215: Three Year Overall Survival

	Radiothe	erapy	Chemoradio	therapy		Risk Ratio			Risk F	latio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	Year		M-H, Fixed	I, 95% CI	
Wobbes 2001	98	111	100	110	55.2%	0.97 [0.89, 1.06]	2001				
Kumar 2007	53	60	53	65	27.9%	1.08 [0.93, 1.26]	2007		+	÷	
Gao 2009	0	0	0	0		Not estimable	2009				
Lui 2012	35	57	30	54	16.9%	1.11 [0.81, 1.51]	2012		-	-	
Total (95% CI)		228		229	100.0%	1.03 [0.94, 1.12]			•		
Total events	186		183								
Heterogeneity: Chi ² =	2.15, df=1	2 (P = 0	.34); I ² = 7%					L			4.0
Test for overall effect	: Z = 0.57 (F	P = 0.57)					0.01	0.1 1 Favours (RT)	10 Favours [Chei	10 [mo + RT

Figure 216: Five Year Survival

	Radiothe	Radiotherapy Chemoradiotherap				Risk Ratio		Risk Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixe	d, 95% Cl		
Kumar 2007	57	60	57	65	62.5%	1.08 [0.97, 1.21]					
Lui 2012	41	57	32	54	37.5%	1.21 [0.92, 1.60]		-			
Total (95% CI)		117		119	100.0%	1.13 [1.00, 1.28]			•		
Total events	98		89								
Heterogeneity: Chi ² =	: 0.89, df = 1	1 (P = 0	.35); I² = 0%				0.01	01		10	100
Test for overall effect	: Z = 1.94 (F	° = 0.05)				0.01	Favours [RT]	Favours	[Chemo	

Figure 217: Ten Year Overall Survival

	Radiothe	erapy	Chemoradiot	herapy		Risk Ratio			Risk Ra	tio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	Year		M-H, Fixed,	95% CI		
Lui 2012	46	57	42	54	100.0%	1.04 [0.86, 1.26]	2012		_			
Total (95% CI)		57		54	100.0%	1.04 [0.86, 1.26]			•			
Total events	46		42									
Heterogeneity: Not a								0.01	0.1 1			100
Test for overall effect	:Z=0.38 (F	P = 0.70)						Favours [RT] F	avours [Ch	emo + F	

Figure 218: Treatment-Related Mortality

	Radiothe	erapy	Chemoradiot	herapy		Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixed, 95%	CI	
Lui 2012	2	57	5	54	100.0%	0.38 [0.08, 1.87]				
Total (95% CI)		57		54	100.0%	0.38 [0.08, 1.87]				
Total events	2		5							
Heterogeneity: Not a) Test for overall effect		P = 0.23)				L.01	0.1 1 Favours [RT] Favou	10 rs [CRT]	100

Figure 219: One Year Progression-free Survival

	Radiothe	erapy	Chemoradioth	егару		Risk Ratio		Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H, Random, 95% Cl	
Gao 2009	24	35	14	33	50.5%	1.62 [1.02, 2.55]			
Kumar 2007	0	0	0	0		Not estimable			
Lui 2012	0	0	0	0		Not estimable			
Wobbes 2001	18	111	34	110	49.5%	0.52 [0.32, 0.87]			
Total (95% CI)		146		143	100.0%	0.93 [0.30, 2.89]		-	
Total events	42		48						
Heterogeneity: Tau ² =	= 0.61; Chi ^a	² = 11.11	l, df = 1 (P = 0.0	009); I ^z =	91%				400
Test for overall effect	-						0.01	0.1 1 10 Favours [CRT] Favours [RT]	100

Figure 220: Three Year Progression-free Survival

	Radiothe	erapy	Chemoradiot	herapy		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
Gao 2009	0	0	0	0		Not estimable	
Kumar 2007	0	0	0	0		Not estimable	
Lui 2012	0	0	0	0		Not estimable	
Wobbes 2001	8	111	9	110	100.0%	0.88 [0.35, 2.20]	
Total (95% CI)		111		110	100.0%	0.88 [0.35, 2.20]	-
Total events	8		9				
Heterogeneity: Not ap	oplicable						
Test for overall effect:	Z = 0.27 (F	P = 0.79)				Favours [experimental] Favours [control]

Figure 221: Treatment-related Toxicity: nausea and vomiting



Figure 222: Treatment-related toxicity: oesophagitis

	Radiothe	erapy	Chemoradiot	herapy		Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixed, 95% Cl		
Gao 2009	22	33	24	35	49.3%	0.97 [0.70, 1.35]				
Kumar 2007	15	60	25	65	50.7%	0.65 [0.38, 1.11]				
Lui 2012	0	0	0	0		Not estimable				
Wobbes 2001	0	0	0	0		Not estimable				
Total (95% CI)		93		100	100.0%	0.81 [0.60, 1.09]		•		
Total events	37		49							
Heterogeneity: Chi ² =	: 1.84, df=	1 (P = 0	.17); I² = 46%						 	
Test for overall effect	: Z = 1.38 (F	P = 0.17)				0.01	0.1 1 Favours [CRT] Favours [R	10 [T]	1

H.14.2 Comparison 2: 5-FU-based chemoradiotherapy versus non-5-FU-based chemoradiotherapy

Figure 223: One Year Overall Survival

	5FU-base	I CRT	Non 5FU-bas	ed CRT		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	Year	M-H, Fixed, 95% Cl
Ajani 2008	9	37	11	35	100.0%	0.77 [0.37, 1.64]	2008	
Total (95% CI)		37		35	100.0%	0.77 [0.37, 1.64]		-
Total events	9		11					
Heterogeneity: Not ap							0.01	
Test for overall effect:	: Z = 0.67 (P	= 0.50)					0.01	5-FU Based CRT non-5-FU Based CRT

Figure 224: Two Year Overall Survival

	5FU-base	d CRT	Non 5FU-bas	ed CRT		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	Year	M-H, Fixed, 95% CI
Ajani 2008	29	37	23	35	100.0%	1.19 [0.89, 1.60]	2008	
Total (95% CI)		37		35	100.0%	1.19 [0.89, 1.60]		•
Total events	29		23					
Heterogeneity: Not ap Test for overall effect		= 0.24)					0.01	I 0.1 1 10 100 5-FU Based CRT Non-5-FU Based CRT

Figure 225: Treatment-related Mortality

	5FU-based	I CRT	Non 5FU-bas	ed CRT		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
Ajani 2008	1	37	2	35	100.0%	0.47 [0.04, 4.99]	
Total (95% CI)		37		35	100.0%	0.47 [0.04, 4.99]	
Total events	1		2				
Heterogeneity: Not ap Test for overall effect:		- 0.52)					L.01 0.1 1 10 100
restion overall effect.	. <u>2</u> – 0.02 (F :	- 0.03)					Favours 5-FU Based CRT Favours Non-5-FU CRT

Figure 226: Treatment-related Morbidity: grade 4/5 toxicity

	5FU-based	I CRT	Non 5FU-bas	ed CRT		Risk Ratio		Ris	k Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fiz	(ed, 95% Cl		
Ajani 2008	11	37	15	35	100.0%	0.69 [0.37, 1.30]		-	+		
Total (95% CI)		37		35	100.0%	0.69 [0.37, 1.30]					
Total events	11		15								
Heterogeneity: Not ap Test for overall effect:		= 0.25)					L.01	0.1 Favours (5FU CRT		0 5FU CR	100 2 1]

H.15 First-line palliative chemotherapy

What is the optimal palliative first-line systemic chemotherapy for locally advanced and/or metastatic oesophago-gastric cancer?

H.15.1 Comparison 1: Combination versus single-agent chemotherapy

Study or Subgroup	log[Hazard ratio]	SE	Combination Chemo Total	Single-agent therapy Total	Weight	Hazard ratio IV, Fixed, 95% Cl	Hazard ratio IV, Fixed, 95% Cl
Colucci 1995	-0.36	0.26	35	36	11.7%	0.70 [0.42, 1.16]	
Loehrer 1994	0	0	64	94		Not estimable	
Ohtsu 2003	-0.14	0.14	105	105	40.2%	0.87 [0.66, 1.14]	
Bouche 2004	-0.43	0.19	89	45	21.9%	0.65 [0.45, 0.94]	_
Lutz 2007	-0.27	0.1734	108	37	26.2%	0.76 [0.54, 1.07]	
Total (95% CI)			337	223	100.0%	0.77 [0.65, 0.91]	◆
Heterogeneity: Chi ² =	1.69, df = 3 (P = 0.6	4); I ² = 0%)				0.1 0.2 0.5 1 2 5 10
Test for overall effect:	Z = 2.96 (P = 0.003))					Favours Combination Favours Single Agent

Figure 228: Treatment-related mortality

	Combination C	hemo	Single-agent f	therapy		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI
Colucci 1995	0	35	1	36	32.7%	0.33 [0.01, 8.46]	
Ohtsu 2003	4	105	1	105	21.5%	4.12 [0.45, 37.48]	
Bouche 2004	1	89	1	45	29.4%	0.50 [0.03, 8.18]	
Lutz 2007	1	108	0	37	16.4%	1.05 [0.04, 26.25]	
Total (95% CI)		337		223	100.0%	1.31 [0.38, 4.55]	
Total events	6		3				
Heterogeneity: Chi ² =	2.20, df = 3 (P =	0.53); I² =	= 0%				
Test for overall effect:	Z = 0.43 (P = 0.6	(7)					0.01 0.1 1 10 100 favours combination favours single agent

Figure 229: Treatment-related toxicity: nausea and vomiting

	Combination C	hemo	Single-agent th	егару		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% Cl
Kim 1993	0	0	0	0		Not estimable	
Loehrer 1994	8	70	6	69	54.7%	1.31 [0.48, 3.59]	
Ohtsu 2003	8	105	5	105	45.3%	1.60 [0.54, 4.73]	
Total (95% CI)		175		174	100.0%	1.44 [0.69, 3.02]	-
Total events	16		11				
Heterogeneity: Chi ^z = Test for overall effect:			= 0%				0.01 0.1 1 10 100 Favours combination Favours single agent

Figure 230: Treatment-related toxicity: diarrhoea

	Combination C	hemo	Single-agent the	erapy		Risk Ratio		Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H, Random, 95% CI	
Loehrer 1994	2	70	5	69	59.2%	0.39 [0.08, 1.96]		_	
Ohtsu 2003	3	105	0	105	40.8%	7.00 [0.37, 133.87]			
Total (95% CI)		175		174	100.0%	1.28 [0.07, 21.75]			
Total events	5		5						
Heterogeneity: Tau² = Test for overall effect:			P = 0.09); I ^z = 669	6			L 0.01	0.1 1 10 Favours combination Favours single agent	100

H.15.2 Comparison 2: 5-FU/cisplatin combinations with or without anthracycline

Figure 231: Overall survival

Study or Subgroup	log[Hazard ratio]		5-FU/P/anthracycline Total		Weight	Hazard ratio IV, Fixed, 95% Cl	Hazar IV, Fixed	d ratio I, 95% Cl	
Yun 2010	0	0	0	0		Not estimable	,	(
KRGGC 1992	-0.56	0.38	25	22	44.5%	0.57 [0.27, 1.20]	_	<u> </u>	
Kim 2001	-0.19	0.34	60	60	55.5%	0.83 [0.42, 1.61]			
Total (95% CI)			85	82	100.0%	0.70 [0.43, 1.15]		-	
Heterogeneity: Chi² = Test for overall effect:		7); I² =	0%				0.2 0.5 5-FU/cis/anthracycline	2 5-FU/cisplatin	5

Figure 232: Progression-free survival

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% Cl	Hazard Ratio IV, Fixed, 95% CI
Yun 2010	-0.0468	0.254	100.0%	0.95 [0.58, 1.57]	
Total (95% CI) Heterogeneity: Not ag Test for overall effect:			100.0%	0.95 [0.58, 1.57]	0.01 0.1 1 10 100 Favours [triplet] Favours [doublet]

H.15.3 Comparison 3: 5-FU/anthracycline combinations with or without cisplatin

Figure 233: Overall survival

			5-FU/anthracycline/P	5-FU/anthracycline		Hazard ratio	Hazard ratio
Study or Subgroup	log[Hazard ratio]	SE	Total	Total	Weight	IV, Fixed, 95% Cl	IV, Fixed, 95% Cl
Kikuchi 1990	-0.54	0.25	32	33	26.5%	0.58 [0.36, 0.95]	_
Cullinan 1994	0.07	0.15	51	132		Not estimable	
Roth 1999	-0.3	0.15	54	56	73.5%	0.74 [0.55, 0.99]	
Total (95% CI)			86	89	100.0%	0.70 [0.54, 0.89]	•
Heterogeneity: Chi ² =			0%				
Test for overall effect:	Z = 2.83 (P = 0.005)	I					5-FU/anthracycline/P 5-FU/anthracycline

H.15.4 Comparison 4: Irinotecan versus non-irinotecan containing combinations

Figure 234: Overall survival

			Irinotecan	Non-Irinotecan		Hazard Ratio	Hazard Ratio
Study or Subgroup	log[Hazard Ratio]	SE	Total	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Bouche 2004	-0.174	0.23	44	45	15.9%	0.84 [0.54, 1.32]	
Dank 2008	-0.08	0.12	170	163	58.5%	0.92 [0.73, 1.17]	
Park 2008	-0.1805	0.3628	45	45	6.4%	0.83 [0.41, 1.70]	
Moehler 2009	-0.256	0.21	53	50	19.1%	0.77 [0.51, 1.17]	
Total (95% CI)			312	303	100.0%	0.87 [0.73, 1.05]	•
Heterogeneity: Chi ² = Test for overall effect:		0); I² = 09	6				0.1 0.2 0.5 1 2 5 10 Favours irinotecan Favours non-irinotecan

Figure 235: Progression-free survival

			Irinotecan			Hazard Ratio		Hazard		
Study or Subgroup	log[Hazard Ratio]	SE	Total	Total	Weight	IV, Fixed, 95% CI		IV, Fixed	, 95% CI	
Park 2008	-0.2437	0.2319	45	45	19.2%	0.78 [0.50, 1.23]	4			
Dank 2008	-0.21	0.12	170	163	71.7%	0.81 [0.64, 1.03]			-	
Moehler 2009	0.131	0.338	53	50	9.0%	1.14 [0.59, 2.21]			•	
Total (95% CI)			268	258	100.0%	0.83 [0.68, 1.01]				
Heterogeneity: Chi² = Test for overall effect:		1); I² = 09	6				0.5	0.7 Favours irinotecan	1.5 Favours non-irinotecan	2

Figure 236: Treatment-related mortality

	Irinote	can	Non-Irinot	tecan		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Bouche 2004	0	45	1	45	16.3%	0.33 [0.01, 7.97]	
Dank 2008	1	170	5	163	55.6%	0.19 [0.02, 1.62]	
Moehler 2009	0	53	2	50	28.0%	0.19 [0.01, 3.84]	·
Total (95% CI)		268		258	100.0%	0.21 [0.05, 0.98]	
Total events	1		8				
Heterogeneity: Chi ² =	0.09, df=	2 (P =	0.96); I^z = 0)%			
Test for overall effect:	Z=1.99	(P = 0.0)5)				higher without irinotecan higher with irinotecan

H.16 Second-line palliative chemotherapy

What is the optimal palliative second-line chemotherapy for locally-advanced or metastatic oesophago-gastric cancer?

