National Institute for Health and Care Excellence

Version 1.0

Pancreatic Cancer in adults:

diagnosis and management

Appendix H

Forest Plots and Summary ROC Curves

31 July 2017

Draft for Consultation

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

Disclaimer
The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

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Appendix H: Forest plots and Summary ROC curves

H.1 People with jaundice

Figure 1: Forest plot of spiral CT

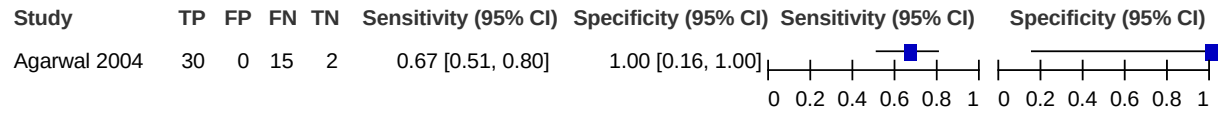


Figure 2: Forest plot of EUS

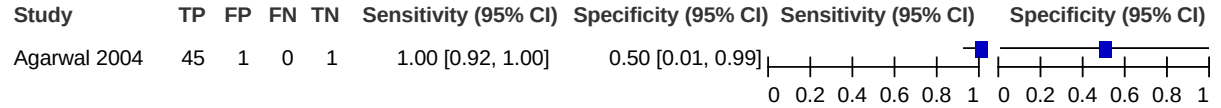


Figure 3: Forest plots for EUS-FNA

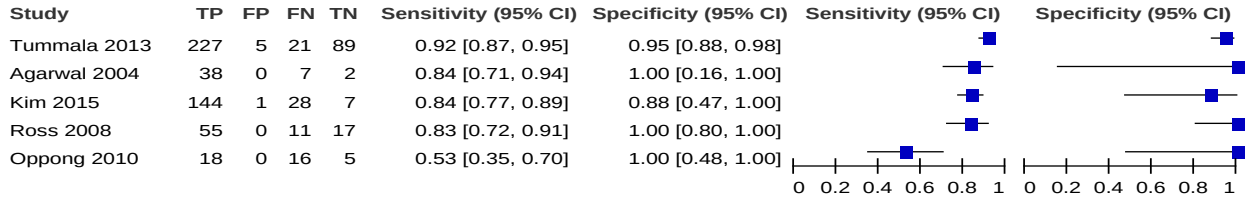


Figure 4: EUS-FNA - Summary ROC curve

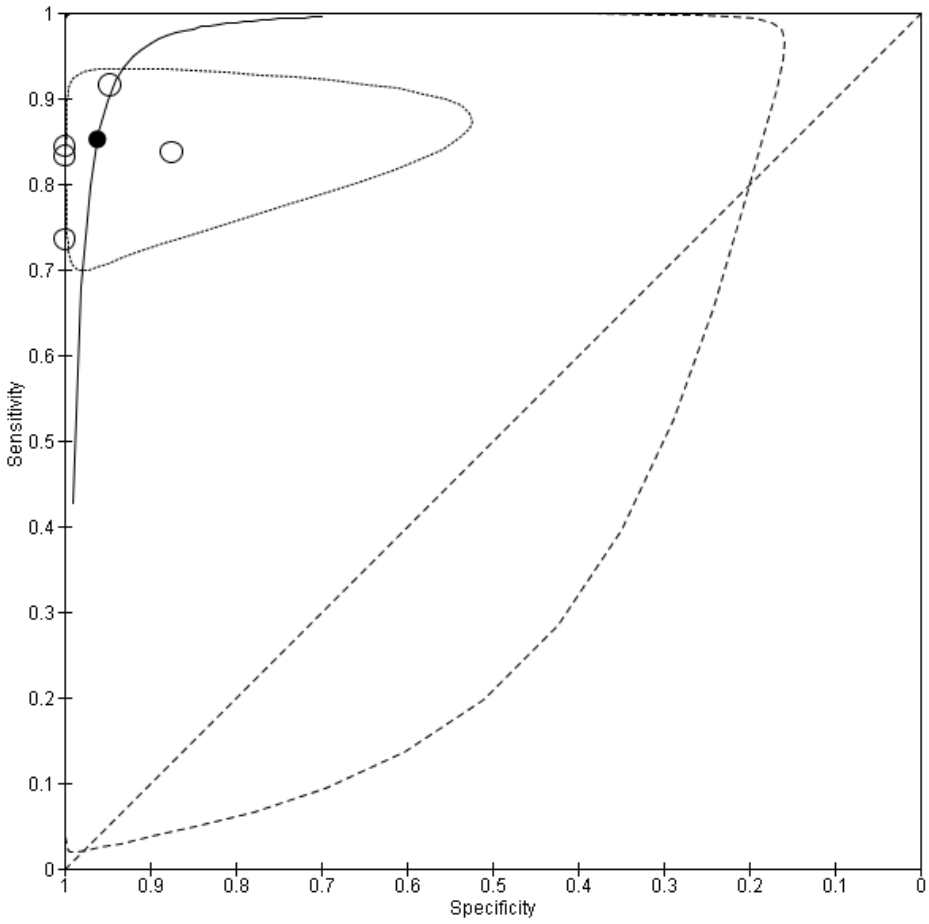
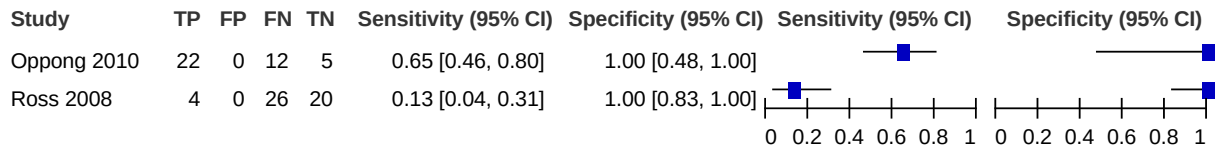


Figure 5: Forest plot of ERCP + BB.



H.2 People without jaundice but with a pancreatic abnormality

Figure 6: Forest plot of computer tomography

Study	TP	FP	FN	TN	Type of observational study	Index test type	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Tamm 2007 CT	96	5	3	13	Retrospective cohort	Not applicable	0.97 [0.91, 0.99]	0.72 [0.47, 0.90]		

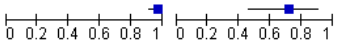


Figure 7: Forest plot of EUS

Study	TP	FP	FN	TN	Type of study	Index test type	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Krishna 2009	110	35	0	68	Prospective cohort	Cytology	1.00 [0.97, 1.00]	0.66 [0.56, 0.75]		
Tamm 2007 EUS	98	9	1	9	Retrospective cohort	Histology	0.99 [0.95, 1.00]	0.50 [0.26, 0.74]		

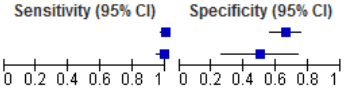


Figure 8: Forest plot of EUS-FNA

Study	TP	FP	FN	TN	Type of study	Index test type	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Bang 2012	25	0	0	3	RCT	Cytology	1.00 [0.86, 1.00]	1.00 [0.29, 1.00]		
Fabbri 2011	44	0	2	4	Prospective cohort	Cytology	0.96 [0.85, 0.99]	1.00 [0.40, 1.00]		
Ramesh 2015 19-gauge	41	0	2	7	RCT	Cytology	0.95 [0.84, 0.99]	1.00 [0.59, 1.00]		
Lee 2014	53	0	3	2	RCT	Histology + Cytology	0.95 [0.85, 0.99]	1.00 [0.16, 1.00]		
Hikichi 2009 Group 2	27	0	2	6	Retrospective cohort	Cytology	0.93 [0.77, 0.99]	1.00 [0.54, 1.00]		
Wakatsuki 2005	39	0	3	11	Retrospective cohort	Cytology	0.93 [0.81, 0.99]	1.00 [0.72, 1.00]		
Hikichi 2009 Group 1	26	0	2	10	Retrospective cohort	Cytology	0.93 [0.76, 0.99]	1.00 [0.69, 1.00]		
Ramesh 2015 25-gauge	40	0	4	6	RCT	Cytology	0.91 [0.78, 0.97]	1.00 [0.54, 1.00]		
Fritscher-Ravens 2002	99	0	17	84	Retrospective cohort	Cytology	0.85 [0.78, 0.91]	1.00 [0.96, 1.00]		
Mishra 2006	40	0	7	5	Prospective cohort	Cytology	0.85 [0.72, 0.94]	1.00 [0.48, 1.00]		
Iglesias-Garcia 2007	32	0	6	24	Prospective cohort	Cytology	0.84 [0.69, 0.94]	1.00 [0.86, 1.00]		
Yusuf 2009 22-gauge	314	0	60	166	Retrospective cohort	Cytology	0.84 [0.80, 0.88]	1.00 [0.98, 1.00]		
Seicean 2016	89	0	18	11	Prospective cohort	Histology	0.83 [0.75, 0.90]	1.00 [0.72, 1.00]		
Bournet 2009	122	0	29	27	Prospective cohort	Cytology	0.81 [0.74, 0.87]	1.00 [0.87, 1.00]		
Bournet 2015	97	0	29	60	Prospective cohort	Histology + Cytology	0.77 [0.69, 0.84]	1.00 [0.94, 1.00]		
Wittmann 2006	29	0	19	36	Prospective cohort	Histology + Cytology	0.60 [0.45, 0.74]	1.00 [0.90, 1.00]		
Krishna 2009	106	1	4	102	Prospective cohort	Cytology	0.96 [0.91, 0.99]	0.99 [0.95, 1.00]		
Yusuf 2009 25-gauge	180	3	16	103	Retrospective cohort	Cytology	0.92 [0.87, 0.95]	0.97 [0.92, 0.99]		
Tamm 2007 EUS-FNA	81	1	18	17	Retrospective cohort	Unclear	0.82 [0.73, 0.89]	0.94 [0.73, 1.00]		
Kliment 2010	151	5	12	39	Prospective cohort	Cytology	0.93 [0.87, 0.96]	0.89 [0.75, 0.96]		
Touchefeu 2009	62	3	18	8	Prospective cohort	Histology + Cytology	0.78 [0.67, 0.86]	0.73 [0.39, 0.94]		
Harewood 2002	154	6	10	15	Prospective cohort	Cytology	0.94 [0.89, 0.97]	0.71 [0.48, 0.89]		