H.16.1 Second line chemotherapy versus placebo or best supportive care for oesophago-gastric cancer

Figure 237: Overall survival with second line chemotherapy for oesophagogastric cancer: results from individual studies

ID		HR (95% CI)
Olaparib + Paclitaxel v Paclitaxel		
Bang 2015	e	0.56 (0.35, 0.87)
Bang 2016	-8-	0.79 (0.63, 1.00)
Subtotal (I-squared = 42.7%, p = 0.187)	$\overline{\mathbf{a}}$	0.74 (0.60, 0.90)
Docetaxel v Placebo / BSC		
Ford 2014		0.67 (0.49, 0.92)
Subtotal (I-squared = .%, p = .)	$\overline{\mathbf{a}}$	0.67 (0.49, 0.92)
Irinotecan + Cisplatin v Irinotecan		
Higuchi 2014		1.00 (0.69, 1.44)
Nishikawa 2015	_	0.83 (0.60, 1.17)
Subtotal (I-squared = 0.0%, p = 0.475)	\diamond	0.91 (0.71, 1.16)
Paclitaxel v Irinotecan		
Hironaka 2013		1 12 (0 86 1 40)
		1.13 (0.86, 1.49)
Subtotal (I-squared = .%, p = .)	\leftarrow	1.13 (0.86, 1.49)
Docetaxel v Docetaxel + Fluoropyrimidine	_	
Maruta 2007		3.11 (1.22, 7.97)
Subtotal (I-squared = .%, p = .)		3.11 (1.22, 7.95)
Docetaxel v Docetaxel + Oxaliplatin		
Kim JY 2015		1.17 (0.67, 2.04)
Subtotal (I-squared = .%, p = .)		1.17 (0.67, 2.04)
FOLFIRI + Sunitinib v Placebo / BSC		
Moehler 2013		0.82 (0.50, 1.34)
Subtotal (I-squared = .%, p = .)		0.82 (0.50, 1.34)
Fluoropyrimidine v Paclitaxel		
Nishina 2016		0.89 (0.57, 1.38)
Subtotal (I-squared = .%, p = .)		0.89 (0.57, 1.38)
Docetaxel v Irinotecan		
Roy 2013		1.06 (0.70, 1.64)
Subtotal (I-squared = .%, p = .)		1.06 (0.69, 1.63)
Irinotecan v Irinotecan + 5FU/leucovorin		
Sym 2013		1.04 (0.62, 1.75)
Sym 2013 Subtotal (I-squared = .%, p = .)		1.04 (0.62, 1.75) 1.04 (0.62, 1.75)
Subiolal (I-squaled%, p)		1.04 (0.02, 1.75)
S-1 + Irinotecan v Irinotecan		
Tanabe 2015		0.99 (0.78, 1.25)
Subtotal (I-squared = .%, p = .)	\checkmark	0.99 (0.78, 1.25)
Irinotecan v Placebo / BSC	_	
Thuss-Patience 2011		0.48 (0.25, 0.92)
Subtotal (I-squared = .%, p = .)	<>	0.48 (0.25, 0.92)
Docetaxel / Irinotecan v Placebo / BSC		
Kang 2012		0.71 (0.54, 0.97)
Subtotal (I-squared = .%, p = .)	\diamond	0.71 (0.53, 0.96)

	HR (95% CI)
Docetaxel v Placebo / BSC Ford 2014 Subtotal (I-squared = .%, p = .)	0.67 (0.48, 0.92) 0.67 (0.48, 0.93)
Irinotecan + Cisplatin v Irinotecan Higuchi 2014 Nishikawa 2015 Subtotal (I-squared = 0.0%, p = 0.355)	0.68 (0.47, 0.98) 0.86 (0.62, 1.20) 0.77 (0.60, 0.99)
Paclitaxel v Irinotecan Hironaka 2013 Subtotal (I-squared = .%, p = .)	1.14 (0.88, 1.49) 1.14 (0.88, 1.48)
Docetaxel v Docetaxel + Oxaliplatin Kim JY 2015 Subtotal (I-squared = .%, p = .)	0.50 (0.27, 0.91) 0.50 (0.27, 0.92)
FOLFIRI + Sunitinib v Placebo / BSC Moehler 2013 Subtotal (I-squared = .%, p = .)	 1.11 (0.70, 1.74) 1.11 (0.70, 1.75)
Fluoropyrimidine v Paclitaxel Nishina 2016 Subtotal (I-squared = .%, p = .)	0.58 (0.38, 0.88) 0.58 (0.38, 0.88)
Docetaxel v Irinotecan Roy 2013 Subtotal (I-squared = .%, p = .)	0.84 (0.55, 1.28) 0.84 (0.55, 1.29)
Irinotecan v Irinotecan + 5FU/leucovorin Sym 2013 Subtotal (I-squared = .%, p = .)	1.13 (0.68, 1.89) 1.13 (0.68, 1.88)
S-1 + Irinotecan v Irinotecan Tanabe 2015 Subtotal (I-squared = .%, p = .)	0.85 (0.67, 1.07) 0.85 (0.67, 1.07)
Olaparib + Paclitaxel v Paclitaxel Bang 2016 Subtotal (I-squared = .%, p = .)	0.84 (0.67, 1.04) 0.84 (0.67, 1.05)

Figure 238: Progression-free survival with second line chemotherapy for oesophagogastric cancer: results from individual studies

Figure 239: Overall (OS) and progression free survival (PFS) with second line chemotherapy vs placebo or best supportive care for oesophagogastric cancer: results from network meta-analyses

Outcome	HR (95% CI)
S-1 + Irinotecan OS PFS	0.56 (0.35, 0.90) 0.68 (0.37, 1.23)
Irinotecan OS PFS	0.57 (0.38, 0.85) 0.80 (0.46, 1.38)
Docetaxel + Fluoropyrimidine OS ← ← ←	0.21 (0.08, 0.55)
Irinotecan + mFOLFIRI OS PFS	0.54 (0.28, 1.05) 0.71 (0.33, 1.49)
Docetaxel / Irinotecan OS	0.71 (0.54, 0.94)
Olaparib + Paclitaxel OS PFS	0.47 (0.28, 0.81) 0.76 (0.40, 1.45)
Docetaxel OS PFS	0.65 (0.48, 0.86) 0.67 (0.48, 0.94)
Paclitaxel OS PFS	0.64 (0.39, 1.05) 0.91 (0.50, 1.66)
Irinotecan + Cisplatin OS PFS	0.51 (0.32, 0.83) 0.62 (0.34, 1.12)
Docetaxel + Oxaliplatin OS PFS	0.55 (0.29, 1.03) 1.34 (0.67, 2.70)
FOLFIRI + Sunitinib OS PFS	0.82 (0.50, 1.33) 1.11 (0.70, 1.76)
Fluoropyrimidine OS PFS	0.57 (0.29, 1.11) 0.53 (0.25, 1.10)
.1 .5 1 5	

Figure 240: Treatment related morbidity with second line chemotherapy for oesophagogastric cancer: results from network meta-analyses. Effects are plotted treatment vs paclitaxel.

Dutcome		RR (95% CI)
Docetaxel		
Nausea	•	0.50 (0.02, 14.29)
Neutropaenic fever/sepsis	•	1.32 (0.17, 10.00)
Neutropaenia		4.76 (1.01, 25.00)
Diarrhoea	•	0.12 (0.00, 3.85)
rinotecan + mFOLFIRI		
Nausea		2.38 (0.04, 100.00)
Neutropaenic fever/sepsis		3.23 (0.05, 100.00)
Neutropaenia		1.82 (0.79, 4.17)
Diarrhoea	—	1.92 (0.05, 100.00)
Treatment-related death		1.60 (0.02, 126.99)
Docetaxel + Fluoropyrimidine		
Nausea	•	0.17 (0.00, 16.67)
Neutropaenic fever/sepsis	•	0.66 (0.03, 14.29)
Neutropaenia		2.86 (0.38, 20.00)
Irinotecan		
Nausea		2.50 (0.49, 12.50)
Neutropaenic fever/sepsis		3.33 (0.93, 11.11)
Neutropaenia	Les Č	1.37 (0.94, 2.00)
Diarrhoea	<u>·</u>	0.99 (0.06, 16.67)
Treatment-related death		
rreatment-related death		4.96 (0.24, 102.03)
S-1+ Irinotecan		1 10 /0 00 0 00
Nausea		1.43 (0.22, 9.09)
Neutropaenic fever/sepsis	· · · · · · · · · · · · · · · · · · ·	33.33 (3.57, 250.00)
Neutropaenia	_ 	2.00 (1.19, 3.33)
Diarrhoea	•	0.68 (0.04, 12.50)
Treatment-related death		0.98 (0.01, 70.67)
Fluoropyrimidine		
Nausea		7.14 (0.39, 100.00)
Neutropaenic fever/sepsis	—	5.26 (0.26, 100.00)
Neutropaenia		2.44 (1.01, 5.88)
Diarrhoea		11.11 (0.65, 250.00)
Treatment-related death		3.12 (0.13, 74.80)
Docetaxel + Oxaliplatin		
Nausea	•	1.61 (0.02, 100.00)
Neutropaenic fever/sepsis		16.67 (0.48, 250.00)
Neutropaenia		100.00 (3.57, 250.00)
Diarrhoea -		0.40 (0.00, 50.00)
lrinotecan + Cisplatin		
Nausea		2.17 (0.33, 14.29)
Neutropaenic fever/sepsis	•	0.49 (0.02, 12.50)
Neutropaenia	· ·	1.61 (0.99, 2.63)
Diarrhoea	•	0.21 (0.01, 5.56)
Treatment-related death		→ 5.11 (0.04, 713.53)
		= 0.11(0.0 4 , /10.00)
Olaparib + Paclitaxel Nausea		1.02 (0.02, 50.41)
Neutropaenic fever/sepsis		3.05 (0.13, 73.40)
Neutropaenia		1.37 (1.09, 1.73)
Diarrhoea		0.34 (0.07, 1.61)
Treatment-related death		1.02 (0.02, 50.41)
Docetaxel / Irinotecan		
Neutropaenic fever/sepsis		0.65 (0.01, 50.00)
Neutropaenia	•	0.61 (0.02, 16.67)
Docetaxel + Cisplatin		
Neutropaenic fever/sepsis		1.89 (0.14, 25.00)
Neutropaenia	├ ─◆──	5.56 (0.85, 33.33)
Placebo / BSC		
Neutropaenic fever/sepsis	→	0.10 (0.00, 3.39)
Neutropaenia	+	0.13 (0.01, 3.19)
FOLFIRI + Sunitinib		
Neutropaenia		0.37 (0.01, 10.00)

H.17 Luminal obstruction

What is the optimal management of luminal obstruction for adults with oesophagogastric cancer not amenable to treatment with curative intent?

H.17.1 Self-expanding metallic stent versus plastic tube

Figure 241: Dysphagia improvement

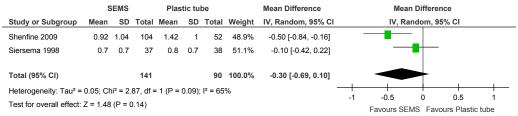


Figure 242: Persistent or recurrent dysphagia

	SEM	s	Plast	ic		Risk Ratio		Risk	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H, Ran	dom, 95% Cl	
De Palma 1996	7	19	11	20	15.6%	0.67 [0.33, 1.36]			+	
Knyrim 1993	7	21	7	21	13.0%	1.00 [0.43, 2.35]			+	
O'Donnell 2002	11	25	15	25	19.1%	0.73 [0.42, 1.27]			+	
Roseveare 1998	3	15	4	16	7.5%	0.80 [0.21, 3.00]				
Sanyika 1999	2	20	13	20	7.2%	0.15 [0.04, 0.60]				
Shenfine 2009	24	104	34	52	22.3%	0.35 [0.24, 0.53]				
Siersema 1998	10	37	11	38	15.3%	0.93 [0.45, 1.93]		_	•	
Total (95% CI)		241		192	100.0%	0.60 [0.39, 0.91]		•		
Total events	64		95							
Heterogeneity: Tau ² =	0.16; Chi ²	= 13.7	0, df = 6 ((P = 0.0	03); l² = 56	:%			+ +	
Test for overall effect:	Z = 2.40 (P = 0.0	2)				0.01	0.1 Favours SEMS	1 10 Favours Plastic	100 tube

Figure 243: Procedure-related mortality

	SEM	s	Plastic	tube		Risk Ratio		1	Risk Rat	tio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	М-Н,	Fixed,	95% CI	
De Palma 1996	0	19	3	20	18.1%	0.15 [0.01, 2.72]	←	-		_	
Knyrim 1993	0	21	3	21	18.6%	0.14 [0.01, 2.61]	←	-			
O'Donnell 2002	0	25	0	25		Not estimable					
Roseveare 1998	0	15	0	16		Not estimable					
Sanyika 1999	0	20	0	20		Not estimable					
Shenfine 2009	8	104	6	52	42.4%	0.67 [0.24, 1.82]					
Siersema 1998	1	37	4	38	20.9%	0.26 [0.03, 2.19]		•		-	
Total (95% CI)		241		192	100.0%	0.39 [0.17, 0.88]					
Total events	9		16								
Heterogeneity: Chi ² = 2	2.12, df =	3 (P = 0	0.55); l² =	0%			<u> </u>				
Test for overall effect:	Z = 2.28 (P = 0.0	2)				0.01	0.1 Favours SE	1 EMS Fa	10 Ivours Plastic	100 tube

0							• •		,		
	SEM	s	Plastic	tube		Risk Ratio		Ris	sk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fi	ixed, 95% Cl		
De Palma 1996	4	19	9	20	7.5%	0.47 [0.17, 1.27]			+		
Knyrim 1993	6	21	10	21	8.5%	0.60 [0.27, 1.35]			+		
O'Donnell 2002	8	25	13	25	11.1%	0.62 [0.31, 1.22]			+		
Roseveare 1998	2	15	3	16	2.5%	0.71 [0.14, 3.68]			•		
Sanyika 1999	1	20	12	20	10.2%	0.08 [0.01, 0.58]		-			
Shenfine 2009	45	104	42	52	47.7%	0.54 [0.41, 0.69]		-	-		
Siersema 1998	5	37	15	38	12.6%	0.34 [0.14, 0.85]			-		
Total (95% CI)		241		192	100.0%	0.48 [0.38, 0.60]		•			
Total events	71		104								
Heterogeneity: Chi ² =	5.41, df =	6 (P = (0.49); I² =	0%					+	+	4.04
Test for overall effect:	Z = 6.20 (P < 0.0	0001)				0.01	0.1 Favours SEM	1 S Favours F	10 Plastic t	100 ube

Figure 244: All procedure-related morbidity (unspecified)