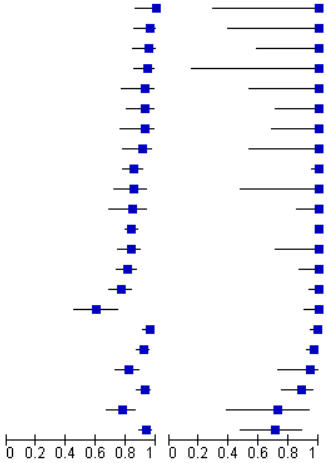


Figure 9: EUS-FNA - Summary ROC curve

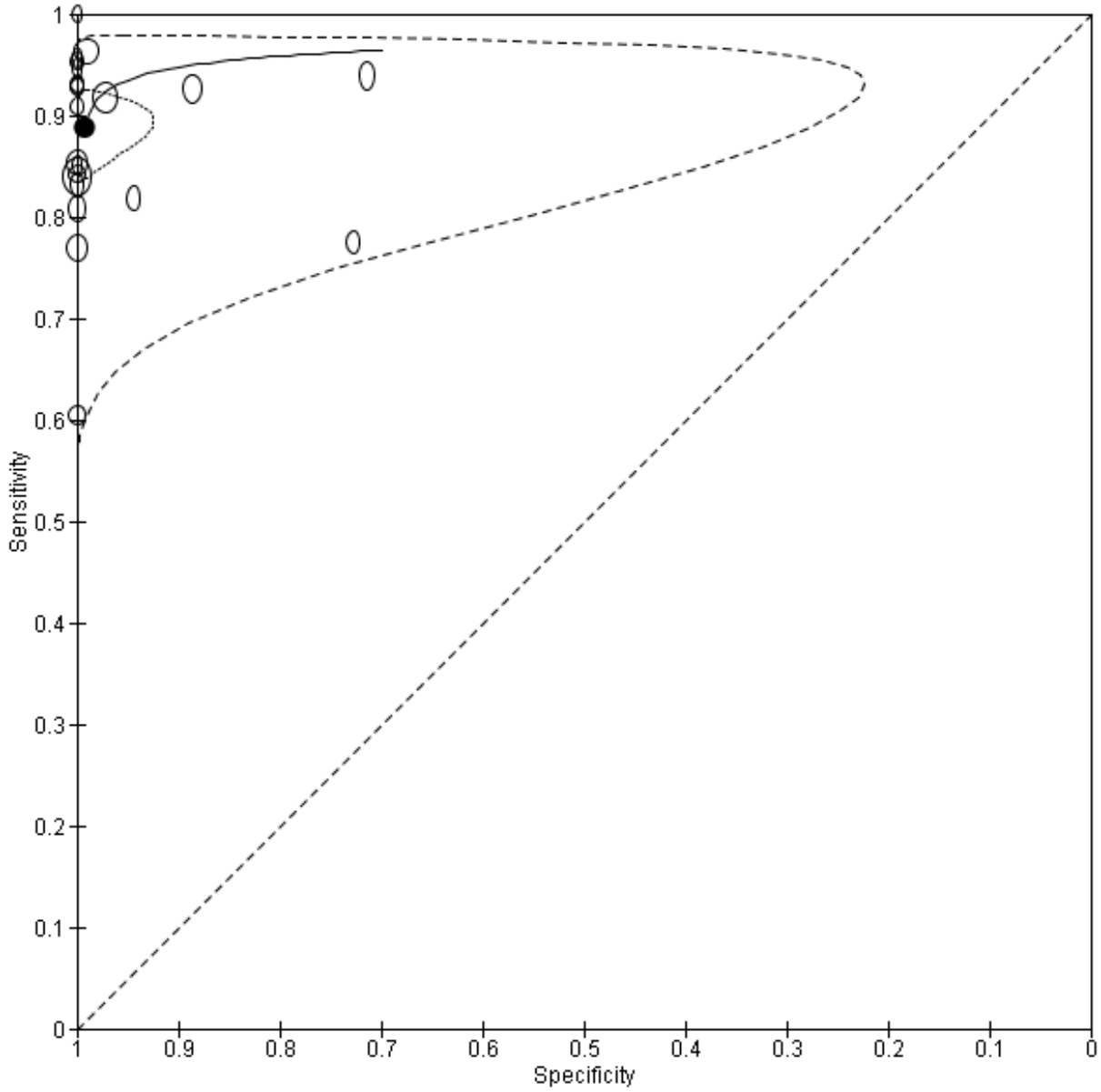
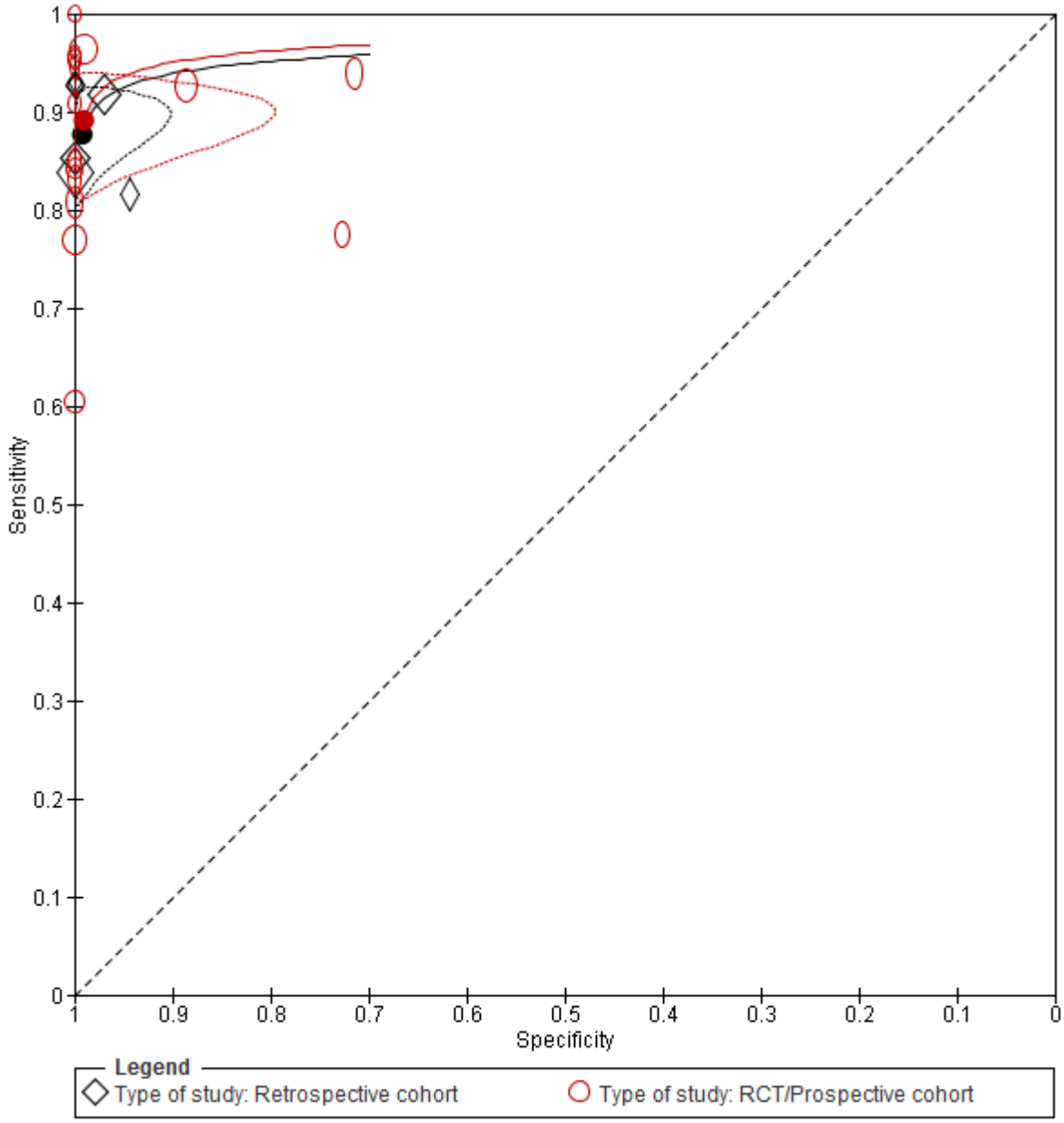


Figure 10: EUS-FNA - Summary ROC curve (subgroup analysis by type of study)



Note: Red and black dotted line represent the 95% confidence region for, respectively, the RCT/prospective cohort and retrospective cohort study groups.

Figure 11: Forest plot of EUS-Core

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bang 2012	22	0	3	3	0.88 [0.69, 0.97]	1.00 [0.29, 1.00]
Lee 2014	54	0	3	1	0.95 [0.85, 0.99]	1.00 [0.03, 1.00]
Strand 2014	6	1	18	7	0.25 [0.10, 0.47]	0.88 [0.47, 1.00]
Wittmann 2006	11	0	16	9	0.41 [0.22, 0.61]	1.00 [0.66, 1.00]