Figure 245: Procedure-related morbidity

1.9.1 Perforation	SEMS Events		Events	ube Total	Weight	Risk Ratio M-H, Fixed, 95% Cl	Risk Ratio M-H, Fixed, 95% Cl
De Palma 1996	0	19	3	20	21.3%	0.15 [0.01, 2.72]	
Knyrim 1993	0	21	3	21	21.8%	0.14 [0.01, 2.61]	• • • • • • • • • • • • • • • • • • •
O'Donnell 2002	0	25	0	25		Not estimable	
Roseveare 1998	0	15	0	16		Not estimable	
Sanyika 1999	0	20	2	20	15.6%	0.20 [0.01, 3.92]	
Shenfine 2009	2	104	2	52	16.6%	0.50 [0.07, 3.45]	
Siersema 1998	1	37	4	38	24.6%	0.26 [0.03, 2.19]	
Subtotal (95% CI)		241		192	100.0%	0.24 [0.08, 0.71]	\bullet
Total events	3		14				
Heterogeneity: Chi ² = 0	0.79, df = 4	(P = 0).94); l² = (0%			
Test for overall effect: 2							
1.9.2 Fistula							
De Palma 1996	0	19	0	20		Not estimable	_
Knyrim 1993	1	21	2	21	50.2%	0.50 [0.05, 5.10]	
D'Donnell 2002	1	25	0	25	12.6%	3.00 [0.13, 70.30]	
Roseveare 1998	0	15	0	16		Not estimable	
Sanyika 1999	0	20	0	20		Not estimable	
Siersema 1998	0	37	1	38	37.2%	0.34 [0.01, 8.14]	
Subtotal (95% CI)		137		140	100.0%	0.76 [0.17, 3.28]	
Fotal events	2		3				
Heterogeneity: Chi ² = 1	i.10, df = 2	(P=0	.58); l² = (0%			
est for overall effect:	Z = 0.37 (P	, = 0.7 [,]	1)				
I.9.3 Haemorrhage							
De Palma 1996	0	19	0	20		Not estimable	
Knyrim 1993	0	21	1	21	5.6%	0.33 [0.01, 7.74]	
D'Donnell 2002	5	25	2	25	7.4%	2.50 [0.53, 11.70]	
Roseveare 1998	0	15	0	16		Not estimable	
Sanyika 1999	0	20	2	20	9.3%	0.20 [0.01, 3.92]	
Shenfine 2009	20	104	12	52	59.4%	0.83 [0.44, 1.57]	
Siersema 1998	3	37	5	38	18.3%	0.62 [0.16, 2.40]	_
Subtotal (95% CI)		241	Ŭ		100.0%	0.83 [0.50, 1.38]	. ◆
Total events	28		22	.=		· · · · · · · · · · · · · · · · · · ·	-
leterogeneity: Chi ² = 3		(P = (٦%			
Fest for overall effect: 2				,,,,			
	- 0.72 (0.11	,				
I.9.4 Chest pain							
D'Donnell 2002	11	25	14	25	40.0%	0.79 [0.45, 1.38]	
Sanyika 1999	2	20	5	25	12.7%	0.50 [0.11, 2.31]	
Shenfine 2009	20	104	8	52	30.4%	1.25 [0.59, 2.64]	
Siersema 1998	12	37	6	38	16.9%	2.05 [0.86, 4.90]	
Subtotal (95% CI)	12	186	0		100.0%	1.11 [0.75, 1.63]	•
Total events	45		33				Ĩ
Heterogeneity: Chi ² = 4		(P = (33%			
Test for overall effect: 2							
			-,				
1.9.5 Sepsis							_
Knyrim 1993	0	21	2	21	100.0%	0.20 [0.01, 3.93]	
Sanyika 1999	0	20	0	20		Not estimable	
Subtotal (95% CI)		41		41	100.0%	0.20 [0.01, 3.93]	
Total events	0		2				
Heterogeneity: Not app	olicable						
Test for overall effect: 2	Z = 1.06 (P	= 0.29	3)				
1.9.6 Migration							
De Palma 1996	0	19	2	20	5.5%	0.21 [0.01, 4.11]	
	0	21		21	3.4%	0.33 [0.01, 7.74]	
	0	21	1			0.32 [0.07, 1.43]	
Knyrim 1993		25	1 6	24	13.9%	0.02 [0.07, 1.40]	
Knyrim 1993 D'Donnell 2002	0			24 16	13.9% 4.4%	0.53 [0.05, 5.29]	
Knyrim 1993 D'Donnell 2002 Roseveare 1998	0 2	25	6				
(nyrim 1993 D'Donnell 2002 Roseveare 1998 Sanyika 1999	0 2 1	25 15	6 2	16	4.4%	0.53 [0.05, 5.29]	
Knyrim 1993 D'Donnell 2002 Roseveare 1998 Sanyika 1999 Shenfine 2009	0 2 1 1	25 15 20	6 2 6	16 20	4.4% 13.6%	0.53 [0.05, 5.29] 0.17 [0.02, 1.26] 0.35 [0.18, 0.68] 0.14 [0.01, 2.67]	
Knyrim 1993 D'Donnell 2002 Roseveare 1998 Sanyika 1999 Shenfine 2009 Siersema 1998 Subtotal (95% CI)	0 2 1 1 12	25 15 20 104	6 2 6 17	16 20 52 37	4.4% 13.6% 51.3%	0.53 [0.05, 5.29] 0.17 [0.02, 1.26] 0.35 [0.18, 0.68]	
Knyrim 1993 D'Donnell 2002 Roseveare 1998 Sanyika 1999 Shenfine 2009 Siersema 1998	0 2 1 1 12	25 15 20 104 37	6 2 6 17	16 20 52 37	4.4% 13.6% 51.3% 7.9%	0.53 [0.05, 5.29] 0.17 [0.02, 1.26] 0.35 [0.18, 0.68] 0.14 [0.01, 2.67]	
Knyrim 1993 D'Donnell 2002 Roseveare 1998 Sanyika 1999 Shenfine 2009 Siersema 1998 Subtotal (95% CI) Fotal events Heterogeneity: Chi ² = 1	0 2 1 12 0 16 1.08, df = 6	25 15 20 104 37 241	6 2 6 17 3 37 0.98); ² = 1	16 20 52 37 190	4.4% 13.6% 51.3% 7.9%	0.53 [0.05, 5.29] 0.17 [0.02, 1.26] 0.35 [0.18, 0.68] 0.14 [0.01, 2.67]	
Knyrim 1993 D'Donnell 2002 Roseveare 1998 Sanyika 1999 Shenfine 2009 Siersema 1998 Subtotal (95% CI) Fotal events Heterogeneity: Chi ² = 1	0 2 1 12 0 16 1.08, df = 6	25 15 20 104 37 241	6 2 6 17 3 37 0.98); ² = 1	16 20 52 37 190	4.4% 13.6% 51.3% 7.9%	0.53 [0.05, 5.29] 0.17 [0.02, 1.26] 0.35 [0.18, 0.68] 0.14 [0.01, 2.67]	
Knyrim 1993 D'Donnell 2002 Roseveare 1998 Sanyika 1999 Shenfine 2009 Siersema 1998 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 1 Fest for overall effect: 2	0 2 1 12 0 16 1.08, df = 6	25 15 20 104 37 241	6 2 6 17 3 37 0.98); ² = 1	16 20 52 37 190	4.4% 13.6% 51.3% 7.9%	0.53 [0.05, 5.29] 0.17 [0.02, 1.26] 0.35 [0.18, 0.68] 0.14 [0.01, 2.67]	
Knyrim 1993 D'Donnell 2002 Roseveare 1998 Sanyika 1999 Shenfine 2009 Siersema 1998 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = Fest for overall effect: 2 J.9.9 Reflux	0 2 1 12 0 16 1.08, df = 6 Z = 4.29 (P	25 15 20 104 37 241 ; (P = 0 ? < 0.00	6 2 6 17 3 37 0.98); ² = (001)	16 20 52 37 190	4.4% 13.6% 51.3% 7.9% 100.0%	0.53 [0.05, 5.29] 0.17 [0.02, 1.26] 0.35 [0.18, 0.68] 0.14 [0.01, 2.67] 0.31 [0.18, 0.53]	
Knyrim 1993 YDonnell 2002 Koseveare 1998 Sanyka 1999 Shenfine 2009 Sitersema 1998 Subtotal (95% CI) Total events Heterogeneity: Chi ² = 1 est for overall effect: 2 .9.9 Reflux YDonnell 2002	0 2 1 1 12 0 16 1.08, df = 6 Z = 4.29 (P	25 15 20 104 37 241 6 (P = 0 9 < 0.00 25	6 2 6 17 3 37 0.98); I ² = (001)	16 20 52 37 190 0%	4.4% 13.6% 51.3% 7.9%	0.53 [0.05, 5.29] 0.17 [0.02, 1.26] 0.35 [0.18, 0.68] 0.14 [0.01, 2.67] 0.31 [0.18, 0.53]	
Knyrim 1993 D'Donnell 2002 Rosevear 1998 Sanyika 1999 Siersema 1998 Subtotal (95% CI) Total events Lesorgeneity: Chi ² = 1 Fest for overall effect: 2 L9.9 Roflux D'Donnell 2002 Sanyika 1999	0 2 1 1 12 0 16 1.08, df = 6 Z = 4.29 (P	25 15 20 104 37 241 ; (P = 0 ? < 0.00 25 1	6 2 6 17 3 37 0.98); ² = (001) 3 0	16 20 52 37 190 0% 25 1	4.4% 13.6% 51.3% 7.9% 100.0%	0.53 (0.05, 5.29) 0.17 (0.02, 1.26) 0.35 (0.18, 0.68) 0.14 (0.01, 2.67) 0.31 (0.18, 0.53] 1.33 (0.33, 5.36) Not estimable	
Knyrim 1993 7/Donnell 2002 Roseveare 1998 Sanyka 1999 Shenfine 2009 Siersema 1998 Subtotal (95%, Cl) Fotal events Leterogeneity: Chi ² = 1 Fest for overall effect: 2 I.9.9 Roflux 7/Donnell 2002 Sanyika 1999 Siersema 1998	0 2 1 1 12 0 16 1.08, df = 6 Z = 4.29 (P	25 15 20 104 37 241 5 (P = 0 5 < 0.00 25 1 37	6 2 6 17 3 37 0.98); I ² = (001)	16 20 52 37 190 0% 25 1 37	4.4% 13.6% 51.3% 7.9% 100.0%	0.53 [0.05, 5.29] 0.17 [0.02, 1.26] 0.35 [0.18, 0.68] 0.14 [0.01, 2.67] 0.31 [0.18, 0.53] 1.33 [0.33, 5.36] Not estimable 1.50 [0.27, 8.46]	
Knyrim 1993 2/Donnell 2002 Roseveare 1998 Sanyka 1999 Shenfine 2009 Shenfine 2009 Subtotal (95% C1) rotal events Leterogeneity: Chi ² = : 1.9.9 Reflux 2/Donnell 2002 Sanyka 1999 Subtotal (95% C1)	0 2 1 1 12 0 16 1.08, df = 6 Z = 4.29 (P 4 0 3	25 15 20 104 37 241 ; (P = 0 ? < 0.00 25 1	6 2 6 17 3 37 0.98); ² = (001) 3 0 2	16 20 52 37 190 0% 25 1 37	4.4% 13.6% 51.3% 7.9% 100.0%	0.53 (0.05, 5.29) 0.17 (0.02, 1.26) 0.35 (0.18, 0.68) 0.14 (0.01, 2.67) 0.31 (0.18, 0.53] 1.33 (0.33, 5.36) Not estimable	
Knyrim 1993 2/Donnell 2002 Roseveare 1998 Sanyka 1999 Siersema 1998 Subtotal (95% Cl) 10 Cala events Heterogeneity: Chi ² = 1 Heterogeneity: Chi ² = 1 Heterogeneity: Chi ² = 1 Heterogeneity: Chi ² = 1 Heterogeneity: Chi ² = 1 Subtotal (95% Cl) Folal events	0 2 1 1 12 0 1.08, df = 6 Z = 4.29 (P 4 0 3 7	25 15 20 104 37 241 (P = 0) 25 1 37 63	6 2 6 17 3 37 0.98); ² = (001) 3 0 2 5	16 20 52 37 190 0% 25 1 37 63	4.4% 13.6% 51.3% 7.9% 100.0%	0.53 [0.05, 5.29] 0.17 [0.02, 1.26] 0.35 [0.18, 0.68] 0.14 [0.01, 2.67] 0.31 [0.18, 0.53] 1.33 [0.33, 5.36] Not estimable 1.50 [0.27, 8.46]	
Knyrim 1993 YDonnell 2002 Roseveare 1998 Sanyka 1999 Shenfine 2009 Silersema 1998 Subtotal (95% CI) Total events Heterogeneity: Chi² = 1 JDonnell 2002 Sanyka 1999 Siersema 1998 Subtotal (95% CI) Total events Heterogeneity: Chi² = 1 Colal events Heterogeneity: Chi² = 1	0 2 1 1 12 0 16 1.08, df = 6 Z = 4.29 (P 4 0 3 7 0.01, df = 1	25 15 20 104 37 241 6 (P = 0 25 1 37 63 (P = 0	6 2 6 17 3 37 0.98); ² = (0.01) 3 0 2 5 0.92); ² = (16 20 52 37 190 0% 25 1 37 63	4.4% 13.6% 51.3% 7.9% 100.0%	0.53 [0.05, 5.29] 0.17 [0.02, 1.26] 0.35 [0.18, 0.68] 0.14 [0.01, 2.67] 0.31 [0.18, 0.53] 1.33 [0.33, 5.36] Not estimable 1.50 [0.27, 8.46]	
Gnyrim 1993 YDonnell 2002 Koseveare 1998 asnyka 1999 Shenfne 2009 Silersema 1998 Subtotal (95% CI) Total events teterogeneity: Chi ² = 1 "est for overall effect: 2 .9.9 Reflux YDonnell 2002 anyika 1999 Siersema 1998 Subtotal (95% CI) Otal events teterogeneity: Chi ² = 0	0 2 1 1 12 0 16 1.08, df = 6 Z = 4.29 (P 4 0 3 7 0.01, df = 1	25 15 20 104 37 241 6 (P = 0 25 1 37 63 (P = 0	6 2 6 17 3 37 0.98); ² = (0.01) 3 0 2 5 0.92); ² = (16 20 52 37 190 0% 25 1 37 63	4.4% 13.6% 51.3% 7.9% 100.0%	0.53 [0.05, 5.29] 0.17 [0.02, 1.26] 0.35 [0.18, 0.68] 0.14 [0.01, 2.67] 0.31 [0.18, 0.53] 1.33 [0.33, 5.36] Not estimable 1.50 [0.27, 8.46]	
Knyrim 1993 YDonnell 2002 Koseveare 1998 sanyka 1999 Shenfine 2009 Siersema 1998 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = (0 2 1 1 12 0 16 1.08, df = 6 Z = 4.29 (P 4 0 3 7 0.01, df = 1 Z = 0.61 (P	25 15 20 104 37 241 6 (P = 0 25 1 37 63 (P = 0	6 2 6 17 3 37 0.98); ² = (0.01) 3 0 2 5 0.92); ² = (16 20 52 37 190 0% 25 1 37 63	4.4% 13.6% 51.3% 7.9% 100.0%	0.53 [0.05, 5.29] 0.17 [0.02, 1.26] 0.35 [0.18, 0.68] 0.14 [0.01, 2.67] 0.31 [0.18, 0.53] 1.33 [0.33, 5.36] Not estimable 1.50 [0.27, 8.46]	
Gnyrim 1993 YDonnell 2002 Roseveare 1998 Snykia 1999 Shenfine 2009 Siersema 1998 Subtotal (95% CI) Todal events Heterogeneity: Chi ² = 1 JP3 Reflux YDonnell 2002 Sanyika 1999 Siletotal (95% CI) Total events Heterogeneity: Chi ² = ("Gest for overall effect" 2 "Subtotal (95% CI) Total events Heterogeneity: Chi ² = ("Settorgeneity: Chi ² = (0 2 1 1 12 0 16 1.08, df = 6 Z = 4.29 (P 4 0 3 7 0.01, df = 1 Z = 0.61 (P ion	25 15 20 104 37 241 6 (P = 0 25 1 37 63 (P = 0 25 1 37 63 (P = 0.54)	6 2 6 17 3 37 0.98); ² = (001) 3 0 2 5 0.92); ² = (4)	16 20 52 37 190 0% 25 1 37 63	4.4% 13.6% 51.3% 7.9% 100.0%	0.53 [0.05, 5.29] 0.17 [0.02, 1.26] 0.35 [0.18, 0.68] 0.14 [0.01, 2.67] 0.31 [0.18, 0.53] 1.33 [0.33, 5.36] Not estimable 1.50 [0.27, 8.46] 1.40 [0.47, 4.14]	
Gnyrim 1993 7/Donnell 2002 Koseveare 1998 asnyka 1999 Shenfine 2009 Siersema 1998 subtotal (95% Cl) Total events 9.93 Reflux 2/Donnell 2002 anyka 1999 Siersema 1998 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = (Test for overall effect: 2 	0 2 1 1 20 16 1.08, df = 6 Z = 4.29 (P 4 0 3 3 7 0.01, df = 1 Z = 0.61 (P ion 0	25 15 20 104 37 241 6 (P = 0 25 1 37 63 (P = 0 63 (P = 0.5c) 19	6 2 6 17 3 37 0.98); ² = (001) 3 0 2 0.92); ² = (4) 0	16 20 52 37 190 0% 25 1 37 63 20%	4.4% 13.6% 51.3% 7.9% 100.0% 60.0% 40.0% 100.0%	0.53 [0.05, 5.29] 0.17 [0.02, 1.26] 0.35 [0.18, 0.68] 0.14 [0.01, 2.67] 0.31 [0.18, 0.53] 1.33 [0.33, 5.36] Not estimable 1.50 [0.27, 8.46] 1.40 [0.47, 4.14]	
Gryrim 1993 7/Dornell 2002 Koseveare 1998 sanyka 1999 shenfine 2009 siersema 1998 subtotal (95% Cl) Total events teterogeneity: Chi ² = { .9.9 Reflux 7/Dornell 2002 Sanyka 1999 Subtotal (95% Cl) Total events teterogeneity: Chi ² = { teterogeneity: Chi ² = { teterogeneity: Chi ² = { teterogeneity: Chi ² = { .9.1 Stent malfunct be Palma 1996 Gryrim 1993	$\begin{array}{c} 0 \\ 2 \\ 1 \\ 12 \\ 0 \\ 16 \\ 1.08, df = 6 \\ Z = 4.29 (P \\ 4 \\ 0 \\ 3 \\ 7 \\ 0.01, df = 1 \\ Z = 0.61 (P \\ 100 \\ 0 \\ 2 \\ \end{array}$	$\begin{array}{c} 25\\ 15\\ 20\\ 104\\ 37\\ 241\\ 6\ (P=0\\ 0<0.00\\ 25\\ 1\\ 37\\ 63\\ (P=0\\ 0.5c\\ 19\\ 21\\ \end{array}$	6 6 2 6 17 3 37 7 3 37 9 5 19 10 10 10 10 10 10 10 10 10 10 10 10 10	16 20 52 37 190 0% 25 1 37 63 0% 20 21	4.4% 13.6% 51.3% 7.9% 100.0%	0.53 [0.05, 5.29] 0.17 [0.02, 1.26] 0.35 [0.18, 0.68] 0.14 [0.01, 2.67] 0.31 [0.18, 0.53] 1.33 [0.33, 5.36] Not estimable 1.50 [0.27, 8.46] 1.40 [0.47, 4.14] Not estimable 2.00 [0.20, 20.41]	
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H.17.2 SEMS versus laser

Figure 246: Persistent or recurrent dysphagia

	SEM	s	LASE	R		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H	l, Fixed, 95	% CI	
Adam 1997	14	42	4	18	32.9%	1.50 [0.57, 3.93]				_	
Dallal 2001	4	31	12	34	67.1%	0.37 [0.13, 1.02]					
Total (95% CI)		73		52	100.0%	0.74 [0.38, 1.43]			•		
Total events	18		16								
Heterogeneity: Chi ² =	= 3.89, df =	1 (P = (0.05); l² =	74%							
Test for overall effect	:: Z = 0.90 (P = 0.3	7)				0.01	0.1 Favours S	1 EMS Favo	10 ours LASEF	100 R

Figure 247: Need of intervention for recurrent dysphagia

	SEM	s	LASE	R		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		М-Н,	Random, 9	5% CI	
Adam 1997	15	42	18	18	54.8%	0.37 [0.25, 0.56]		-	-		
Dallal 2001	10	31	13	34	45.2%	0.84 [0.43, 1.64]			-		
Total (95% CI)		73		52	100.0%	0.54 [0.23, 1.26]		•			
Total events	25		31								
Heterogeneity: Tau ² =	0.30; Chi ²	= 4.80	, df = 1 (F	P = 0.03	3); l² = 79%	, D	H				
Test for overall effect:	Z = 1.43 (P = 0.1	5)				0.01	0.1 Favours S	1 EMS Favo	10 ours LASER	100 R