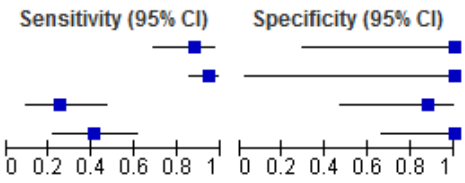


Figure 12: EUS-Core Biopsy - Summary ROC curve

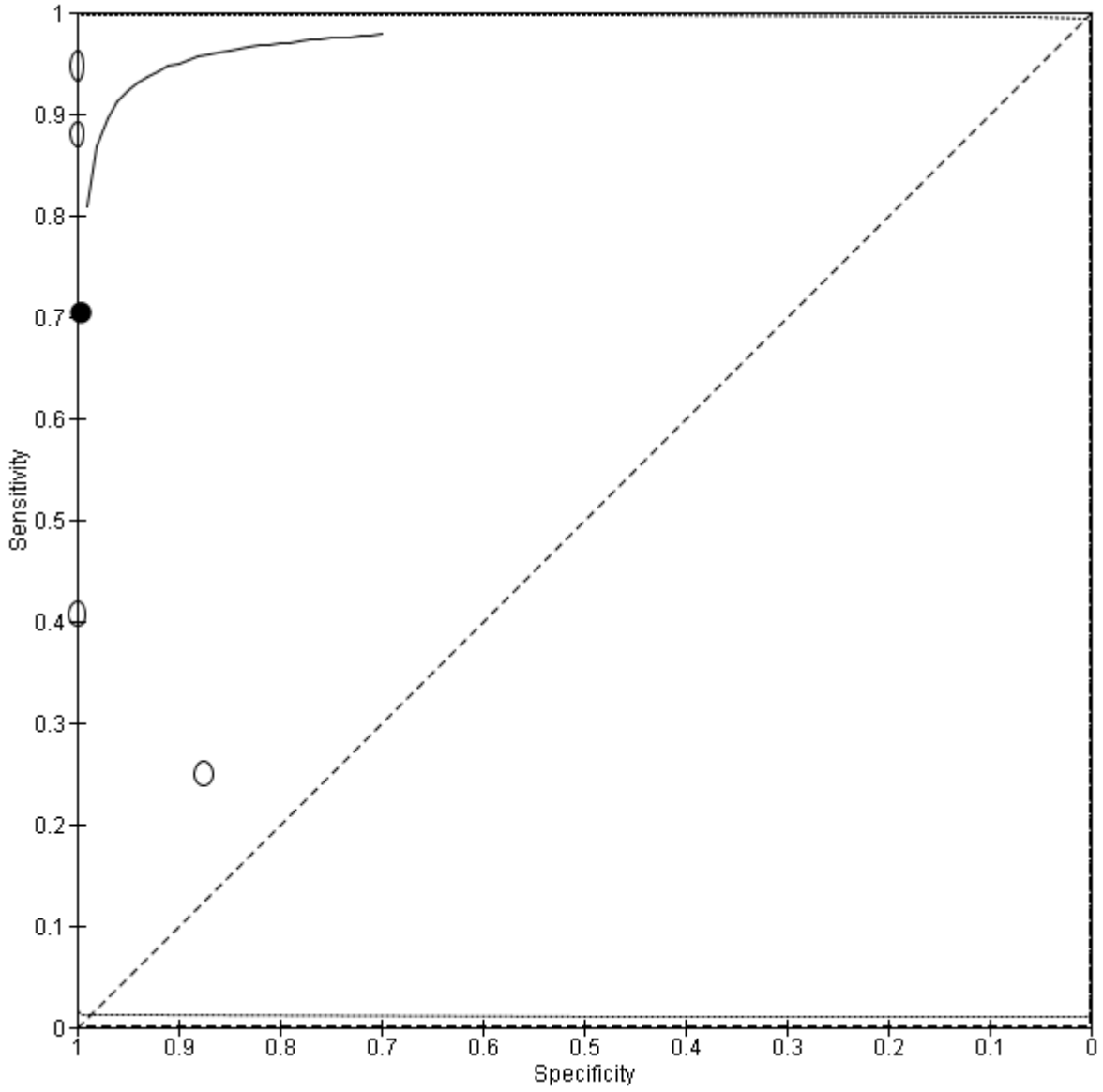


Figure 13: Forest plot of EUS-FNA + Core

Figure 14: Forest plot of PUS-Core

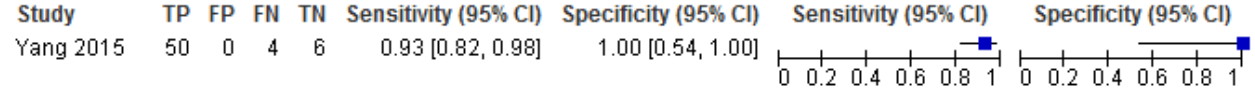
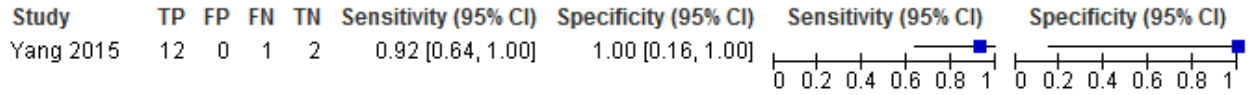


Figure 15: Forest plot of PUS-FNA + Core



H.3 4 Pancreatic Cysts

Figure 16: Forest plot for Cystic fluid CEA at cut-off level of <30-<70 ng/ml for differentiating between MCNs and NMCNs of pancreas

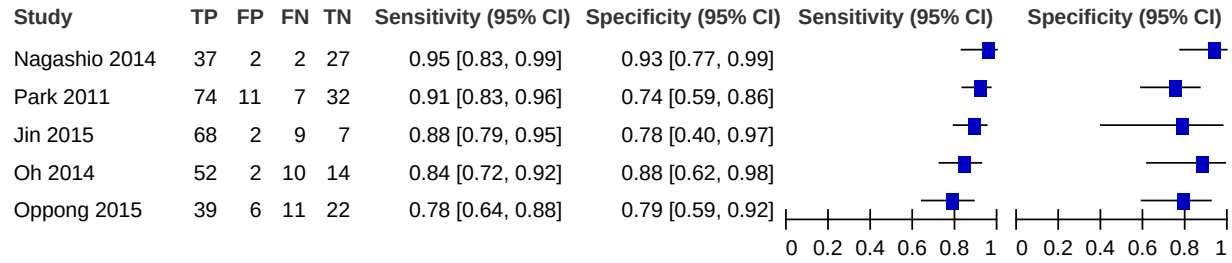


Figure 17: Summary ROC curve of cystic fluid CEA at cut-off level of <30-<70 ng/ml for differentiating between MCNs and NMCNs of pancreas

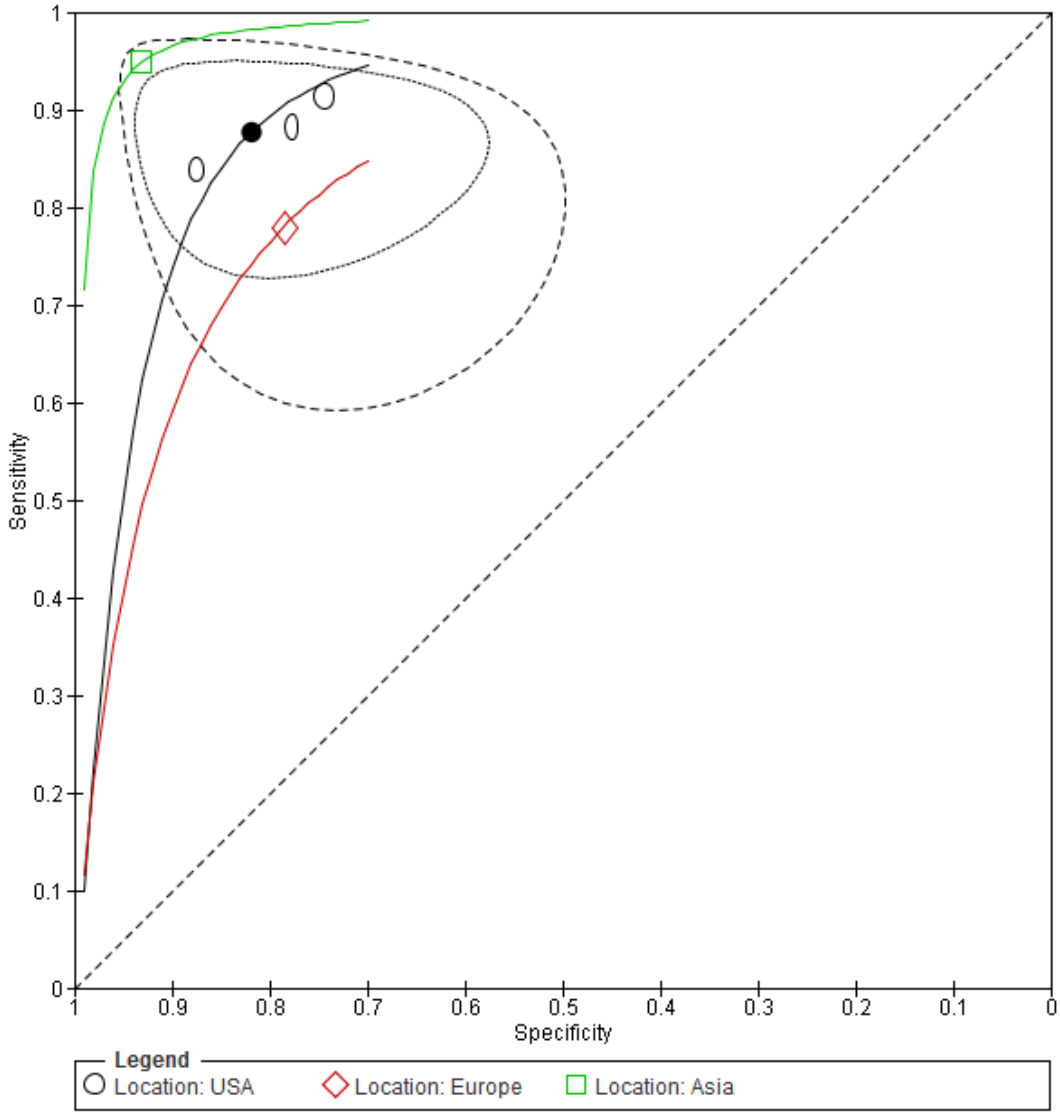


Figure 18: Forest plot for cystic fluid CEA at cut-off level of <192 ng/ml for differentiating between MCNs and NMCNs of pancreas

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Brugge 2004	42	9	14	46	0.75 [0.62, 0.86]	0.84 [0.71, 0.92]
Gaddam 2015	92	17	58	59	0.61 [0.53, 0.69]	0.78 [0.67, 0.86]
Jin 2015	40	1	37	8	0.52 [0.40, 0.63]	0.89 [0.52, 1.00]
Oppong 2015	24	1	26	27	0.48 [0.34, 0.63]	0.96 [0.82, 1.00]

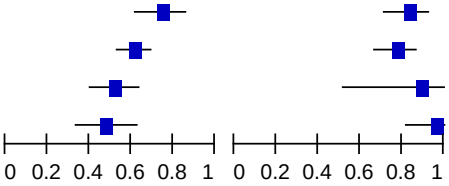


Figure 19: Summary ROC curve of cystic fluid CEA [192 ng/ml] for differentiating between MCNs and NMCNs of pancreas