Figure 248: Procedure-related morbidity

igure 240.			aurc	-101	alca	monorally	
	SEMS	6	LASE	R		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 90% C	I M-H, Fixed, 90% Cl
2.3.1 Perforation							
Adam 1997	0	42	1	18	46.6%	0.15 [0.01, 2.08]	
Dallal 2001	0	31	2	34	53.4%	0.22 [0.02, 2.71]	
Subtotal (90% CI)		73		52	100.0%	0.19 [0.03, 1.15]	
Total events	0		3				
Heterogeneity: Chi ² =	0.03, df = 1	(P = (0.86); I² =	0%			
Test for overall effect:	Z = 1.52 (P	P = 0.1	3)				
2.3.2 Fistula							
Adam 1997	0	42	1	18	38.4%	0.15 [0.01, 2.08]	
Dallal 2001	0	31	3	34	61.6%	0.16 [0.01, 1.82]	_
Subtotal (90% CI)		73		52	100.0%	0.15 [0.02, 0.95]	
Total events	0		4				
Heterogeneity: Chi ² =	0.00, df = 1	(P = (0.98); I² =	0%			
Test for overall effect:	Z = 1.69 (F	P = 0.0	9)				
2.3.3 Haemorrhage							
Adam 1997	1	42	0	18	59.2%	1.33 [0.09, 18.72]	
Dallal 2001	3	31	0	34	40.8%	7.66 [0.66, 89.08]	
Subtotal (90% CI)		73		52	100.0%	3.91 [0.73, 20.80]	
Total events	4		0				
Heterogeneity: Chi ² =	0.65, df = 1	(P = (0.42); I² =	0%			
Test for overall effect:	Z = 1.34 (F	P = 0.1	8)				
2.3.4 Sepsis							
Adam 1997	2	42	0	18	42.1%	2.21 [0.18, 27.12]	
Dallal 2001	2	31	1	34	57.9%	2.19 [0.31, 15.77]	
Subtotal (90% CI)		73		52	100.0%	2.20 [0.46, 10.42]	
Total events	4		1				
Heterogeneity: Chi ² =	0.00, df = 1	(P = ⁻	1.00); I² =	0%			
Test for overall effect:	Z = 0.83 (F	P = 0.4	0)				
2.3.8 All adverse effe	ects						
Adam 1997	20	42	4	18	49.5%	2.14 [0.99, 4.64]	⊢∎ −
Dallal 2001	8	31	6	34	50.5%	1.46 [0.66, 3.22]	- +-
Subtotal (90% CI)		73		52	100.0%	1.80 [1.04, 3.12]	◆
Total events	28		10				
Heterogeneity: Chi ² =	0.33, df = 1	(P = (0.57); l² =	0%			
Test for overall effect:							
	,						
							⊢ ⊢ ⊢ ⊢ ⊢
							0.01 0.1 1 10 1
							Favours SEMS Favours LASER

Figure 249: Overall survival days

		SEMS			laser			Mean Difference		Mea	an Differer	ice	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV,	Fixed, 95%	6 CI	
Adam 1997	93.64	74.91	42	79.49	58.6	18	83.1%	14.15 [-21.15, 49.45]					
Dallal 2001	190.32	166.89	31	213.27	154.09	34	16.9%	-22.95 [-101.27, 55.37]	•	•			
Total (95% CI)			73			52	100.0%	7.89 [-24.30, 40.07]		-			
Heterogeneity: Chi ² =	0.72, df =	1 (P = 0	.40); l²	= 0%					-100	-50	0	50	100
Test for overall effect:	Z = 0.48	(P = 0.63	5)						-100	Favours la	-	ours SEMS	100

Figure 250: Procedure-related mortality

	SEM	s	Lase	r		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% Cl
Adam 1997	3	42	1	18	59.5%	1.29 [0.14, 11.54]	
Dallal 2001	3	31	1	34	40.5%	3.29 [0.36, 30.00]	
Total (95% CI)		73		52	100.0%	2.10 [0.46, 9.57]	-
Total events	6		2				
Heterogeneity: Chi ² =	0.35, df =	1 (P = (0.55); l² =	0%			
Test for overall effect:	Z = 0.96 (P = 0.3	4)				0.01 0.1 1 10 100 Favours SEMS Favours Laser

H.17.3 Laser versus plastic tube

Figure 251: Recurrent dysphagia

	Laser		Plastic	tube		Risk Ratio		I	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	l	M-H, F	Random, 95	% CI	
Alderson 1990	16	20	2	20	52.9%	8.00 [2.11, 30.34]				-	-
Carter 1992	1	20	4	20	47.1%	0.25 [0.03, 2.05]	-				
Total (95% CI)		40		40	100.0%	1.56 [0.05, 46.42]					
Total events	17		6								
Heterogeneity: Tau ² =	5.20; Chi² =	= 7.45,	, df = 1 (P	= 0.006	6); l² = 87%	/o	0.01	0.1	1	10	100
Test for overall effect:	Z = 0.26 (P	= 0.80	0)				0.01	Favours la	iser Favou	irs plastic ti	

Figure 252: Procedure-related morbidity

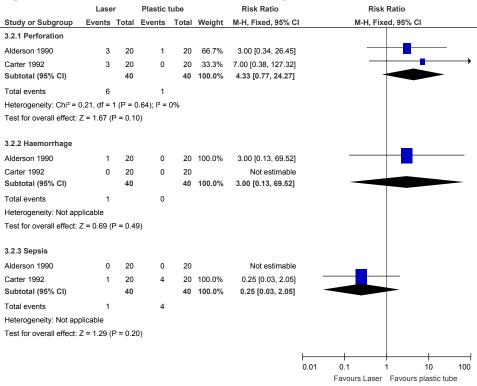


Figure 253: Procedure-related mortality

	Lase	r	Plastic	tube		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H	l, Fixed, 95%	6 CI	
Alderson 1990	1	20	0	20	50.0%	3.00 [0.13, 69.52]					
Carter 1992	1	20	0	20	50.0%	3.00 [0.13, 69.52]					
Total (95% CI)		40		40	100.0%	3.00 [0.33, 27.69]					-
Total events	2		0								
Heterogeneity: Chi ² =	0.00, df =	1 (P = '	1.00); I² =	0%			0.01	0.1		10	100
Test for overall effect:	Z = 0.97 (I	P = 0.3	3)				0.01	Favours L	aser Favou	urs Plastic t	

Figure 254: Dysphagia improvement

-	-		-	-			
	Lase	r	plastic	tube		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Alderson 1990	7	20	2	20	9.5%	3.50 [0.83, 14.83]	
Carter 1992	19	20	19	20	90.5%	1.00 [0.87, 1.15]	
Total (95% CI)		40		40	100.0%	1.24 [0.96, 1.60]	•
Total events	26		21				
Heterogeneity: Chi ² =	10.66, df =	= 1 (P =	0.001); l ²	= 91%			
Test for overall effect:	7 = 1 62 (- - 0 1	1)				0.5 0.7 1 1.5 2
rest for overall effect.	2 - 1.02 (0.1	1)				Favours Plastic tube Favours Laser

Figure 255: All procedure-related morbidity

	Laser Plastic tube				Risk Ratio			Risk Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	M-H	, Fixed, 95%	CI	
Alderson 1990	5	20	4	20	44.4%	1.25 [0.39, 3.99]				-	
Carter 1992	11	20	5	20	55.6%	2.20 [0.93, 5.18]			╞╼	_	
Total (95% CI)		40		40	100.0%	1.78 [0.90, 3.52]					
Total events	16		9								
Heterogeneity: Chi ² =	0.59, df =	1 (P = (0.44); l² =	0%							
Test for overall effect:	Z = 1.65 (I	P = 0.1	0)				0.01	0.1 Favours La	1 aser Favou	10 rs plastic t	100 ube

H.17.4 Laser versus laser plus brachytherapy

Figure 256: Recurrent dysphagia

	Laser+br	achy	Lase	r		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H	Random, 95	5% CI	
Sander 1991	19	19	20	20	39.9%	1.00 [0.91, 1.10]			•		
Spencer 2002	7	11	10	11	35.6%	0.70 [0.43, 1.14]					
Tan 1998	3	12	8	14	24.5%	0.44 [0.15, 1.29]			•		
Total (95% CI)		42		45	100.0%	0.72 [0.31, 1.70]					
Total events	29		38								
Heterogeneity: Tau ² =	0.48; Chi² =	= 20.05,	df = 2 (P	< 0.000	01); I² = 90	1% ł					
Test for overall effect:	Z = 0.75 (P	= 0.45)				(0.01 Favo	0.1 urs Laser +	Brac Favou	10 Jrs Laser	100

Figure 257: Procedure-related morbidity

Study or Subgroup			Laser and E			Risk Ratio	Risk Ratio
4.2.1 Perforation	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
Sander 1991	1	20	0	19	49.5%	2.86 [0.12, 66.11]	
Spencer 2002	0	11	0	11	43.370	Not estimable	
Fan 1998			0		E0 E9/		
Subtotal (95% CI)	1	14 45	0	12	50.5% 100.0%	2.60 [0.12, 58.48] 2.72 [0.30, 24.87]	
	0	40	0		100.070	2.12 [0.00, 24.01]	
Total events	2	0.00	0	07) 12	0.01		
Heterogeneity: Tau ² = Test for overall effect: 3				.97); 1- =	0%		
4.2.2 Haemorrhage							
Sander 1991	0	20	0	19		Not estimable	
Spencer 2002	0	11	0	11		Not estimable	
Tan 1998	1	14	0	12	100.0%	2.60 [0.12, 58.48]	
Subtotal (95% CI)		45			100.0%	2.60 [0.12, 58.48]	
Total events	1		0				
Heterogeneity: Not app							
Test for overall effect:		e = 0.55	.)				
	_ 0.00 (1	5.00	,				
4.2.3 Fistula							
Ries 1989	3	20	2	17	43.8%	1.27 [0.24, 6.76]	
Sander 1991	3	20	3	19	56.2%	0.95 [0.22, 4.14]	
Spencer 2002	0	11	0	11		Not estimable	
Tan 1998	0	14	0	12		Not estimable	L
Subtotal (95% CI)		65		59	100.0%	1.08 [0.36, 3.26]	
Total events	6		5				
Heterogeneity: Tau ² =	0.00; Chi ²	= 0.07,	df = 1 (P = 0	.80); I ² =	0%		
Test for overall effect:	Z = 0.14 (P	e = 0.89)				
4.2.4 Sepsis							
Spencer 2002	0	11	0	11		Not estimable	
Tan 1998	0	14	0	12		Not estimable	
Subtotal (95% CI)		25		23		Not estimable	
Total events	0		0				
Heterogeneity: Not app	olicable						
neterogeneity. Not upp	photobio						
Test for overall effect:		able					
Test for overall effect:		able					
		able 20	4	19	51.9%	0.11 [0.01, 1.84]	•
Test for overall effect: 4.2.6 Oesophagitis	Not applica		4 0	19 11	51.9%	0.11 [0.01, 1.84] Not estimable	• -
Test for overall effect: 4.2.6 Oesophagitis Sander 1991	Not applica	20			51.9% 48.1%		
Test for overall effect: 4.2.6 Oesophagitis Sander 1991 Spencer 2002	Not applica 0 0	20 11	0	11 12		Not estimable	
Test for overall effect: 4.2.6 Oesophagitis Sander 1991 Spencer 2002 Tan 1998	Not applica 0 0	20 11 14	0	11 12	48.1%	Not estimable 2.60 [0.12, 58.48]	
Test for overall effect: 4.2.6 Oesophagitis Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI) Total events	Not applica 0 1 1	20 11 14 45	0 0 4	11 12 42	48.1% 100.0%	Not estimable 2.60 [0.12, 58.48]	
Test for overall effect: 4.2.6 Oesophagitis Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI)	Not applica 0 1 2.90; Chi ²	20 11 14 45 = 2.25,	0 0 4 df = 1 (P = 0	11 12 42	48.1% 100.0%	Not estimable 2.60 [0.12, 58.48]	
Test for overall effect: 4.2.6 Oesophagitis Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI) Total events Heterogeneity: Tau ² =	Not applica 0 1 2.90; Chi ²	20 11 14 45 = 2.25,	0 0 4 df = 1 (P = 0	11 12 42	48.1% 100.0%	Not estimable 2.60 [0.12, 58.48]	
Test for overall effect: 4.2.6 Oesophagitis Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect: : 4.2.7 All adverse effect	Not applica 0 1 2.90; Chi ² Z = 0.44 (P	20 11 14 45 = 2.25, 9 = 0.66	0 0 df = 1 (P = 0	11 12 42	48.1% 100.0% 56%	Not estimable 2.60 [0.12, 58.48] 0.49 [0.02, 11.70]	
Test for overall effect: 4.2.6 Oesophagitis Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI) Total events Heterogeneity: Tau ² =	Not applica 0 1 2.90; Chi ² Z = 0.44 (P	20 11 14 45 = 2.25,	0 0 4 df = 1 (P = 0	11 12 42	48.1% 100.0%	Not estimable 2.60 [0.12, 58.48]	
Test for overall effect: 4.2.6 Oesophagitis Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect: : 4.2.7 All adverse effect Ries 1989	Not applica 0 1 2.90; Chi ² Z = 0.44 (P cts	20 11 14 45 = 2.25, 9 = 0.66	0 0 df = 1 (P = 0	11 12 42 .13); I ² =	48.1% 100.0% 56%	Not estimable 2.60 [0.12, 58.48] 0.49 [0.02, 11.70]	
Test for overall effect: 1 4.2.6 Oesophagitis Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect: 1 4.2.7 All adverse effec Ries 1989 Sander 1991	Not applica 0 1 2.90; Chi ² Z = 0.44 (P cts 3	20 11 14 45 = 2.25, P = 0.66	0 0 df = 1 (P = 0 ;) 2	11 12 42 .13); I ² =	48.1% 100.0% 56% 25.7%	Not estimable 2.60 [0.12, 58.48] 0.49 [0.02, 11.70] 1.27 [0.24, 6.76]	
Test for overall effect: 1 4.2.6 Oesophagitis Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect: 1 4.2.7 All adverse effect Ries 1989 Sander 1991 Spencer 2002	Not applica 0 0 1 2.90; Chi ² : Z = 0.44 (F cts 3 4	20 11 14 45 = 2.25, 20 20	0 0 df = 1 (P = 0 ;) 2 7	11 12 42 .13); ² = 17 19	48.1% 100.0% 56% 25.7% 44.6%	Not estimable 2.60 [0.12, 58.48] 0.49 [0.02, 11.70] 1.27 [0.24, 6.76] 0.54 [0.19, 1.56]	
Test for overall effect: 1 4.2.6 Oesophagitis Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect: 1 4.2.7 All adverse effect Ries 1989 Sander 1991 Spencer 2002 Tan 1998	Not applica 0 0 1 2.90; Chi ² : Z = 0.44 (F cts 3 4 0	20 11 14 45 = 2.25, 20 20 11	0 0 df = 1 (P = 0 ;) 2 7 3	11 12 42 .13); ² = 17 19 11 12	48.1% 100.0% 56% 25.7% 44.6% 10.9%	Not estimable 2.60 [0.12, 58.48] 0.49 [0.02, 11.70] 1.27 [0.24, 6.76] 0.54 [0.19, 1.56] 0.14 [0.01, 2.48]	
Test for overall effect: 4.2.6 Oesophagitis Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect: : 4.2.7 All adverse effect	Not applica 0 0 1 2.90; Chi ² : Z = 0.44 (F cts 3 4 0	20 11 14 45 = 2.25, 20 20 11 14	0 0 df = 1 (P = 0 ;) 2 7 3	11 12 42 .13); ² = 17 19 11 12	48.1% 100.0% 56% 25.7% 44.6% 10.9% 18.9%	Not estimable 2.60 [0.12, 58.48] 0.49 [0.02, 11.70] 1.27 [0.24, 6.76] 0.54 [0.19, 1.56] 0.14 [0.01, 2.48] 3.43 [0.44, 26.66]	
Test for overall effect: 1 4.2.6 Oesophagitis Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect: 1 4.2.7 All adverse effect Ries 1989 Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI)	Not applica 0 1 2.90; Chi ² : Z = 0.44 (P cts 3 4 0 4 11	20 11 14 45 = 2.25, 20 20 20 11 14 65	0 0 df = 1 (P = 0)) 2 7 3 1 1 3	11 12 42 .13); I ² = 17 19 11 12 59	48.1% 100.0% 56% 25.7% 44.6% 10.9% 18.9% 100.0%	Not estimable 2.60 [0.12, 58.48] 0.49 [0.02, 11.70] 1.27 [0.24, 6.76] 0.54 [0.19, 1.56] 0.14 [0.01, 2.48] 3.43 [0.44, 26.66]	
Test for overall effect: 1 4.2.6 Oesophagitis Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect: 1 4.2.7 All adverse effect Ries 1989 Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI) Total events	Not applica 0 0 1 2.90; Chi2 : $Z = 0.44 (Pcts3404110.30; Chi2 :$	20 11 14 45 = 2.25, 20 20 20 11 14 65 = 4.15,	0 0 df = 1 (P = 0)) 2 7 3 1 1 3 df = 3 (P = 0	11 12 42 .13); I ² = 17 19 11 12 59	48.1% 100.0% 56% 25.7% 44.6% 10.9% 18.9% 100.0%	Not estimable 2.60 [0.12, 58.48] 0.49 [0.02, 11.70] 1.27 [0.24, 6.76] 0.54 [0.19, 1.56] 0.14 [0.01, 2.48] 3.43 [0.44, 26.66]	
Test for overall effect: 1 4.2.6 Oesophagitis Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect: 1 4.2.7 All adverse effect Ries 1989 Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI) Total events Heterogeneity: Tau ² =	Not applica 0 0 1 2.90; Chi2 : $Z = 0.44 (Pcts3404110.30; Chi2 :$	20 11 14 45 = 2.25, 20 20 20 11 14 65 = 4.15,	0 0 df = 1 (P = 0)) 2 7 3 1 1 3 df = 3 (P = 0	11 12 42 .13); I ² = 17 19 11 12 59	48.1% 100.0% 56% 25.7% 44.6% 10.9% 18.9% 100.0%	Not estimable 2.60 [0.12, 58.48] 0.49 [0.02, 11.70] 1.27 [0.24, 6.76] 0.54 [0.19, 1.56] 0.14 [0.01, 2.48] 3.43 [0.44, 26.66]	
Test for overall effect: 1 4.2.6 Oesophagitis Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect: 1 4.2.7 All adverse effect Ries 1989 Sander 1991 Spencer 2002 Tan 1998 Subtotal (95% CI) Total events Heterogeneity: Tau ² =	Not applica 0 0 1 2.90; Chi2 : $Z = 0.44 (Pcts3404110.30; Chi2 :$	20 11 14 45 = 2.25, 20 20 20 11 14 65 = 4.15,	0 0 df = 1 (P = 0)) 2 7 3 1 1 3 df = 3 (P = 0	11 12 42 .13); I ² = 17 19 11 12 59	48.1% 100.0% 56% 25.7% 44.6% 10.9% 18.9% 100.0%	Not estimable 2.60 [0.12, 58.48] 0.49 [0.02, 11.70] 1.27 [0.24, 6.76] 0.54 [0.19, 1.56] 0.14 [0.01, 2.48] 3.43 [0.44, 26.66]	