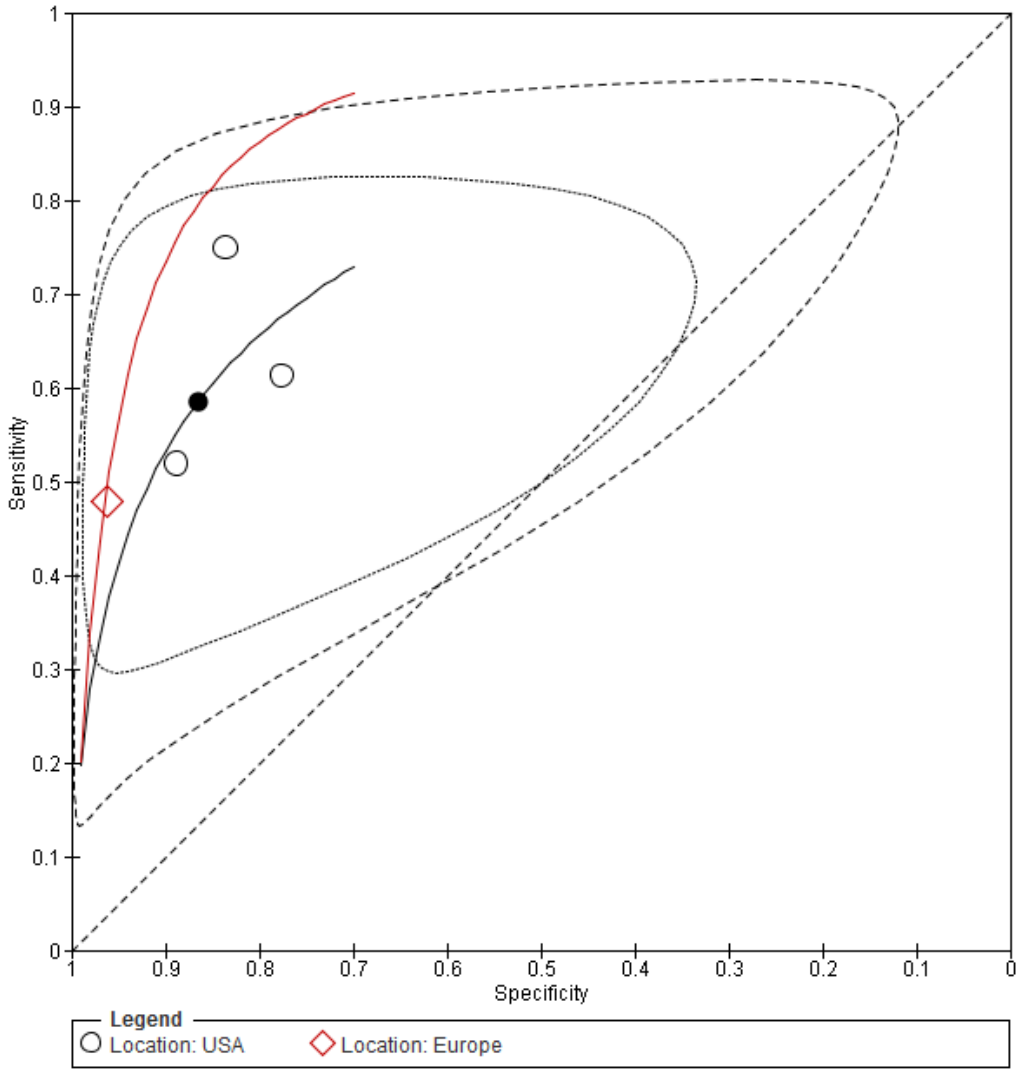


Figure 20: Forest plots for other studies on cystic fluid CEA at various cut-off levels for differentiating between MCNs and NMCNs of pancreas

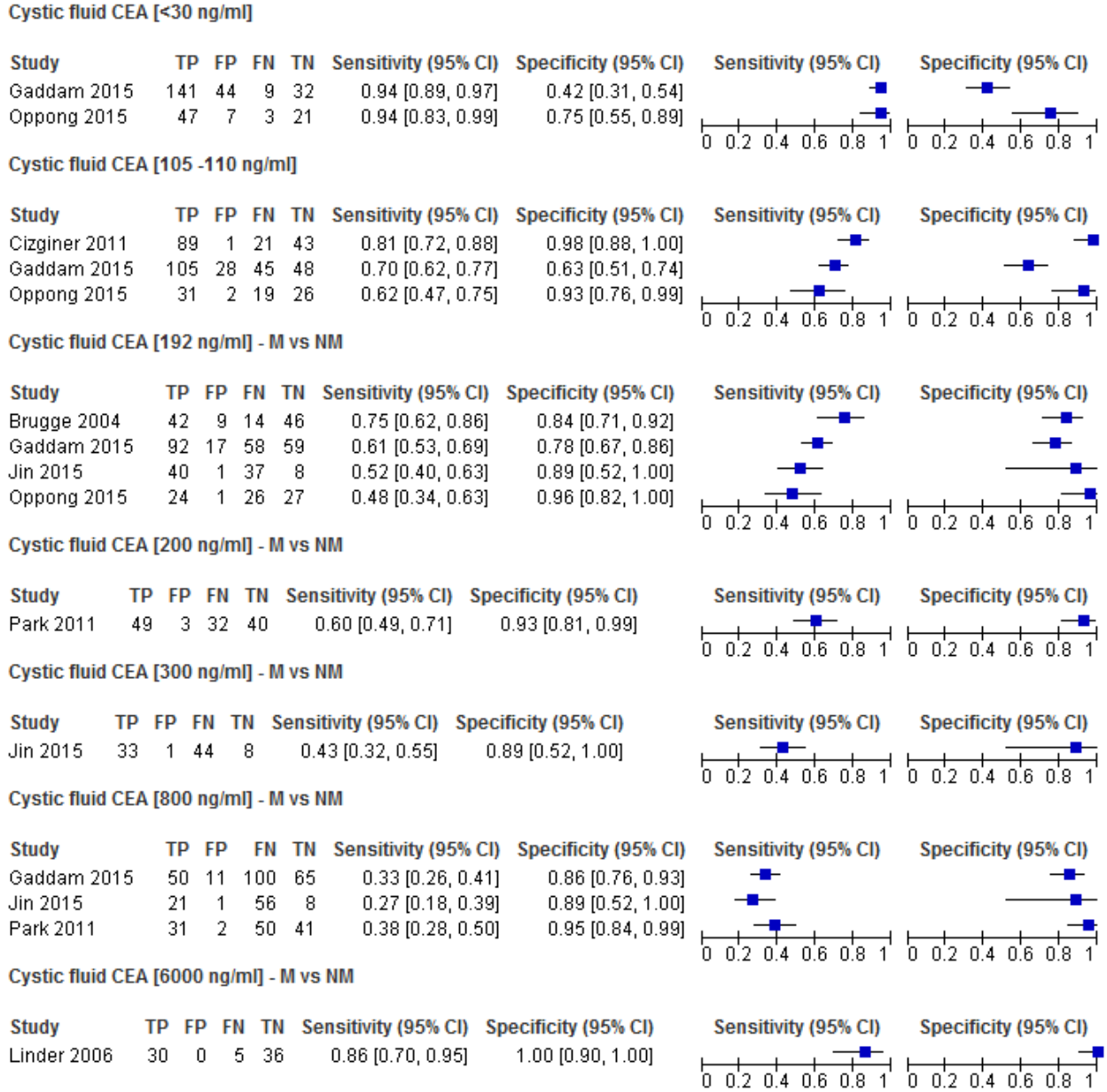


Figure 21: Forest plot for cystic fluid CEA in differentiating between (potentially) malignant and benign PCLs

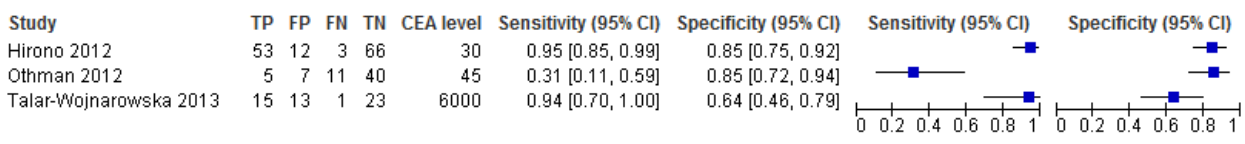


Figure 22: Forest plot for serum CEA at unspecified cut-off level for differentiating between (potentially) malignant and benign PCLs

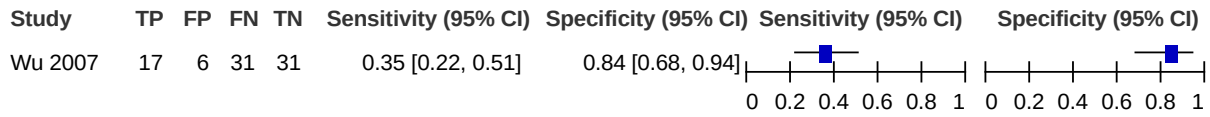


Figure 23: Forest plot for cystic fluid CA 19-9 at cut-off level of <35-<45 ng/ml] for differentiating between (potentially) malignant and benign PCLs

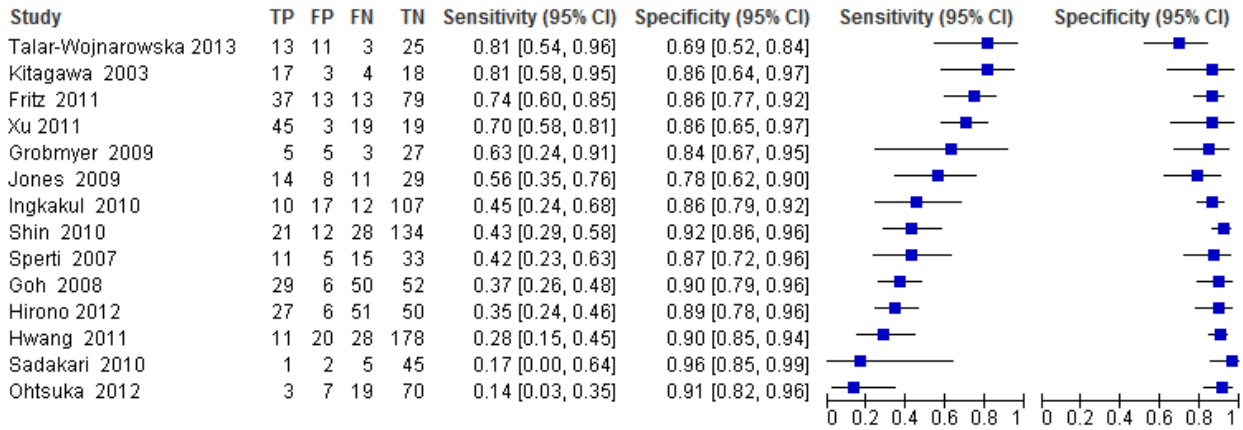


Figure 24: Summary ROC curve for cystic fluid CA 19-9 at cut-off level of <35-<45 ng/ml] for differentiating between (potentially) malignant and benign PCLs

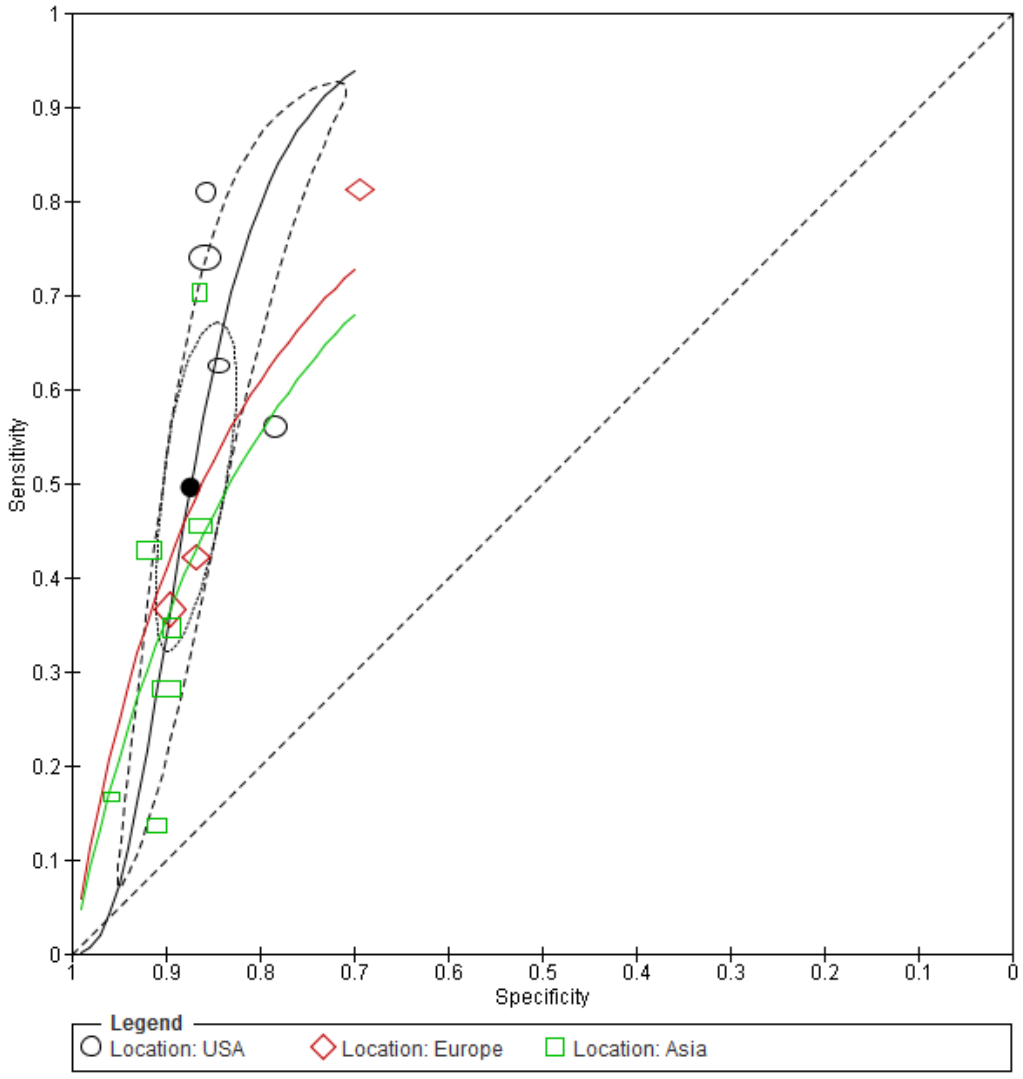


Figure 25: Forest plot for serum CA 19-9 at unspecified cut-off level for differentiating between (potentially) malignant and benign PCLs

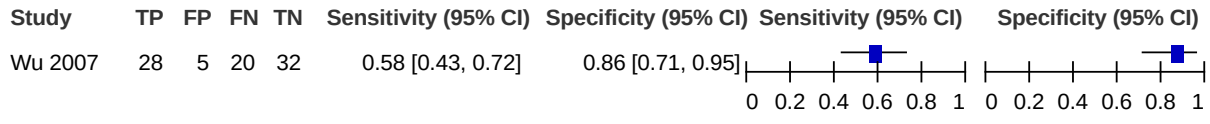


Figure 26: Forest plot for EUS-FNA-based cytology for differentiating between MCNs and NMCNs of pancreas

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Frossard 2003	38	2	1	26	0.97 [0.87, 1.00]	0.93 [0.76, 0.99]
Oppong 2015	52	4	20	26	0.72 [0.60, 0.82]	0.87 [0.69, 0.96]
Cizginer 2011	61	2	80	51	0.43 [0.35, 0.52]	0.96 [0.87, 1.00]
Brugge 2004	19	9	36	45	0.35 [0.22, 0.49]	0.83 [0.71, 0.92]
Pitman 2010	11	0	28	73	0.28 [0.15, 0.45]	1.00 [0.95, 1.00]
Zhang 2010	7	3	18	26	0.28 [0.12, 0.49]	0.90 [0.73, 0.98]

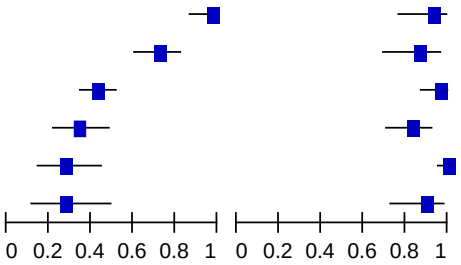


Figure 27: Summary ROC curve for EUS-FNA-based cytology for differentiating between MCNs and NMCNs of pancreas

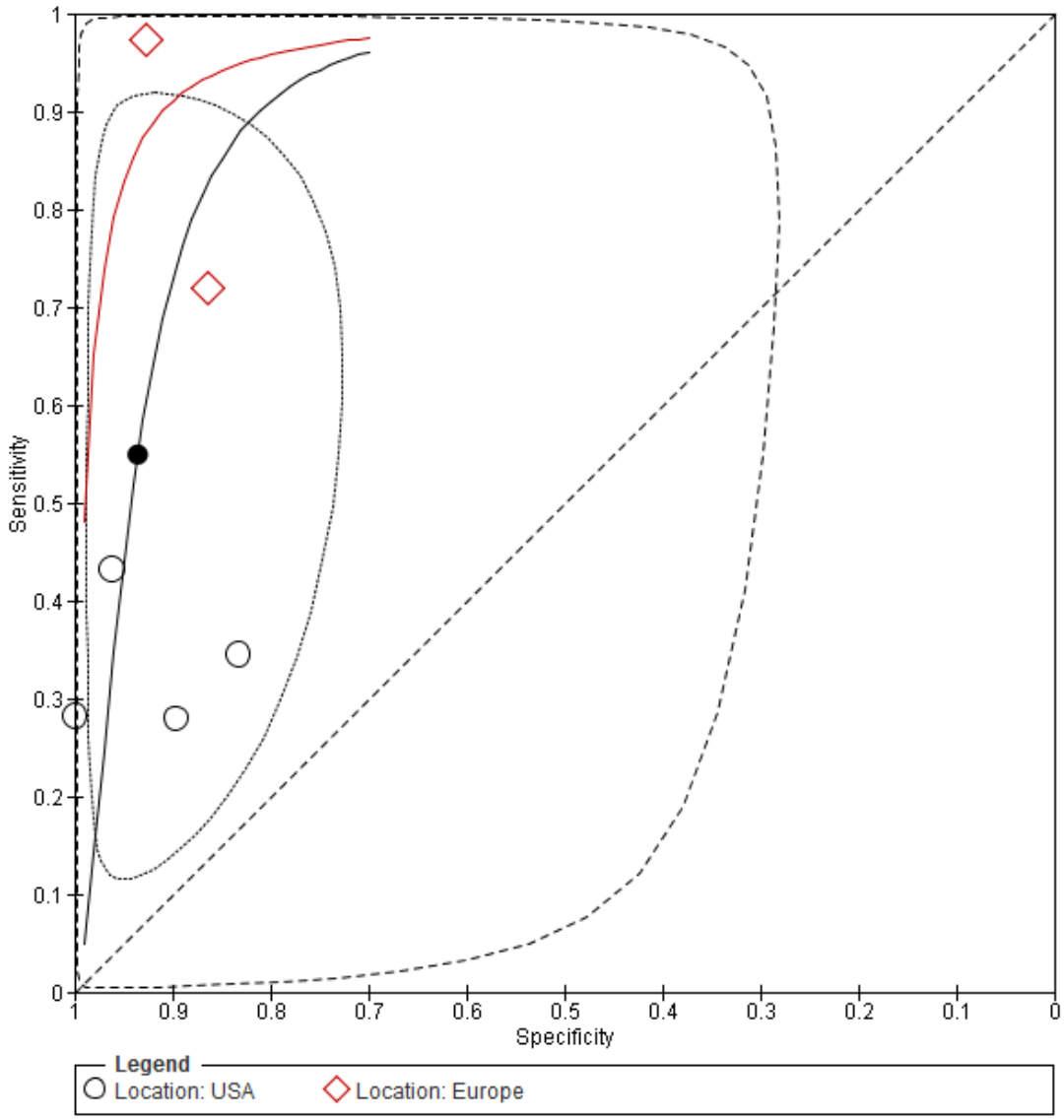


Figure 28: Forest plot for EUS-FNA-based cytology to differentiate between (potentially) malignant and benign PCLs

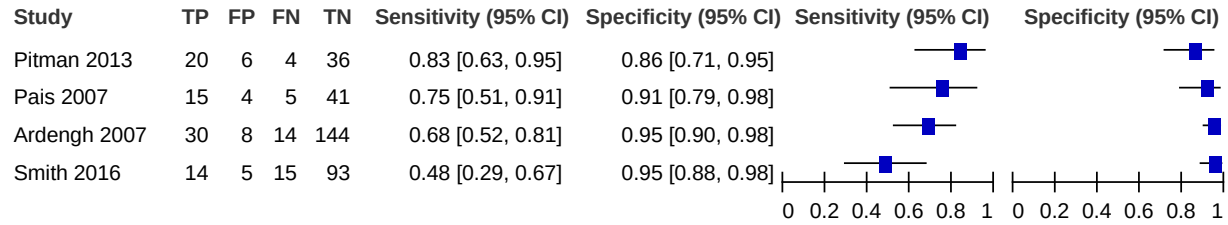


Figure 29: Summary ROC curve for EUS-FNA-based cytology to differentiate between (potentially) malignant and benign PCLs