Figure 258: Procedure-related mortality

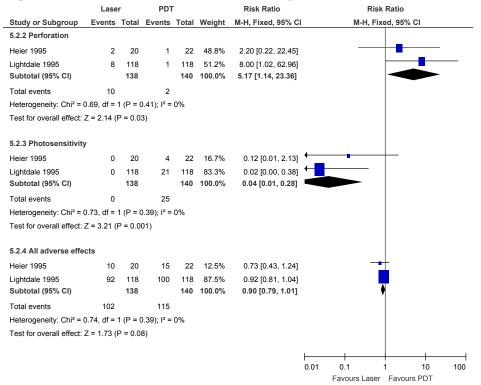
	Lase	aser Laser + Brachy				Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	l Events Total Weight M-H, Fixed, 95				M-H, Fixed, 95% Cl
Ries 1989	0	20	0	17		Not estimable	
Sander 1991	0	20	0	19		Not estimable	
Spencer 2002	0	11	0	11		Not estimable	_
Tan 1998	2	14	0	12	100.0%	4.33 [0.23, 82.31]	
Total (95% CI)		65		59	100.0%	4.33 [0.23, 82.31]	
Total events	2		0				
Heterogeneity: Not ap	plicable						
Test for overall effect: Z = 0.98 (P = 0.			3)				0.01 0.1 1 10 100 Favours Laser Favours Laser + Brac

H.17.5 Laser versus photodynamic therapy

Figure 259: Dysphagia improvement

	PDT	-	Laser Risk Ratio				Risk Ratio				
Study or Subgroup					M-H, Fixed, 95% C	1	M-H	, Fixed, 95	% CI		
Heier 1995	19	22	15	20	21.6%	1.15 [0.85, 1.56]			_ _		
Lightdale 1995	52	118	57	118	78.4%	0.91 [0.69, 1.20]			-		
Total (95% CI)		140		138	100.0%	0.96 [0.77, 1.20]			•		
Total events	71		72								
Heterogeneity: Chi ² =	1.48, df =	1 (P = ().22); l² =	32%			H				
Test for overall effect:	Z = 0.32 (P = 0.7	5)				0.01	0.1 Favours La	1 aser Favo	10 urs PDT	100

Figure 260: Procedure-related morbidity



H.17.6 Different types of SEMS

H.17.6.1 Covered Ultraflex versus covered Wallstent

Figure 261: Dysphagia improvement

	Ult	rafle	x	Wa	llster	nt		Mean Difference	e Mean Difference			ence	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV,	Fixed, 95	% CI	
Sabharwal 2003	1	0.4	31	0.9	0.5	22	52.5%	0.10 [-0.15, 0.35]		_			
Siersema 2001	0.7	0.5	34	0.5	0.6	33	47.5%	0.20 [-0.06, 0.46]					
Total (95% CI)			65			55	100.0%	0.15 [-0.04, 0.33]					
Heterogeneity: Chi ² =	0.29, df	= 1 (F	P = 0.59	9); I² = 0)%				-0.5	-0.25		0.25	0.5
Test for overall effect:	Z = 1.58	8 (P =	0.11)							Favours ultra	-		

Figure 262: Persistent or recurrent dysphagia

	ultraflex	stent	Wallst	Wallstent Risk Ratio				Ris	k Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	M-H, Fi	xed, 95% C	1	
Sabharwal 2003	3	31	1	22	11.4%	2.13 [0.24, 19.14]			<u> </u>		
Siersema 2001	10	34	9	33	88.6%	1.08 [0.50, 2.31]		_			
Total (95% CI)		65		55	100.0%	1.20 [0.58, 2.47]		-			
Total events	13		10								
Heterogeneity: Chi ² =	0.34, df = 1	(P = 0.5	6); I ² = 0	%			-		1		
Test for overall effect:	Z = 0.49 (P	= 0.62)					0.01	0.1 Favours Ultrafle:	Tavours	10 Wallster	100 nt

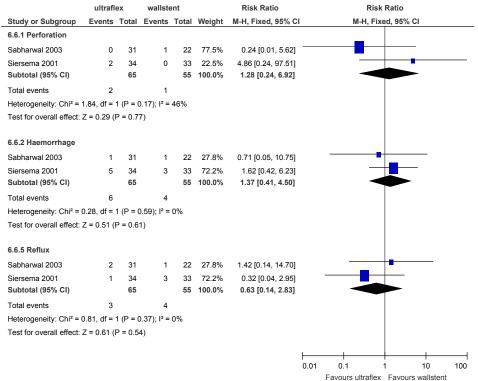
Figure 263: Procedure-related mortality

	Ultraflex	stent	Wallstent Risk Ratio								
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-I	H, Fixed, 95	% CI	
Sabharwal 2003	0	31	0	22		Not estimable					
Siersema 2001	1	34	1	33	100.0%	0.97 [0.06, 14.88]					
Total (95% CI)		65		55	100.0%	0.97 [0.06, 14.88]					
Total events	1		1								
Heterogeneity: Not ap	plicable								<u> </u>		
Test for overall effect:	= 0.98)					0.01	0.1 Favours Ult	ז raflex Favo	10 urs Wallster	100 nt	

Figure 264: Procedure-related morbidity (unspecified)

	ultrafl	ex	wallste	ent		Risk Ratio	Risk Ratio)	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C		M-I	H, Fixed, 95	5% CI	
Sabharwal 2003	7	31	5	22	18.1%	0.99 [0.36, 2.73]			_ <u>+</u> _		
Siersema 2001	21	34	26	33	81.9%	0.78 [0.57, 1.08]					
Total (95% CI)		65		55	100.0%	0.82 [0.59, 1.14]			•		
Total events	28		31								
Heterogeneity: Chi ² =	0.22, df =	1 (P = 0	0.64); I² =	0%				0.1	1	10	100
Test for overall effect:	Z = 1.18 (P = 0.2	4)				0.01	U.I Favours ult	raflex Favo		

Figure 265: Procedure-related morbidity



H.17.6.2 Irradiation stent versus covered stent

Figure 266: Dysphagia score

	Irradia	ation SE	MS	Conver	ntional S					Mea	n Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV,	Fixed, 95% C	I	
Guo 2008 (1)	1.22	0.42	27	1.17	0.38	26	65.8%	0.05 [-0.17, 0.27]					
Zhu 2014	1.51	1.05	73	1.25	0.78	75	34.2%	0.26 [-0.04, 0.56]			- -		
Total (95% CI)			100			101	100.0%	0.12 [-0.05, 0.30]			•		
Heterogeneity: Chi ² =	1.25, df =	1 (P =	0.26); l²	= 20%					-2				+
Test for overall effect:	Z = 1.37	(P = 0.1	7)						-2	-1 Favours irradiation SE	0 MS Favours	conventiona	2 I SEMS
Footnotes													

(1) at one month

Figure 267: Fistula formation

	Irradiation	SEMS	Conventional SEMS Risk Ratio			Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	1	N	I-H, Fixed, 95%	CI	
Guo 2008	1	27	0	26	9.4%	2.89 [0.12, 67.96]					
Zhu 2014	6	73	5	75	90.6%	1.23 [0.39, 3.86]				_	
Total (95% CI)		100		101	100.0%	1.39 [0.48, 4.03]				•	
Total events	7		5								
Heterogeneity: Chi ² =	0.25, df = 1 (P	e = 0.62);	l ² = 0%				0.01			10	100
Test for overall effect: Z = 0.60 (P = 0.55)							0.01	0.1 Favours irradiation	SEMS Favour	10 s conventional S	

Figure 268: Haemorrhage

Guo 2008 9 27 7 26 59.1% 1.24 [0.54, 2.83] Zhu 2014 5 73 5 75 40.9% 1.03 [0.31, 3.40] Total (95% Cl) 100 101 100.0% 1.15 [0.58, 2.29] Total events 14 12 Heterogeneity: Chi² = 0.06, df = 1 (P = 0.80); l² = 0% 0.01 0.1 1 10 100											
Guo 2008 9 27 7 26 59.1% 1.24 [0.54, 2.83] Zhu 2014 5 73 5 75 40.9% 1.03 [0.31, 3.40] Total (95% Cl) 100 101 100.% 1.15 [0.58, 2.29] Total events 14 12 Heterogeneity: Chi ² = 0.06, df = 1 (P = 0.80); l ² = 0% 0.01 0.1 1 10 Total events 14 12 10 100 100 100		Irradiation SEMS		Conventiona	I SEMS	Risk Ratio			Ris	k Ratio	
Zhu 2014 5 73 5 75 40.9% 1.03 [0.31, 3.40] Total (95% Cl) 100 101 100.0% 1.15 [0.58, 2.29] Total events 14 12 Heterogeneity: Chi ² = 0.06, df = 1 (P = 0.80); l ² = 0% 0.01 0.1 1 10 100	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fi	xed, 95% Cl	
Total (95% Cl) 100 101 100.0% 1.15 [0.58, 2.29] Total events 14 12 Heterogeneity: Chi ² = 0.06, df = 1 (P = 0.80); l ² = 0% 0.01 0.1 1 10 100	Guo 2008	9	27	7	26	59.1%	1.24 [0.54, 2.83]			-	
Total events 14 12 Heterogeneity: Chi ² = 0.06, df = 1 (P = 0.80); l ² = 0% 0.01 0.1 1 10 100 Test for overall effect: 7 = 0.40 (P = 0.69) 0.01 0.1 1 10 100	Zhu 2014	5	73	5	75	40.9%	1.03 [0.31, 3.40]			•	
Heterogeneity: Chi ² = 0.06, df = 1 (P = 0.80); l ² = 0% Image: chi = 1 Image: chi = 1 <td>Total (95% CI)</td> <td></td> <td>100</td> <td></td> <td>101</td> <td>100.0%</td> <td>1.15 [0.58, 2.29]</td> <td></td> <td>-</td> <td></td> <td></td>	Total (95% CI)		100		101	100.0%	1.15 [0.58, 2.29]		-		
Test for overall effect: Z = 0.40 (P = 0.69) 0.01 0.1 1 10 100	Total events	14		12							
Test for overall effect: $7 = 0.40$ (P = 0.69)	Heterogeneity: Chi ² =	0.06, df = 1 (P	= 0.80);	l ² = 0%				H		+	
	Test for overall effect: Z = 0.40 (P = 0.69)							0.01		Favours co	

Figure 269: Severe chest pain

	Irradiation	SEMS	Conventiona	I SEMS		Risk Ratio		Ris	k Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, F	xed, 95% Cl		
Guo 2008	8	27	7	26	32.5%	1.10 [0.47, 2.60]			—		
Zhu 2014	17	73	15	75	67.5%	1.16 [0.63, 2.15]		-			
Total (95% CI)		100		101	100.0%	1.14 [0.69, 1.89]			•		
Total events	25		22								
Heterogeneity: Chi ² =	0.01, df = 1 (P	= 0.92);	l ² = 0%					+	+		
Test for overall effect:	Z = 0.53 (P =	0.60)					0.01	0.1 Favours irradiation SEM	Favours co	10 nventional S	100 SEMS

H.17.6.3 Polyflex versus Ultraflex

Figure 270: Major complications (</= 7 days)

•	-				•	• •					
	Polyflex \$	SEMS	Ultraflex \$	SEMS		Risk Ratio		1	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C		M-H	Fixed, 95%	% CI	
Conio 2007	4	47	2	54	48.5%	2.30 [0.44, 11.99]					
Verschuur 2008	3	41	2	42	51.5%	1.54 [0.27, 8.73]		_			
Total (95% CI)		88		96	100.0%	1.91 [0.58, 6.27]					
Total events	7		4								
Heterogeneity: Chi ² =	0.11, df = 1	(P = 0.7	4); l² = 0%				0.01	0.1	1	10	100
Test for overall effect:	Z = 1.06 (P	= 0.29)					0.01	U.I Favours poly	/flex Favo		

Figure 271: Major complications (> 7 days)

	Polyflex \$	SEMS	Ultraflex \$	SEMS		Risk Ratio		F	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C		М-Н,	Fixed, 95	% CI	
Conio 2007	20	47	17	54	69.6%	1.35 [0.81, 2.26]			-		
Verschuur 2008	5	41	7	42	30.4%	0.73 [0.25, 2.12]					
Total (95% CI)		88		96	100.0%	1.16 [0.73, 1.85]			•		
Total events	25		24								
Heterogeneity: Chi ² =	1.06, df = 1	(P = 0.3	0); l² = 5%								
Test for overall effect:	Z = 0.64 (P	= 0.52)					0.01	0.1 Favours poly	flex Favo	10 urs ultrafle:	100 x

Figure 272: Gastro-oesophageal reflux

	Polyflex	SEMS	Ultraflex S	SEMS		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M	H, Fixed, 95	% CI	
Conio 2007 (1)	0	47	2	54	70.2%	0.23 [0.01, 4.66]				_	
Verschuur 2008	2	41	1	42	29.8%	2.05 [0.19, 21.73]					
Total (95% CI)		88		96	100.0%	0.77 [0.15, 3.92]				-	
Total events	2		3								
Heterogeneity: Chi ² =	1.28, df = 1	(P = 0.2	6); I² = 22%				0.01	0.1		10	100
Test for overall effect:	Z = 0.31 (P	= 0.75)					0.01		olyflex Favo		
Footnotes											
(1) within a week											

Figure 273: Retrosternal pain

	Polyflex S	SEMS	Ultraflex \$	SEMS		Risk Ratio			Risk Ratio)	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	M-I	H, Fixed, 95	5% CI	
Conio 2007 (1)	4	12	8	10	81.5%	0.42 [0.18, 0.98]					
Verschuur 2008	1	41	2	42	18.5%	0.51 [0.05, 5.43]			•		
Total (95% CI)		53		52	100.0%	0.43 [0.19, 1.00]		•			
Total events	5		10								
Heterogeneity: Chi ² =	0.03, df = 1	(P = 0.8	7); l² = 0%								
Test for overall effect:	Z = 1.96 (P	= 0.05)					0.01	0.1 Favours po	lyflex Favo	10 ours ultrafle	100 ex

Footnotes

(1) denominator= number of patients with retrosternal pain before intervention

H.17.7 Anti-reflux stent versus open stent

Figure 274: Dysphagia score at one month

		-	-										
	antiref	lux gr	oup	stand	lard op	pen	5	Std. Mean Difference		Std. Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixe	d, 95% Cl		
Wenger 2006	51	32	19	36	21	22	38.6%	0.55 [-0.07, 1.18]			•		
Wenger 2010	56	30	28	45	22	37	61.4%	0.42 [-0.07, 0.92]					
Total (95% CI)			47			59	100.0%	0.47 [0.08, 0.86]					
Heterogeneity: Chi ² =	0.10, df =	1 (P =	0.75);	l² = 0%					-100	-50	0	50	100
Test for overall effect:	Z = 2.38 ((P = 0.	02)						-100	Favours [antireflux group]			100

Figure 275: Overall survival days

	anti-ı	reflux s	tent	ор	en stent			Mean Difference			Mean Diffe	erence	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI			IV, Fixed,	95% CI	
Homs 2004c	107	57.37	15	87	17.33	15	82.0%	20.00 [-10.33, 50.33]					
Wenger 2006	70.37	42.13	19	167.06	148.05	22	18.0%	-96.69 [-161.39, -31.99]			-		
Total (95% CI)			34			37	100.0%	-1.02 [-28.48, 26.44]					
Heterogeneity: Chi² = 10.24, df = 1 (P = 0.001); l² = 90%										-50		50	100
Test for overall effect: Z = 0.07 (P = 0.94)									-100 Fa		-	avours open s	

Figure 276: Reflux scores

	antiref	lux gr	oup	stand	lard op	ben		Mean Difference		Mea	an Difference	Э	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, R	andom, 95%	CI	
Wenger 2006	37	39	19	24	17	22	47.0%	13.00 [-5.92, 31.92]					
Wenger 2010	41	42	28	30	27	37	53.0%	11.00 [-6.82, 28.82]				_	
Total (95% CI)			47			59	100.0%	11.94 [-1.03, 24.91]					
Heterogeneity: Tau ² =	-			1 (P = 0.	88); I²	= 0%			-100	-50	0	50	100
Test for overall effect:	Z = 1.80 (P = 0.	07)							Favours [antireflux gr	oup] Favour	s [standard open]

Figure 277: Procedure-related morbidity

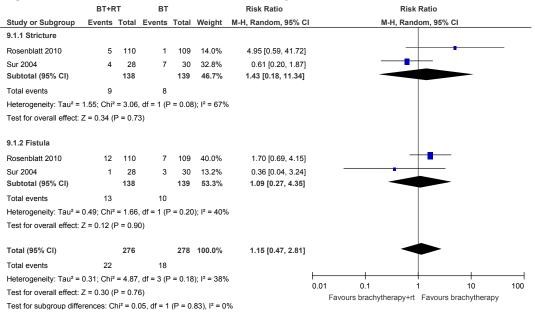
	Favours [expering the second s	mental]	Contr	ol		Risk Ratio		F	lisk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H, R	andom, 95%	CI	
Homs 2004c	7	15	5	15	30.5%	1.40 [0.57, 3.43]					
Wenger 2006	3	19	8	22	20.1%	0.43 [0.13, 1.41]					
Wenger 2010	12	28	13	37	49.4%	1.22 [0.66, 2.25]					
Total (95% CI)		62		74	100.0%	1.03 [0.58, 1.86]			•		
Total events	22		26								
Heterogeneity: Tau ² =	0.08; Chi ² = 2.85, d	lf = 2 (P =	0.24); l² =	30%						-+	
Test for overall effect:	Z = 0.11 (P = 0.91)						0.01	0.1 Favours antiref	lux Favours	10 standard o	100 open

Figure 278: Pneumonia

	With anti-	reflux	Without ant	i-reflux		Risk Ratio		F	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		М-Н,	Fixed, 95%	СІ	
Homs 2004c	0	15	1	15	37.5%	0.33 [0.01, 7.58]					
Nunes 1999	0	11	2	11	62.5%	0.20 [0.01, 3.74]					
Total (95% CI)		26		26	100.0%	0.25 [0.03, 2.09]	-				
Total events	0		3								
Heterogeneity: Chi ² =	0.05, df = 1 ((P = 0.81); I² = 0%								100
Test for overall effect:	Z = 1.28 (P =	= 0.20)					0.01 Favor	0.1 urs with anti-rei	flux Favour	10 s without	100

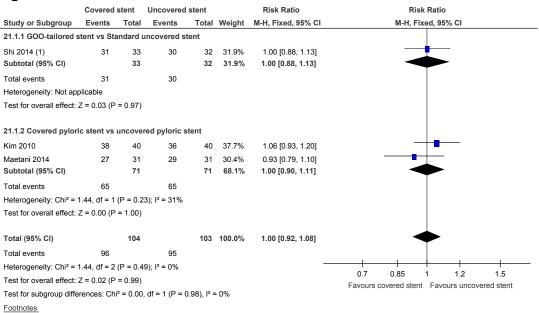
H.17.8 Brachytherapy versus brachytherapy plus radiotherapy

Figure 279: Procedure-related morbidity



H.17.9 Covered stent versus uncovered stent for gastric outlet obstruction

Figure 280: Clinical success



(1) resolution of dysphagia and the ability to restart a low residue diet after stent placement

Figure 281: Major complications

	Covered	stent	Uncovered	stent		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% Cl
21.3.1 GOO-tailored c	overed ste	ent vs S	tandard unc	overed s	tent		
Shi 2014 (1)	11	33	2	32	57.5%	5.33 [1.28, 22.20]	
Subtotal (95% CI)		33		32	57.5%	5.33 [1.28, 22.20]	
Total events	11		2				
Heterogeneity: Not app	olicable						
Test for overall effect: 2	Z = 2.30 (P	= 0.02)					
21.3.2 Covered pylori	c stent vs	Uncove	red pyloric s	stent			
Kim 2010 (2)	2	40	0	40	14.2%	5.00 [0.25, 100.97]	
Maetani 2014 (3)	1	31	1	31	28.3%	1.00 [0.07, 15.28]	
Subtotal (95% CI)		71		71	42.5%	2.33 [0.35, 15.42]	
Total events	3		1				
Heterogeneity: Chi ² = 0	0.62, df = 1	(P = 0.4	3); l² = 0%				
Test for overall effect: 2	Z = 0.88 (P	= 0.38)					
Total (95% CI)		104		103	100.0%	4.06 [1.32, 12.44]	
Total events	14		3				
Heterogeneity: Chi ² = 1	1.17, df = 2	(P = 0.5	6); l ² = 0%				
Test for overall effect: 2	Z = 2.45 (P	= 0.01)					0.01 0.1 1 10 100 Favours covered stent Favours uncovered stent
Test for subgroup diffe	rences: Chi	² = 0.47	, df = 1 (P = 0	0.49), l² =	0%		Favours covered stent Favours uncovered stent
Footnotes							
(1) bleeding							
(2) necessitating surgio	cal interven	tions					

(3) 1 case of perforation in covered stent and 1 case of bleeding in uncovered stent1

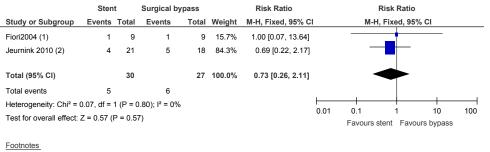
Figure 282: Re-intervention rate

	Covered stent			stent		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% Cl
21.4.1 WAVE-covered	SEMS vs	Uncove	red SEMS				
Lee 2015 (1)	6	42	14	37	67.7%	0.38 [0.16, 0.88]	
Subtotal (95% CI)		42		37	67.7%	0.38 [0.16, 0.88]	\bullet
Total events	6		14				
Heterogeneity: Not app	licable						
Test for overall effect: 2	Z = 2.25 (P	= 0.02)					
21.4.2 GOO-tailored s	tent vs un	covered	stent				
Shi 2014	3	33	7	32	32.3%	0.42 [0.12, 1.47]	
Subtotal (95% CI)		33		32	32.3%	0.42 [0.12, 1.47]	
Total events	3		7				
Heterogeneity: Not app	licable						
Test for overall effect: Z	Z = 1.36 (P	= 0.17)					
Total (95% CI)		75		69	100.0%	0.39 [0.19, 0.79]	•
Total events	9		21				
Heterogeneity: Chi ² = 0	.02, df = 1	(P = 0.9	0); I² = 0%				
Test for overall effect: 2	z = 2.62 (P	= 0.009)				0.01 0.1 1 10 100 Favours uncovered Favours covered
Test for subgroup differ	ences: Chi	² = 0.02	df = 1 (P = 0).90), l² =	• 0%		
Footnotes							

(1) at 16week follow-up

H.17.10 Stent versus bypass surgery for obstructive gastric cancer

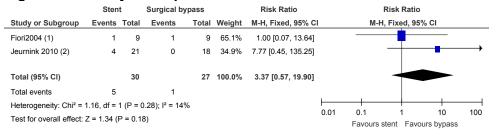
Figure 283: Minor complications



(1) one case of pain in stent and one case of wound infection in bypass $% \label{eq:case}$

(2) moderately severe complications not requiring hospital admission

Figure 284: Major complications



Footnotes

(2) severe complications requiring treatment and/or hospiatlisation

H.18 Curative treatment

What is the effectiveness of nutritional support interventions for adults undergoing curative treatment for oesophago-gastric cancer?

H.18.1 Enteral nutrition versus parenteral nutrition or IV support after surgery

Figure 285: Pneumonia: enteral nutrition versus parenteral nutrition or IV support in people with oesophago-gastric cancer after surgery

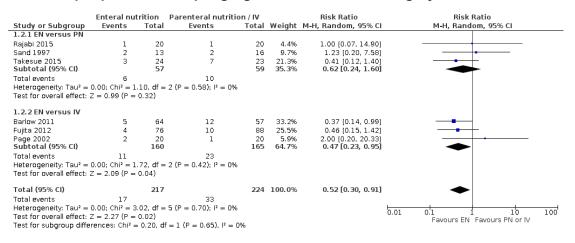


Figure 286: Surgical site infection: enteral nutrition versus parenteral nutrition or IV support in people with oesophago-gastric cancer after surgery

	Enteral nut	rition	Parenteral nutritio	n / IV		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
1.3.1 EN versus PN							
Rajabi 2015	0	20	0	20		Not estimable	
Sand 1997	1	13	1	16	4.3%	1.23 [0.08, 17.83]	
Takesue 2015	5	24	4	23	19.0%	1.20 [0.37, 3.91]	
Subtotal (95% CI)		57		59	23.4%	1.20 [0.41, 3.55]	
Total events	6		5				
Heterogeneity: Tau ² = 1	0.00; Chi² = 0	.00, df =	$1 (P = 0.99); I^2 = 0\%$				
Test for overall effect: 2	Z = 0.33 (P =	0.74)					
1.3.2 EN versus IV							
Barlow 2011	7	64	16	57	33.8%	0.39 [0.17, 0.88]	
Fujita 2012	12	76	13	88	39.6%	1.07 [0.52, 2.20]	+
Page 2002	1	20	0	20	3.2%	3.00 [0.13, 69.52]	
Subtotal (95% CI)		160		165	76.6%	0.74 [0.30, 1.81]	
Total events	20		29				
Heterogeneity: Tau ² = 1	0.30; Chi ² = 4	.13, df =	$2 (P = 0.13); I^2 = 52\%$				
Test for overall effect: 2	Z = 0.67 (P =	0.50)					
Total (95% CI)		217		224	100.0%	0.81 [0.46, 1.42]	•
Total events	26		34				
Heterogeneity: Tau ² = 1	0.08; $Chi^2 = 4$.85, df =	4 (P = 0.30); $l^2 = 18\%$				0.01 0.1 1 10 100
Test for overall effect: 2	Z = 0.74 (P =	0.46)					0.01 0.1 1 10 100 Favours EN Favours PN or IV
Test for subgroup diffe	rences: Chi² =	0.47, df	$= 1 (P = 0.49), I^2 = 09$	%			

Figure 287: Anastamotic leaks: enteral nutrition versus parenteral nutrition or IV support in people with oesophago-gastric cancer after surgery

	Enteral nut	trition	Parenteral nutritio	n / IV		Risk Ratio	Risk Rat	tio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random	, 95% CI
1.4.1 EN versus PN								
Rajabi 2015 Subtotal (95% CI)	0	20 20	0	20 20		Not estimable Not estimable		
Total events	0		0					
Heterogeneity: Not app	olicable							
Test for overall effect:	Not applicable	•						
1.4.2 EN versus IV								
Barlow 2011	2	64	7	57	19.6%	0.25 [0.06, 1.18]		
Fujita 2012	8	76	17	88	74.9%	0.54 [0.25, 1.19]		
Page 2002	0	20	0	20		Not estimable		
Swails 1995	0	13	3	12	5.6%	0.13 [0.01, 2.33]	· · · · · · · · · · · · · · · · · · ·	_
Subtotal (95% CI)		173		177	100.0%	0.43 [0.22, 0.85]	-	
Total events	10		27					
Heterogeneity: Tau ² =	$0.00; Chi^2 = 1$.48, df =	$2 (P = 0.48); I^2 = 0\%$					
Test for overall effect:	Z = 2.42 (P =	0.02)						
Total (95% CI)		193		197	100.0%	0.43 [0.22, 0.85]	-	
Total events	10		27				_	
Heterogeneity: Tau ² =	0.00; $Chi^2 = 1$.48, df =	$2 (P = 0.48); I^2 = 0\%$					10 100
Test for overall effect:	Z = 2.42 (P =	0.02)					0.01 0.1 1 Favours EN Fa	10 100'
Test for subgroup diffe	rences: Not a	pplicable					Tavouis EN Fa	

Figure 288: Short term mortality: enteral nutrition versus parenteral nutrition or IV support in people with oesophago-gastric cancer after surgery

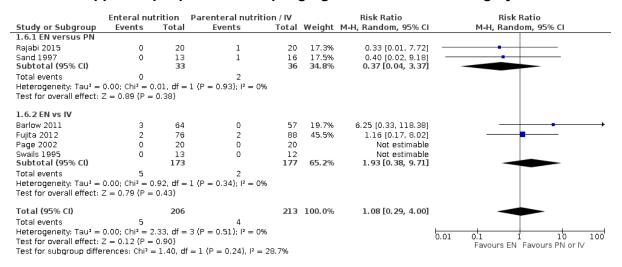
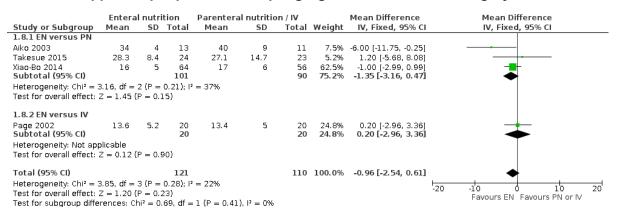


Figure 289: Length of hospital stay: enteral nutrition versus parenteral nutrition or IV support in people with oesophago-gastric cancer after surgery



H.18.2 Immunonutrition in the perioperative period

Figure 290: Pneumonia: immunonutrition versus standard nutrition in people with oesophago-gastric cancer in the perioperative period

	Immunonu	trition	Standard nu	trition		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Farreras 2005	0	30	2	30	0.9%	0.20 [0.01, 4.00]	
Fujitani 2012	5	120	0	111	1.0%	10.18 [0.57, 182.04]	
Liu 2012	5	28	6	24	7.3%	0.71 [0.25, 2.05]	
Lobo 2006	21	54	16	54	28.8%	1.31 [0.77, 2.23]	- +
Marano 2013	2	54	5	55	3.2%	0.41 [0.08, 2.01]	
Okamoto 2009	1	30	2	30	1.5%	0.50 [0.05, 5.22]	
Ryan 2009	7	28	5	25	7.9%	1.25 [0.45, 3.44]	-
Sakurai 2007	2	16	3	14	3.0%	0.58 [0.11, 3.00]	
Senkal 1995	9	77	8	77	10.0%	1.13 [0.46, 2.76]	
Sultan 2012	20	66	23	63	33.7%	0.83 [0.51, 1.35]	
Wei 2014	1	26	1	20	1.1%	0.77 [0.05, 11.56]	
Yildiz 2016	1	21	4	20	1.8%	0.24 [0.03, 1.95]	
Total (95% CI)		550		523	100.0%	0.95 [0.71, 1.26]	•
Total events	74		75				
Heterogeneity: Tau ² =	$0.00; Chi^2 = 9$	9.45, df =	11 ($P = 0.58$);	$ ^2 = 0\%$			0.01 0.1 1 10 100
Test for overall effect: 3	Z = 0.38 (P =	0.70)					'0.01 0.1 1 1'0 100' Favours immunonutrition Favours standard

Figure 291: Surgical site infection: immunonutrition versus standard nutrition in people with oesophago-gastric cancer in the perioperative period

	Immunonut	trition	Standard nu	trition		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
2.3.1 Gastric cancer							
Farreras 2005	1	30	4	30	3.5%	0.25 [0.03, 2.11]	
Fujitani 2012	13	120	8	111	22.4%	1.50 [0.65, 3.49]	
Liu 2012	3	28	2	24	5.5%	1.29 [0.23, 7.07]	
Marano 2013	2	54	3	55	5.2%	0.68 [0.12, 3.90]	
Okamoto 2009	1	30	2	30	2.9%	0.50 [0.05, 5.22]	
Wei 2014	1	26	3	20	3.3%	0.26 [0.03, 2.28]	
Subtotal (95% CI)		288		270	42.7%	0.94 [0.51, 1.72]	•
Total events	21		22				
Heterogeneity: Tau ² =			$5 (P = 0.47); I^2$	= 0%			
Test for overall effect:	Z = 0.22 (P =	0.83)					
2.3.2 Oesophageal o	ancer						
Ryan 2009	0	28	2	25	1.8%	0.18 [0.01, 3.57]	· · · · · · · · · · · · · · · · · · ·
Sakurai 2007	1	16	3	14	3.4%	0.29 [0.03, 2.50]	
Senkal 1995	1	77	2	77	2.8%	0.50 [0.05, 5.40]	
Subtotal (95% CI)		121		116	8.0%	0.32 [0.08, 1.29]	
Total events	2		7				
Heterogeneity: Tau² =			$2 (P = 0.87); I^2$	= 0%			
Test for overall effect:	Z = 1.60 (P =	0.11)					
2.3.3 OG cancer							
Lobo 2006	9	54	8	54	20.8%	1.13 [0.47, 2.70]	
Sultan 2012	9	66	9	63	21.6%	0.95 [0.41, 2.25]	_
Yildiz 2016	2	21	5	20	6.9%	0.38 [0.08, 1.74]	
Subtotal (95% CI)		141		137	49.2%	0.90 [0.51, 1.59]	-
Total events	20		22				
Heterogeneity: Tau ² =			$2 (P = 0.47); I^2$	= 0%			
Test for overall effect:	Z = 0.36 (P =	0.72}					
Total (95% CI)		550		533	100.0%	0.84 [0.56, 1.25]	
	10	550	51	523	100.0%	0.84 [0.56, 1.25]	-
Total events	43 0.00 chil. 0	AF -16	51	17 000			
Heterogeneity: Tau ² =			II (P = 0.67);	I* = U%			0.01 0.1 1 10 100
Test for overall effect:							Favours immunonutrition Favours standard
Test for subgroup diffe	erences: Uni ² =	= 2.03, d 1	= 2 (P = 0.36)	$1^{\circ} = 1.5^{\circ}$	70		

Figure 292: Anastamotic leaks: immunonutrition versus standard nutrition in people with oesophago-gastric cancer in the perioperative period

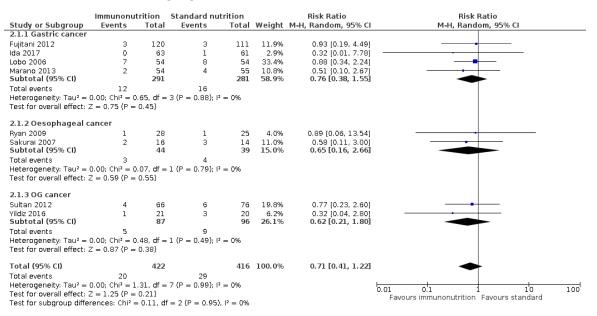


Figure 293: Short term mortality: immunonutrition versus standard nutrition in people with oesophago-gastric cancer in the perioperative period