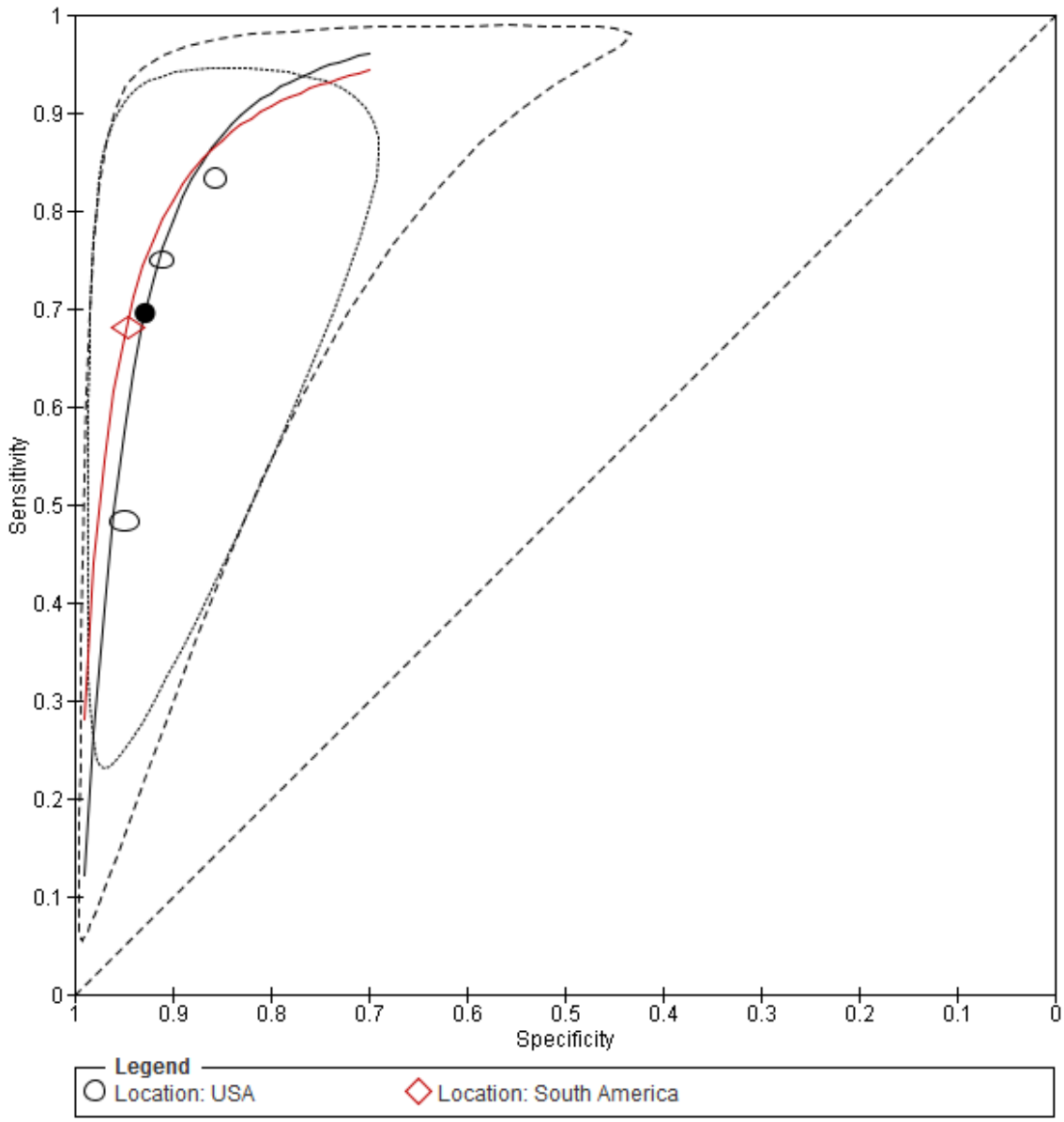


Figure 30: Forest plot for CT to differentiate between benign from (potentially) malignant PCLs

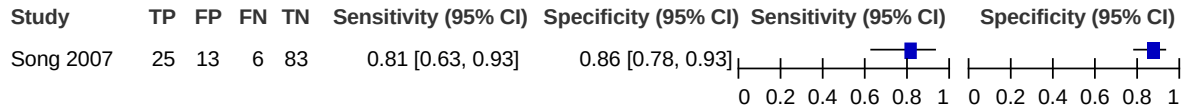


Figure 31 Forest plot for CT to differentiate between benign from (potentially) malignant PCLs

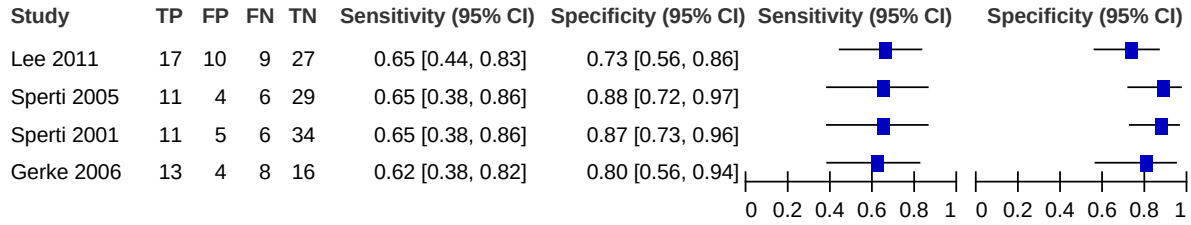


Figure 32: Summary ROC curve for CT to differentiate between MCNs and NMCNs of pancreas

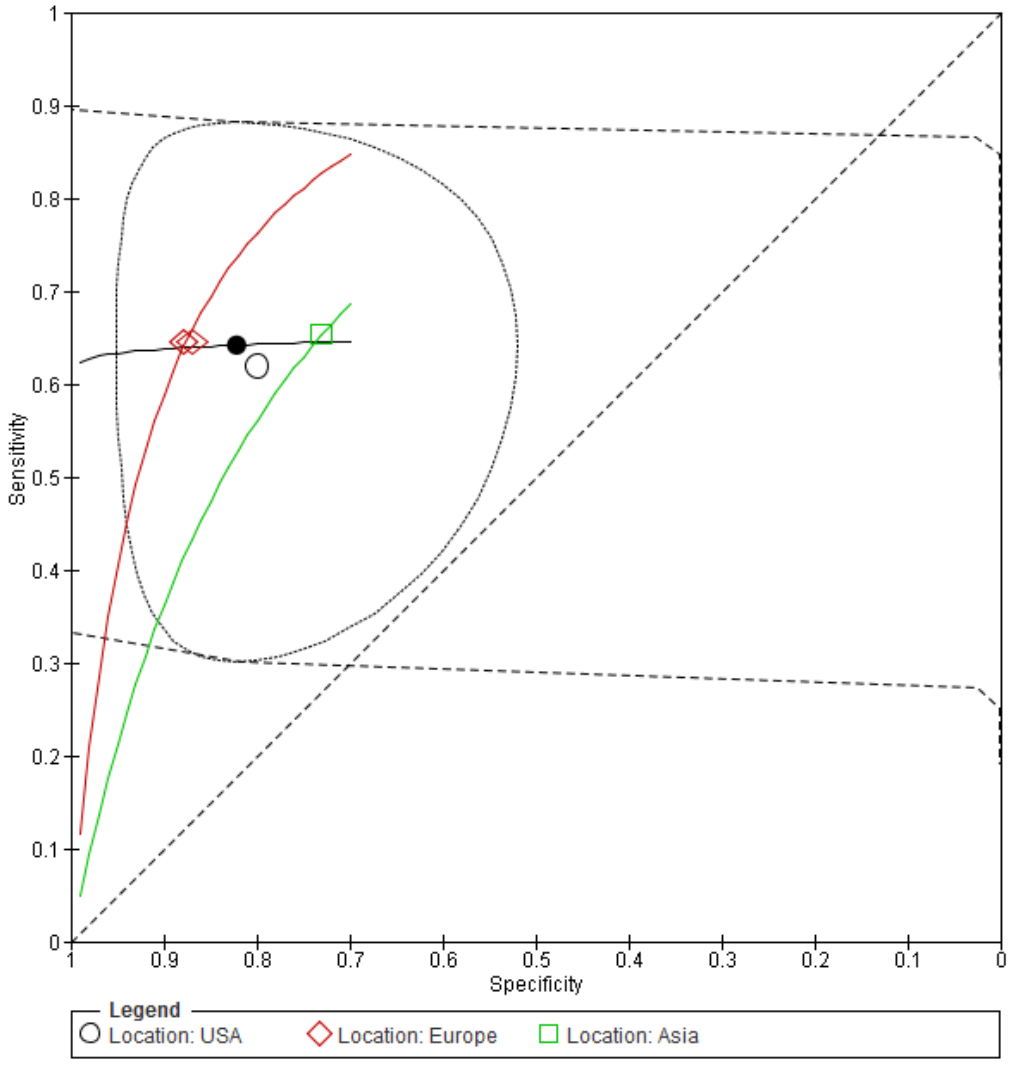


Figure 33: Forest plot for EUS to differentiate between MCNs and NMCNs of pancreas

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Oppong 2015	68	8	13	22	0.84 [0.74, 0.91]	0.73 [0.54, 0.88]
Frossard 2003	33	12	7	15	0.82 [0.67, 0.93]	0.56 [0.35, 0.75]
Brugge 2004	31	30	25	25	0.55 [0.41, 0.69]	0.45 [0.32, 0.59]
Cizginer 2011	50	10	91	43	0.35 [0.28, 0.44]	0.81 [0.68, 0.91]

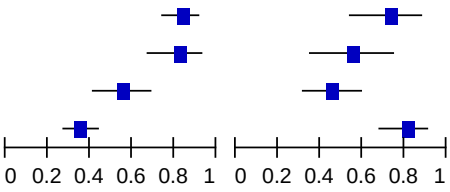


Figure 34: Summary ROC curve for EUS to differentiate between MCNs and NMCNs of pancreas