	Immunonu	trition	Standard nut	trition		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Farreras 2005	1	30	2	30	9.2%	0.50 [0.05, 5.22]	
Fujitani 2012	0	120	0	111		Not estimable	
Marano 2013	1	54	1	55	6.7%	1.02 [0.07, 15.87]	
Okamoto 2009	6	54	6	54	44.6%	1.00 [0.34, 2.91]	+
Ryan 2009	0	28	0	25		Not estimable	
Senkal 1995	3	77	2	77	16.4%	1.50 [0.26, 8.73]	_
Sultan 2012	2	66	2	63	13.6%	0.95 [0.14, 6.57]	
Wei 2014	0	26	0	20		Not estimable	
Yildiz 2016	1	21	2	20	9.4%	0.48 [0.05, 4.85]	
Total (95% CI)		476		455	100.0%	0.93 [0.46, 1.90]	•
Total events	14		15				
Heterogeneity: Tau ² =	0.00: $Chi^2 = 0$.89. df =	$5 (P = 0.97); ^{2}$	= 0%			
Test for overall effect:							0.01 0.1 1 10 100' Favours immunonutrition Favours standard

Figure 294: Overall survival: immunonutrition versus standard nutrition in people with oesophago-gastric cancer – 5 years follow up

	Immunonu		Standard n					Hazard Ratio			Hazard Rati	-	
Study or Subgroup	Events	Total	Events	lotal	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% CI		ExpL(O	-E) / V], Fixed	I, 95% CI	
Klek 2017	0	45	0	54	-1.69	17.89	100.0%	0.91 [0.57, 1.45]					
Total (95% CI)		45		54			100.0%	0.91 [0.57, 1.45]			-		
Total events	0		0										
Heterogeneity: Not ap Test for overall effect:		0.69)							0.01 Favo	0.1 urs immunon	utrition Favo	10 urs standard	100

Figure 295: Length of hospital stay: immunonutrition versus standard nutrition in people with oesophago-gastric cancer in the perioperative period

	Immu	nonutri	tion	Standa	ard nutri	tion		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
2.8.1 Gastric cancer									
Farreras 2005	13	2.75	30	15	3	30	16.1%	-2.00 [-3.46, -0.54]	
Fujitani 2012	18	12.67	120	17	13	111	7.6%	1.00 [-2.31, 4.31]	
Liu 2012	13.2	2.7	28	12.8	3.1	24	15.3%	0.40 [-1.19, 1.99]	
Marano 2013	12.7	2.3	54	15.9	3.4	55	18.3%	-3.20 [-4.29, -2.11]	+
Okamoto 2009 Subtotal (95% CI)	23.8	16.6	30 262	25	10.6	30 250	2.3% 59.5%	-1.20 [-8.25, 5.85] - 1.24 [-3.03, 0.56]	•
Heterogeneity: Tau ² =	2.67; CI	hi ² = 16.	48, df=	4 (P = 0	.002); l²	= 76%			
Test for overall effect: .	Z = 1.35	(P = 0.1	18)						
2.8.2 Oesophageal ca	incer								
Sakurai 2007	26.6	14	16	31.3	16	14	1.0%	-4.70 [-15.53, 6.13]	
Senkal 1995	27	2.3	77	30.6	3.1	77	19.5%	-3.60 [-4.46, -2.74]	+
Subtotal (95% CI)			93			91	20.6%	-3.61 [-4.47, -2.75]	•
Heterogeneity: Tau² = Test for overall effect: .			•	(P = 0.8	(4); I² = (1%			
2.8.3 OG cancer									
Lobo 2006	14.5	2.75	54	17.5	2.5	54	18.8%	-3.00 [-3.99, -2.01]	+
Sultan 2012	18	34.25	66	16	26.25	63	1.1%	2.00 [-8.50, 12.50]	
Subtotal (95% CI)			120			117	19.9%		•
Heterogeneity: Tau² = Test for overall effect: .	•		•	(P = 0.3	(5); I² = (1%			
Total (95% CI)			475			458	100.0%	-2.09 [-3.22, -0.97]	◆
Heterogeneity: Tau ² = Test for overall effect: . Test for subgroup diffe	Z = 3.65	(P = 0.0	0003)						-20 -10 0 10 20 Favours immunonutrition Favours standard

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H.18.3 Additional nutritional support to mitigate toxicity during chemotherapy or chemoradiotherapy

Figure 296: Treatment toxicities: additional nutritional support versus standard nutritional support during chemotherapy or chemoradiotherapy

study or Subgroup	Extra nutritional s Events		Standard Events		Woight	Risk Ratio M-H, Random, 95% Cl	Risk Ratio M-H, Random, 95% Cl
3.1.1 Oral mucositis (c		TOLA	evenus	TOLA	weight	M-H, Kalidolli, 93% Cl	M-H, Kalidolli, 95% Ci
4ivata 2012	7	47	6	44	43.4%	1 00 (0 40 2 00)	
4iyata 2012 4iyata 2017	0	47	5	30	43.4%	1.09 [0.40, 3.00]	
Nyata 2017 Okada 2017	1	10	э 4	30	23.4%	0.09 [0.01, 1.53] 0.23 [0.03, 1.66]	
	2	35	4	36	23.4%		
Sunpaweravong 2014 Subtotal (95% CI)	2	123	1		100.0%	2.06 [0.20, 21.68] 0.59 [0.17, 2.03]	
	10	125	16	119	100.078	0.55[0.17, 2.03]	
otal events		2/D 0	16	,			
leterogeneity: Tau ² = 0. est for overall effect: Z		3 (P = 0.	17); 1* = 419	0			
3.1.2 Oesophagitis (gi	rade 3 or more)						
Sunpaweravong 2014	1	35	1		100.0%	1.03 [0.07, 15.81]	
Subtotal (95% CI)		35		36	100.0%	1.03 [0.07, 15.81]	
otal events	1		1				
leterogeneity: Not appli	cable						
est for overall effect: Z	= 0.02 (P = 0.98)						
8.1.3 Diarrhea (grade							
4iyata 2012	3	47	5	44	28.5%	0.56 [0.14, 2.21]	_
4iyata 2017	5	31	11	30	61.9%	0.44 [0.17, 1.12]	
Sunpaweravong 2014 Subtotal (95% CI)	2	35 113	1	36 110	9.7% 100.0%	2.06 [0.20, 21.68] 0.55 [0.26, 1.14]	
otal events	10		17				
Heterogeneity: Tau ² = 0. Test for overall effect: Z		2 (P = 0	49); l ² = 0%				
3.1.4 Nausea (grade 3							_
4iyata 2012	17	47	21	44	40.9%	0.76 [0.46, 1.24]	
4iyata 2017	16	31	21	30	57.3%	0.74 [0.49, 1.12]	
Sunpaweravong 2014	2	35	1	36	1.8%	2.06 [0.20, 21.68]	
Subtotal (95% CI)		113		110	100.0%	0.76 [0.56, 1.04]	-
otal events	35		43				
Heterogeneity: Tau ² = 0. Test for overall effect: Z		2 (P = 0.)	59); l ² = 0%				
3.1.5 Vomiting (grade	3 or more)						
1iyata 2012	1	47	2	44	49.8%	0.47 [0.04, 4.98]	
Aiyata 2017	0	31	0	30		Not estimable	
iunpaweravong 2014	2	35	1	36	50.2%	2.06 [0.20, 21.68]	
ubtotal (95% CI)		113		110	100.0%	0.98 [0.19, 5.22]	
otal events	3		3				
leterogeneity: Tau ² = 0. est for overall effect: Z		1 (P = 0.3	38); I ² = 0%				
3.1.6 complication rela	ated infection						_
ong 2015 Subtotal (95% CI)	З	25 25	11		100.0% 100.0%	0.27 [0.09, 0.86] 0.27 [0.09, 0.86]	
otal events leterogeneity: Not appli	3 cable		11				
est for overall effect: Z							
							0.01 0.1 1 10

Test for subgroup differences: Chi² = 3.56, df = 5 (P = 0.61), l² = 0%

0.01 0.1 1 10 100 Favours extra nutri, sup. Favours standard care

Figure 297: Completion of planned treatment: additional nutritional support versus standard nutritional support during chemotherapy or chemoradiotherapy

	Extra nutritional s	Standard	care		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Cong 2015	24	25	19	25	11.4%	1.26 [1.00, 1.60]	
Miyata 2012	42	47	39	44	25.0%	1.01 [0.87, 1.17]	_
Miyata 2017	30	31	28	30	34.1%	1.04 [0.92, 1.16]	
Sunpaweravong 2014	32	35	34	36	29.5%	0.97 [0.85, 1.10]	
Total (95% CI)		138		135	100.0%	1.03 [0.95, 1.12]	+
Total events	128		120				
Heterogeneity: Tau ² =	0.00; Chi ² = 4.09, df =	3(P = 0.3)	25); l ² = 27 ⁴	%			
Test for overall effect: 3							0.5 0.7 1 1.5 2' Favours standard care Favours extra nutri. sup.

Figure 298: Weight change: additional nutritional support versus standard nutritional support during chemotherapy or chemoradiotherapy

	Extra nu	tritional su	pport	Sta	ndard ca	re		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Cong 2015	0.6	3.73	25	-4.34	4.6	25	25.2%	4.94 [2.62, 7.26]	_
Miyata 2012	-0.6	3	47	-0.1	3.2	47	29.1%	-0.50 [-1.75, 0.75]	
Miyata 2017	-1.5	3.9	31	-0.1	2.5	30	27.8%	-1.40 [-3.04, 0.24]	
Sunpaweravong 2014	-1	8.7333	35	-2	8.8665	36	17.9%	1.00 [-3.09, 5.09]	
Total (95% CI)			138			138	100.0%	0.89 [-1.77, 3.55]	
Heterogeneity: Tau ² = 5. Test for overall effect: Z :		•	(P = 0.0	001); I²	= 86%				-10 -5 0 5 10 Favours standard care Favours extra nutri, sup.

H.18.4 Oral nutrition supplements

Figure 299: Weight change from baseline: oral nutritional support versus standard care, before or after curative treatment

	Oral supplement Standard diet					Mean Difference	Mean Difference						
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV,	Fixed, 95% CI		
Faber 2015	1.29	1.9097	24	0.39	1.8727	23	54.2%	0.90 [-0.18, 1.98]					
Imamura 2016	-2.88	2.47	53	-4.06	3.36	46	45.8%	1.18 [0.00, 2.36]					
Total (95% CI)			77			69	100.0%	1.03 [0.23, 1.82]				-	
Heterogeneity: Chi ² = Test for overall effect:				= 0%					-4	-2 Favours stan	0 dard Favours	2 oral supj	4 plement

H.18.5 Continued nutrition support after discharge from hospital

Figure 300: Complications: continued nutrition support after discharge from hospital versus standard care

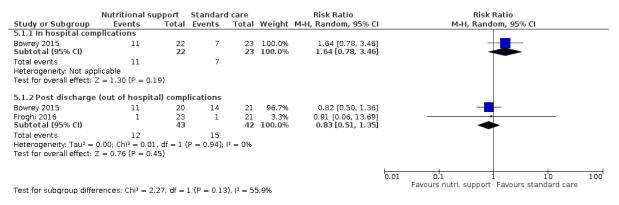


Figure 301: Sarcopenia (change in grip strength in kg): continued nutrition support after discharge from hospital versus standard care

	Nutritio	nal sup	port	Stan	dard o	are		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Bowrey 2015	-1.5	4.4	16	-2	4.1	21	10.8%	0.50 [-2.28, 3.28]	
Carey 2013	1.6	6.2	14	2.9	5.7	13	4.1%	-1.30 [-5.79, 3.19]	
Gavazzi 2016	1.7	2.05	38	0.5	2.44	41	85.0%	1.20 [0.21, 2.19]	
Total (95% CI)			68			75	100.0%	1.02 [0.11, 1.93]	◆
Heterogeneity: Chi ² = 1 Test for overall effect: 3				0%					-10 -5 0 5 10 Favours nutri support Favours standard care

Figure 302: Quality of life: continued nutrition support after discharge from hospital versus standard care

	Nutrition	al sup	port	Stand	lard o	are		Mean Difference	Mean Difference		
Study or Subgroup	Mean			Mean	SD	Total	Weight	IV, Fixed, 95% CI	I IV, Fixed, 95% CI		
5.10.1 Change in QOL	from base	eline to	o 6 mor	nths							
Bowrey 2015 (1) Subtotal (95% CI)	-5	25	16 16	-7	18			2.00 [-12.57, 16.57] 2.00 [-12.57, 16.57]			
Heterogeneity: Not applicable Test for overall effect: Z = 0.27 (P = 0.79)											
5.10.2 QOL at the en	d of follow	up									
Bowrey 2015	69	25	16	73	15	20	59.3%	-4.00 [-17.90, 9.90]]		
Carey 2013 Subtotal (95% CI)	58	26	14 30	64	18	13 33		-6.00 [-22.77, 10.77] -4.81 [-15.52, 5.89]			
	Heterogeneity: $Ch^2 = 0.03$, df = 1 (P = 0.86); P = 0% Test for overall effect: Z = 0.88 (P = 0.38)										
									-100		
Test for subgroup differences: Chi² = 0.55, df = 1 (P = 0.46), l² = 0% Favours standard care Favours nutri, support Footnotes (1) EORTC QLQ-C30 change in global QOL from baseline to 6 months after surgery											

Figure 303: Weight change: continued nutrition support after discharge from hospital versus standard care

	Nutrition	Standard care				Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Bowrey 2015	-7.4	5.2	16	-10.9	7.2	21	22.5%	3.50 [-0.50, 7.50]	· · · · · · · · · · · · · · · · · · ·
Carey 2013	-0.9	5.8	14	-3.2	8.2	13	12.3%	2.30 [-3.09, 7.69]	
Gavazzi 2016	-0.4	5.6	38	-2.4	5	41	65.2%	2.00 [-0.35, 4.35]	
Total (95% CI)			68			75	100.0%	2.37 [0.48, 4.27]	
Heterogeneity: Chi ² = 0 Test for overall effect: 3				0%					-10 -5 0 5 10 Favours standard care Favours Nutritional support

H.19 Palliative care

What is the effectiveness of nutritional interventions in adults with oesophago-gastric cancer receiving palliative care?

No evidence was indentifed for this review.

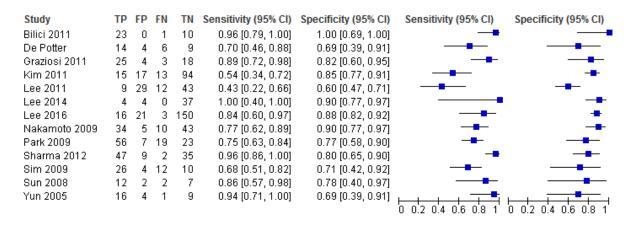
H.20 Routine follow-up

In adults who have undergone treatment for oesophago-gastric cancer with curative intent, with no symptoms or evidence of residual disease, what is the optimal

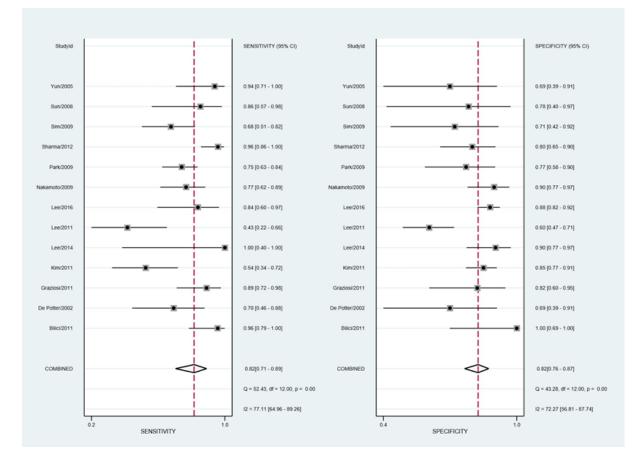
method(s), frequency, and duration of routine follow-up for the detection of concurrent disease?

H.20.1 PET/CT for gastric cancer

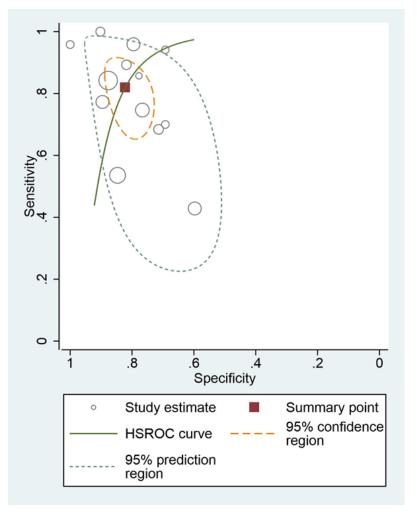
Figure 304: PET/CT for any site recurrence (all studies)











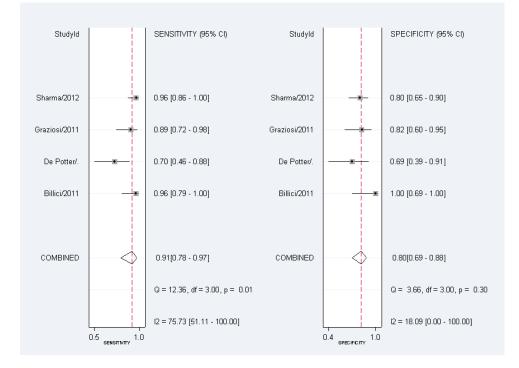


Figure 307: Bivariate analysis: PET/CT for any site recurrence (excluding studies from China, Japan or Korea)



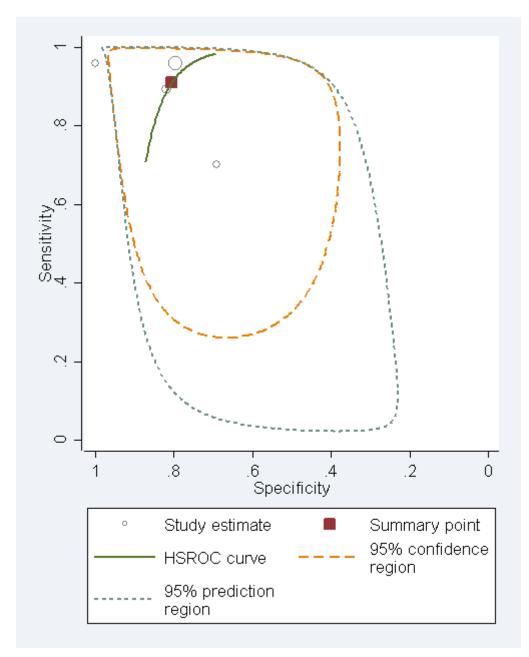
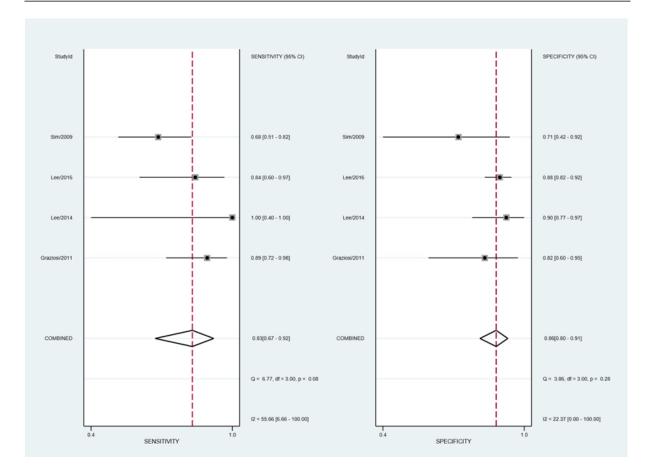


Figure 309: Bivariate analysis: PET/CT for gastric cancer any site recurrence (PET/CT conducted routinely only)





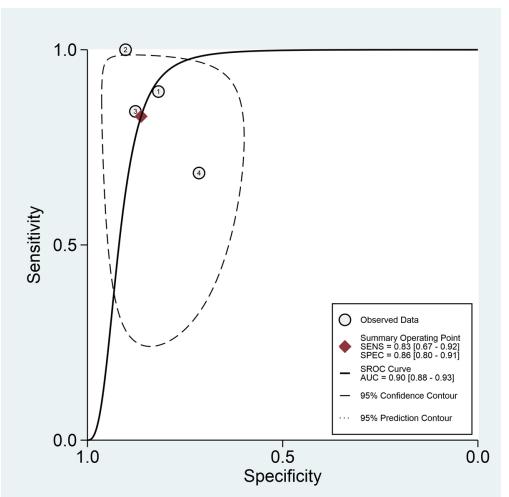


Figure 311: PET/CT for local recurrence

Study	ТР	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Lee 2014	1	3	0	42	1.00 (0.03, 1.00)	0.93 (0.82, 0.99)		

Figure 312: PET/CT for distant recurrence

Study	ТР	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Lee 2014	3	0	3	40	0.50 [0.12, 0.88]	1.00 [0.91, 1.00]	0 0.2 0.4 0.6 0.8 1	

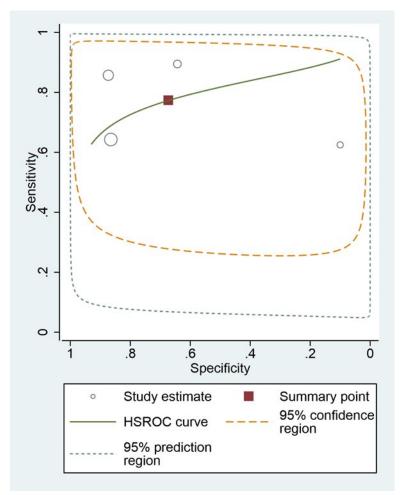
Appendix H Forest Plots

H.20.2 CT for gastric cancer

Figure 313: CT for any site recurrence

Study	ТР	FP	FN	ΤN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Bilici 2011	15	9	9	1	0.63 [0.41, 0.81]	0.10 [0.00, 0.45]		-
Kim 2011	18	15	10	96	0.64 [0.44, 0.81]	0.86 [0.79, 0.92]		-
Lee 2011	18	9	3	62	0.86 [0.64, 0.97]	0.87 [0.77, 0.94]		
Sim 2009	34	5	4	9	0.89 [0.75, 0.97]	0.64 [0.35, 0.87]		
							0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Figure 314: HSROC curve: CT for any site recurrence



Note: Bivariate analysis not reported due to high heterogeneity.

H.20.3 CEA for gastric cancer

Figure 315: CEA for any site recurrence (all studies)

Study	ТР	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Cazin 1998	6	2	5	13	0.55 [0.23, 0.83]	0.87 [0.60, 0.98]		
Kim 2011b	14	3	34	428	0.29 [0.17, 0.44]	0.99 [0.98, 1.00]		•
Lee 2014b	52	99	76	99	0.41 [0.32, 0.50]	0.50 [0.43, 0.57]		-
Marrelli 2001	33	12	42	46	0.44 [0.33, 0.56]	0.79 [0.67, 0.89]		
Ohtsuka 2008	10	18	12	121	0.45 [0.24, 0.68]	0.87 [0.80, 0.92]		-
Qiu 2009	26	11	40	104	0.39 [0.28, 0.52]	0.90 [0.84, 0.95]		

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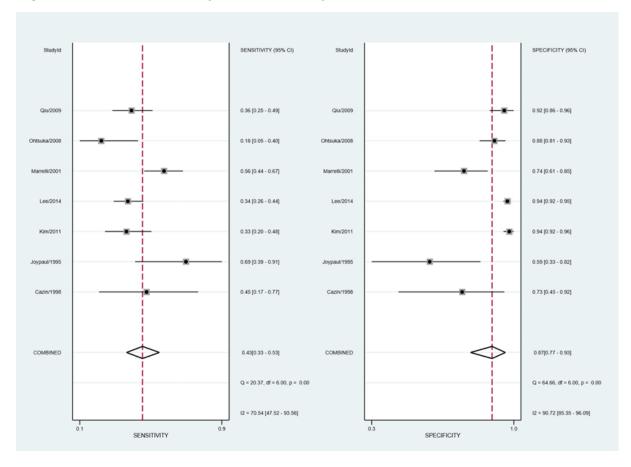


Figure 316: Bivariate analysis: CEA for any site recurrence (all studies)



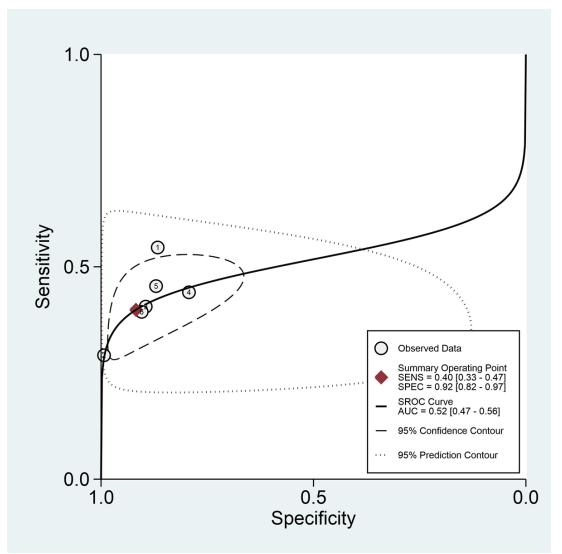
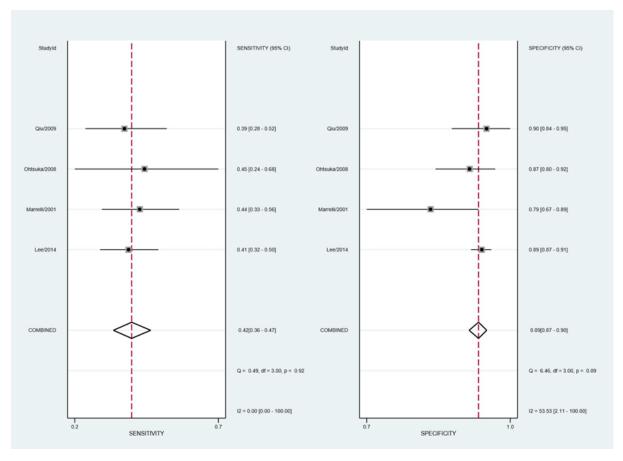


Figure 318: Bivariate analysis: CEA for any site recurrence (CEA cut-off 5ng/mL only)



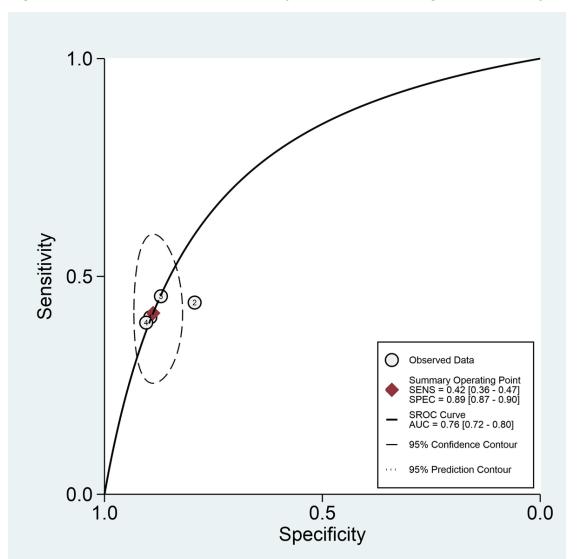


Figure 319: HSROC curve: CEA for any site recurrence (5ng/mL cut off only)

Figure 320: CEA for locoregional recurrence

Study	TP FF	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Kim 2011b	0 13	3	459	0.00 [0.00, 0.71]	0.96 [0.94, 0.98]		

Figure 321: CEA for distant lymph node recurrence

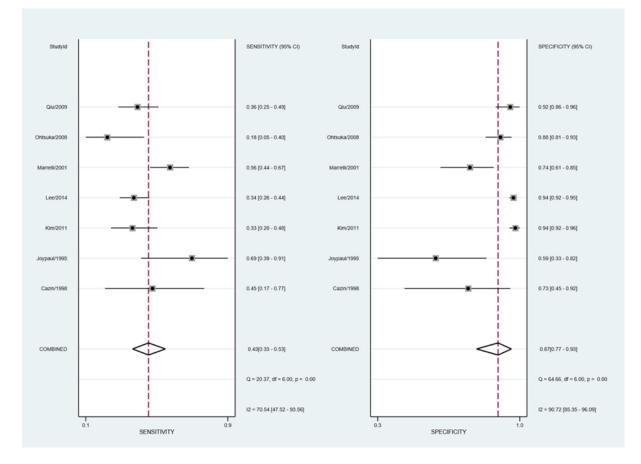
Study	TP F	P	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Kim 2011b	2 1	5	3	459	0.40 [0.05, 0.85]	0.97 [0.95, 0.98]		

H.20.4 CA 19-9 for gastric cancer

Figure 322: CA 19-9 for any site recurrence (all studies)

Study	ТР	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Cazin 1998	5	4	6	11	0.45 [0.17, 0.77]	0.73 [0.45, 0.92]		
Joypaul 1995	9	- 7	4	10	0.69 [0.39, 0.91]	0.59 [0.33, 0.82]		
Kim 2011b	16	24	32	407	0.33 [0.20, 0.48]	0.94 [0.92, 0.96]		•
Lee 2014b	40	57	77	828	0.34 [0.26, 0.44]	0.94 [0.92, 0.95]		•
Marrelli 2001	42	15	33	43	0.56 [0.44, 0.67]	0.74 [0.61, 0.85]		
Ohtsuka 2008	4	17	18	122	0.18 [0.05, 0.40]	0.88 [0.81, 0.93]		-
Qiu 2009	24	9	42	106	0.36 [0.25, 0.49]	0.92 [0.86, 0.96]		

Figure 323: Bivariate analysis: CA 19-9 for any site recurrence (all studies)



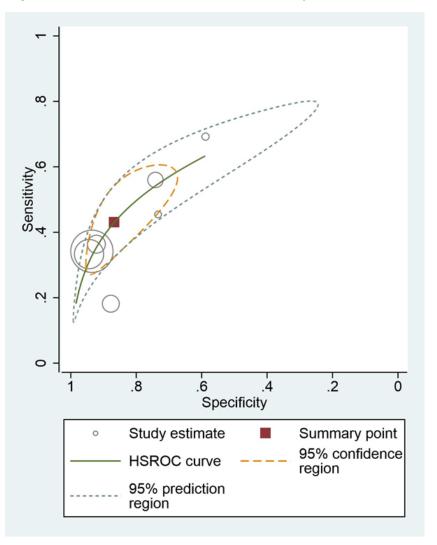
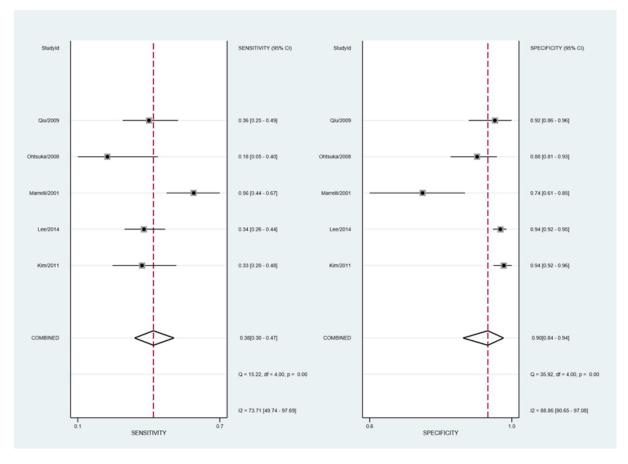
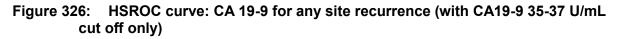


Figure 324: HSROC curve: CA19-9 for any site survival (all studies)

Figure 325: Bivariate analysis: CA 19-9 for any site recurrence (CA 19-9 cut off 35-37 U/mL only)





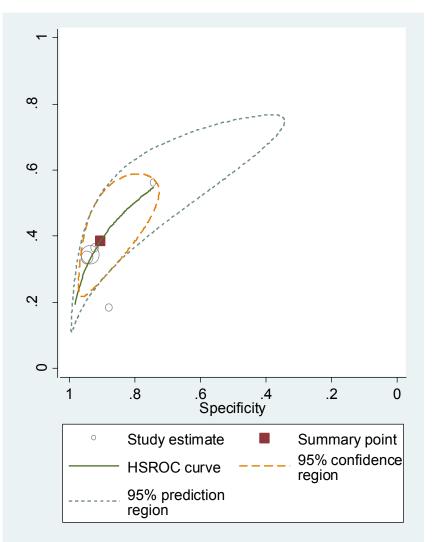


Figure 327: CA 19-9 for locoregional recurrence

Study	ΤР	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Kim 2011b	0	40	3	436	0.00 [0.00, 0.71]	0.92 [0.89, 0.94]		

Figure 328: CA 19-9 for distant lymph node recurrence

Study	ТР	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Kim 2011b	1	39	4	435	0.20 [0.01, 0.72]	0.92 [0.89, 0.94]	0 0.2 0.4 0.6 0.8 1	

H.20.5 CEA and CA19-9 used in combination for gastric cancer

Figure 329: CEA and CA19-9 combination for any site recurrence

Note: Positive test result= both CEA and CA19-9 levels are elevated.

Figure 330: Either CEA or CA 19-9 for any site recurrence

Note: Positive test result= either CEA or CA19-9 levels are elevated.

H.20.6 PET/CT for oesophageal cancer

Figure 331: PET/CT for any site recurrence

Study	TP	FP	FN	ΤN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Kato 2004	26	9	1	19	0.96 [0.81, 1.00]	0.68 [0.48, 0.84]		
Roedl 2008	24	5	3	15	0.89 [0.71, 0.98]	0.75 [0.51, 0.91]		
							0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Figure 332: PET/CT for locoregional recurrence

Figure 333: PET/CT for distant recurrence

H.20.7 CT for oesophageal cancer

Figure 334: CT for any site recurrence

 Study
 TP
 FP
 FN
 TN
 Sensitivity (95% Cl)
 Specificity (95% Cl)
 Sensitivity (95% Cl)
 Specificity (95% Cl)

Figure 335: CT for locoregional recurrence

Study	TP F	Ρ	FN	ΤN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Kato 2004	16	5	3	31	0.84 [0.60, 0.97]	0.86 [0.71, 0.95]		

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Figure 336: CT for distant recurrence

H.20.8 Serum CEA for oesophageal cancer

Figure 337: serum CEA for any site recurrence

Study	ТР	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Clark 1995	29	34	3	27	0.91 [0.75, 0.98]	0.44 [0.32, 0.58]		
Setoyama 2006	26	11	8	61	0.76 [0.59, 0.89]	0.85 [0.74, 0.92]		

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