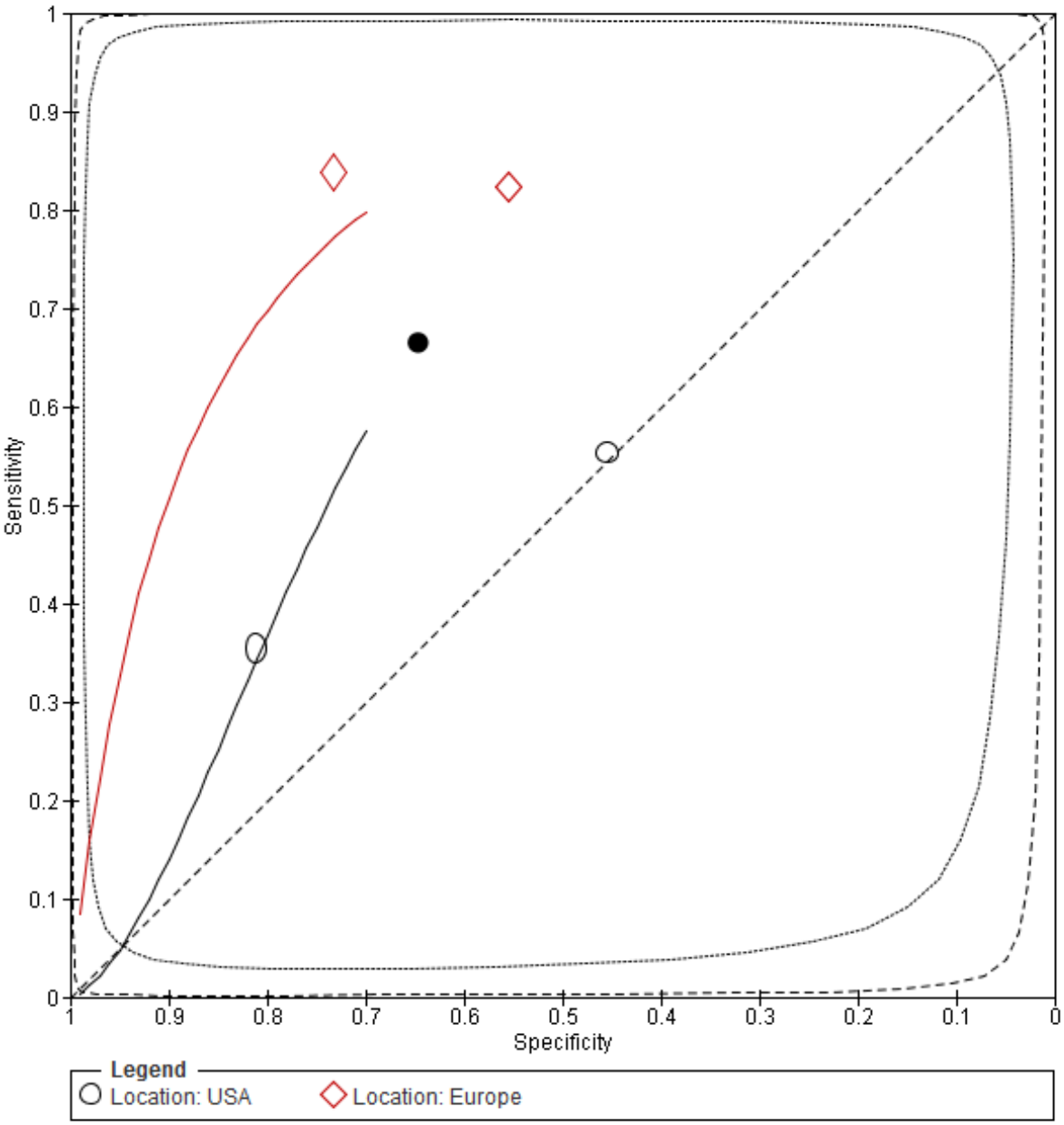


Figure 35: Forest plot for EUS to differentiate between (potentially) malignant and benign PCLs

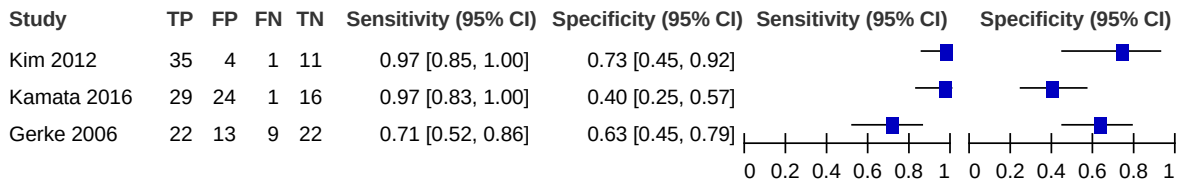


Figure 36: Forest plot for EUS-FNA to differentiate between MCNs and NMCNs of pancreas

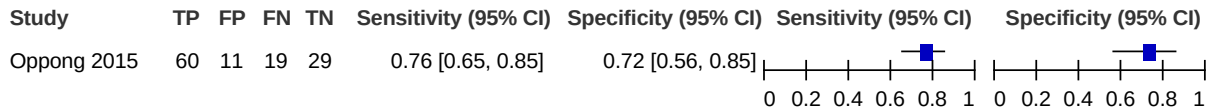


Figure 37: Forest plot for F-18 PET/CT to differentiate between (potentially) malignant and benign PCLs

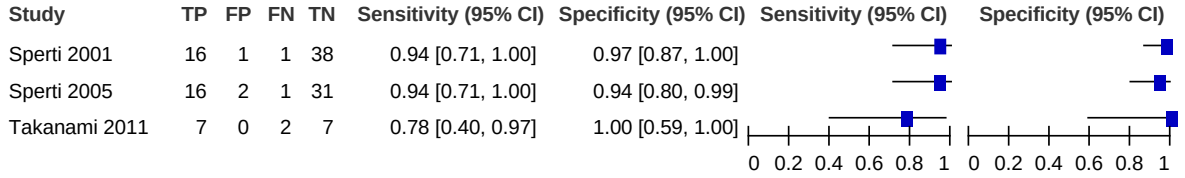


Figure 38: Forest plot for MRI differentiating between MCNs and NMCNs of pancreas

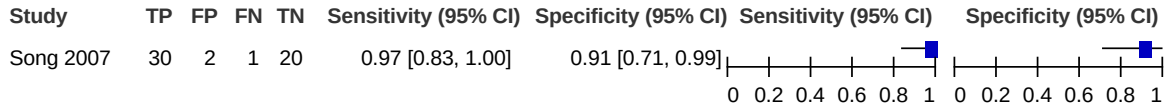


Figure 39: Forest plot for MRI differentiating between (potentially) malignant and benign PCLs

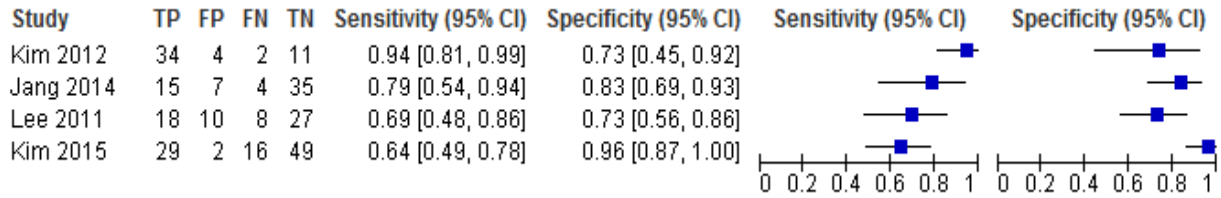
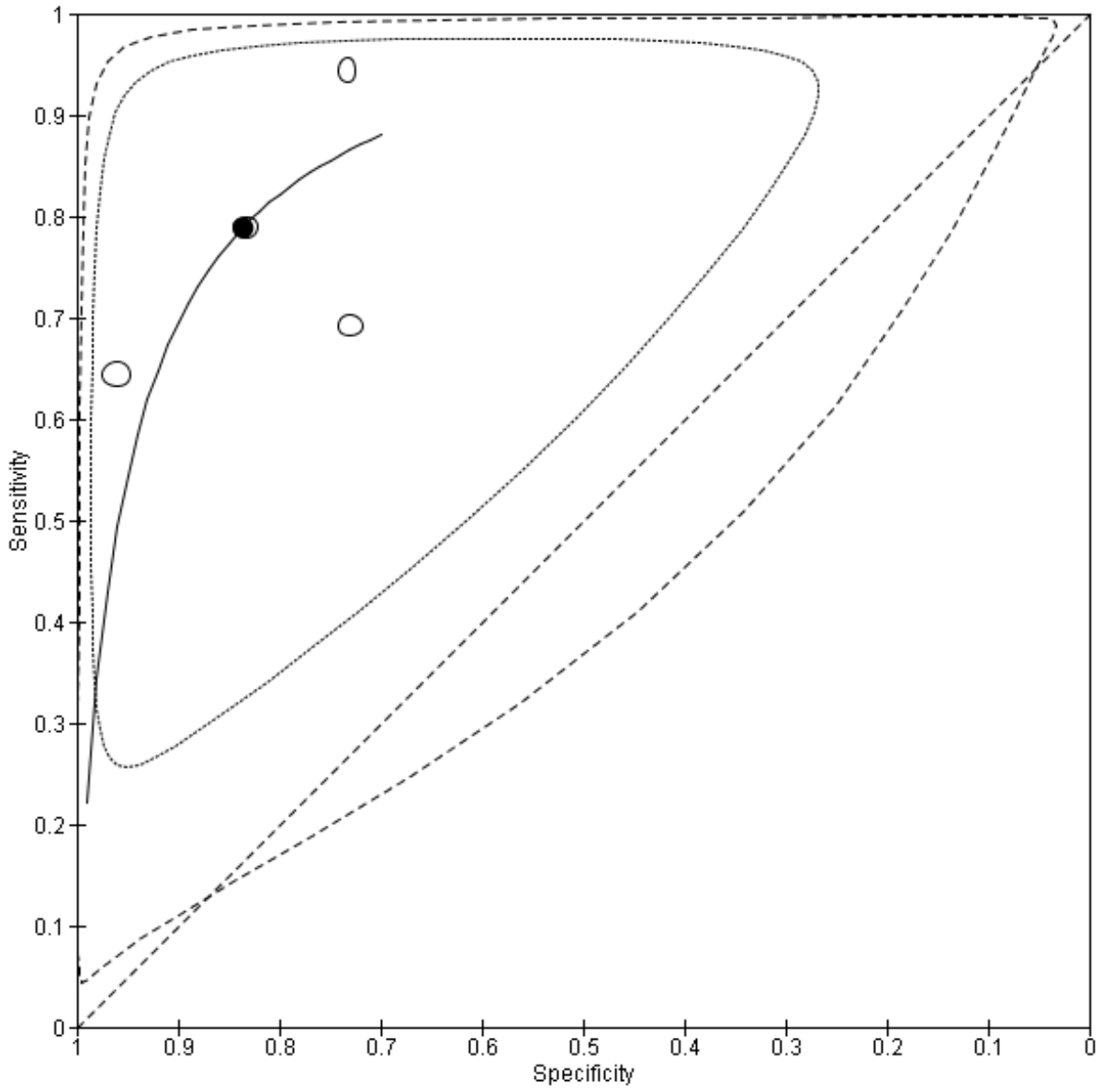
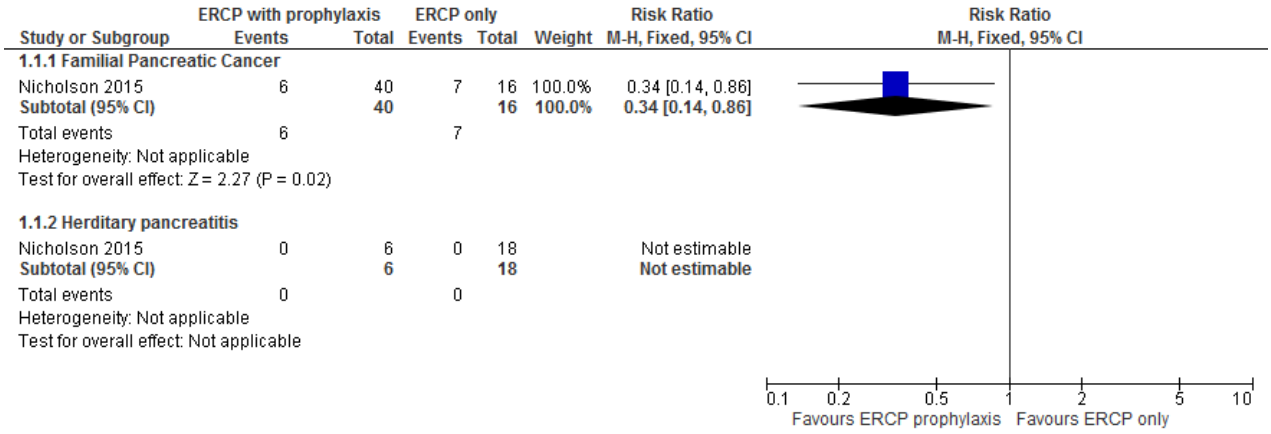


Figure 40: Summary ROC curve for MRI to differentiate between (potentially) malignant and benign PCLs



H.4 People with inherited high risk of pancreatic cancer

Figure 41: # ERCP procedures with post-ERCP pancreatitis

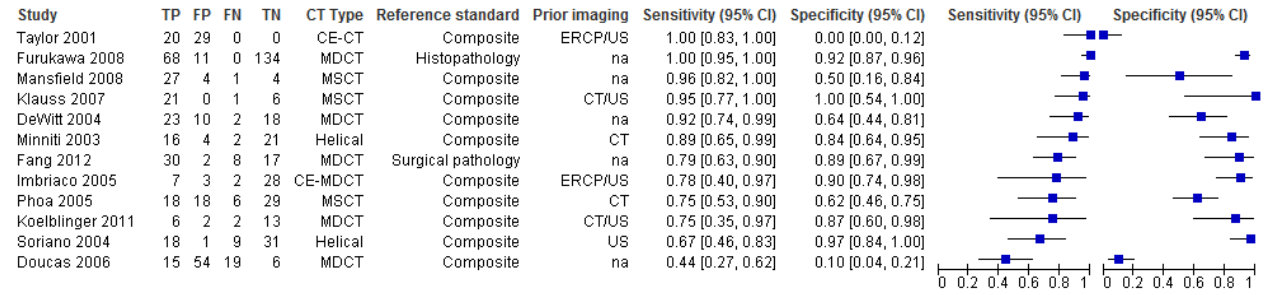


H.5 Referral to specialist multidisciplinary teams

Not applicable for this review.

H.6 Staging

Figure 42: CT for resectability - Forest plots



1 Figure 43: Other types of imaging for resectability - forest plots

CT-3D for resectability

Study	TP	FP	FN	TN	Reference standard	Prior imaging	Sensitivity (95% CI)	Specificity (95% CI)
Fang 2012	38	0	0	19	Surgical pathology	na	1.00 [0.91, 1.00]	1.00 [0.82, 1.00]

EUS for resectability

Study	TP	FP	FN	TN	Reference standard	Prior imaging	Sensitivity (95% CI)	Specificity (95% CI)
DeWitt 2004	22	9	3	19	Composite	na	0.88 [0.69, 0.97]	0.68 [0.48, 0.84]
Mansfield 2008	23	4	5	3	Composite	na	0.82 [0.63, 0.94]	0.43 [0.10, 0.82]
Soriano 2004	5	0	17	30	Composite	US	0.23 [0.08, 0.45]	1.00 [0.88, 1.00]

MRI for resectability

Study	TP	FP	FN	TN	Reference standard	Prior imaging	Sensitivity (95% CI)	Specificity (95% CI)
Koelblinger 2011	5	3	1	14	Composite	CT/US	0.83 [0.36, 1.00]	0.82 [0.57, 0.96]
Fischer 2002	12	2	5	7	Surgical pathology	CT/US	0.71 [0.44, 0.90]	0.78 [0.40, 0.97]
Soriano 2004	13	3	10	27	Composite	US	0.57 [0.34, 0.77]	0.90 [0.73, 0.98]

Abdominal US for resectability

Study	TP	FP	FN	TN	Reference standard	Prior imaging	Sensitivity (95% CI)	Specificity (95% CI)
Minniti 2003	16	6	2	19	Composite	CT	0.89 [0.65, 0.99]	0.76 [0.55, 0.91]

CT+EUS (all)

Study	TP	FP	FN	TN	Reference standard	Prior imaging	Sensitivity (95% CI)	Specificity (95% CI)
Soriano 2004	16	1	6	29	Composite	US	0.73 [0.50, 0.89]	0.97 [0.83, 1.00]

CT + EUS if CT-resectable

Study	TP	FP	FN	TN	Reference standard	Prior imaging	Sensitivity (95% CI)	Specificity (95% CI)
Soriano 2004	46	1	1	4	Composite	US	0.98 [0.89, 1.00]	0.80 [0.28, 0.99]

EUS+CT if EUS-resectable

Study	TP	FP	FN	TN	Reference standard	Prior imaging	Sensitivity (95% CI)	Specificity (95% CI)
Soriano 2004	12	1	7	32	Composite	US	0.63 [0.38, 0.84]	0.97 [0.84, 1.00]

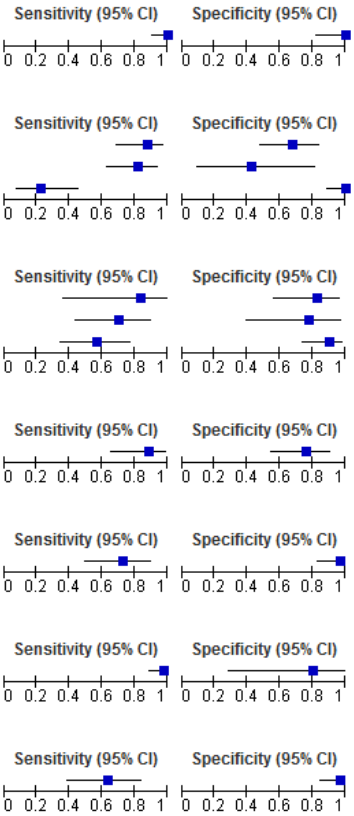


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Figure 44: CT for Resectability - Summary ROC curve

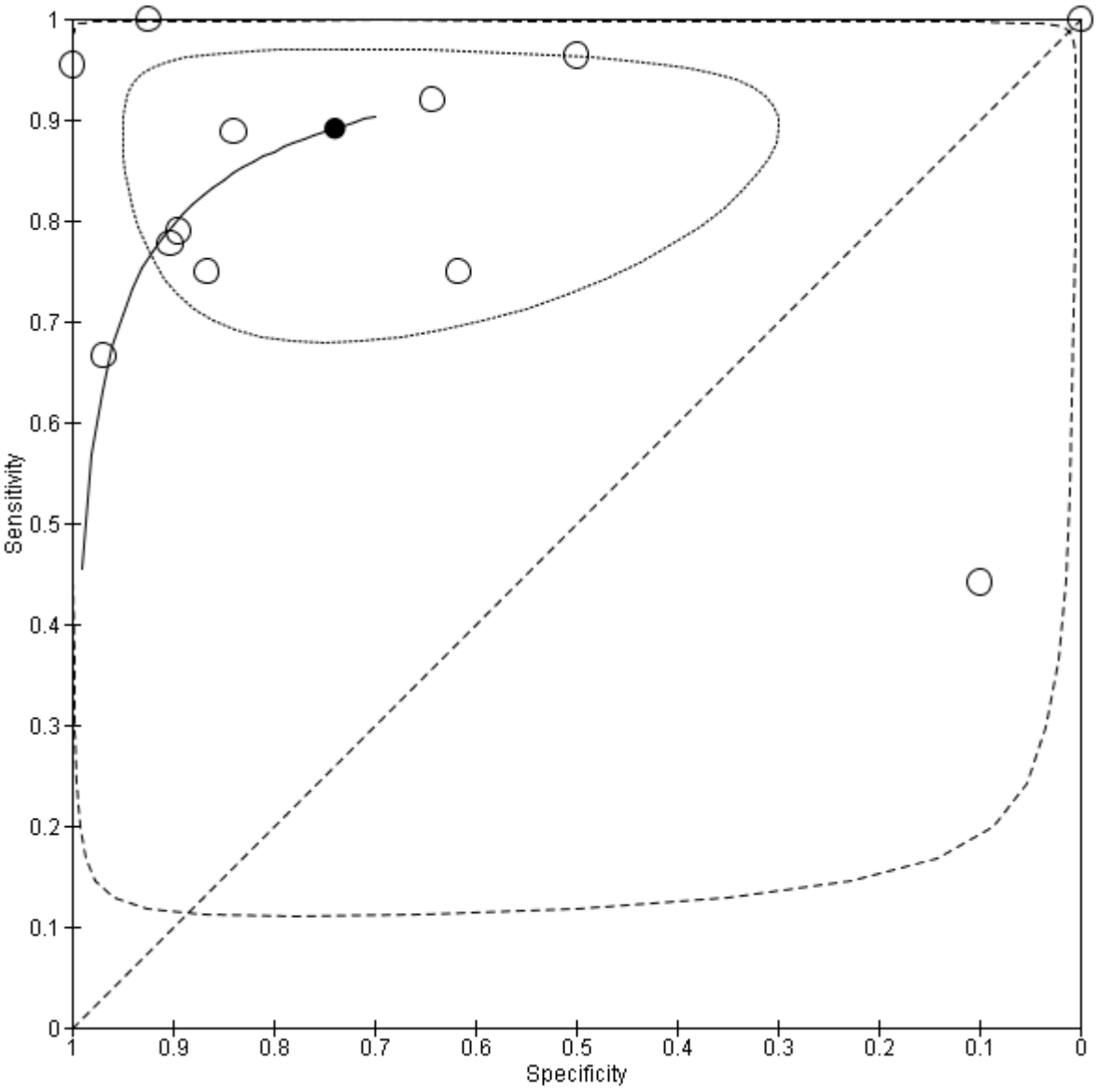


Figure 45: Laparoscopy with laparoscopic ultrasonography for resectability in patients with potentially resectable pancreatic cancer – forest plots

Study	TP	FP	FN	TN	US Type	Reference standard	Prior imaging	Sensitivity (95% CI)	Specificity (95% CI)
Shah 2008	6	2	0	9	Routine	Surgical pathology	CT	1.00 [0.54, 1.00]	0.82 [0.48, 0.98]
Taylor 2001	20	2	0	4	Doppler	Composite	CT	1.00 [0.83, 1.00]	0.67 [0.22, 0.96]
Kwon 2002	39	3	0	10	Doppler	Composite	US/CT/ERCP/EUS	1.00 [0.91, 1.00]	0.77 [0.46, 0.95]
Schacter 2000	33	4	0	30	Doppler	Laparotomy	US/CT/ERCP/EUS	1.00 [0.89, 1.00]	0.88 [0.73, 0.97]
Doucas 2006	15	21	0	28	Routine	Surgical pathology	CT	1.00 [0.78, 1.00]	0.57 [0.42, 0.71]
Fristrup 2006	38	14	0	0	Routine	Composite	CT/US	1.00 [0.91, 1.00]	0.00 [0.00, 0.23]

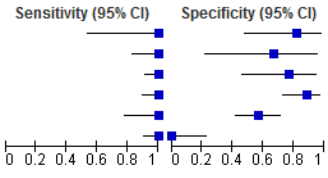


Figure 46: Laparoscopy with laparoscopic ultrasonography for resectability in patients with potentially resectable pancreatic cancer – summary ROC curve

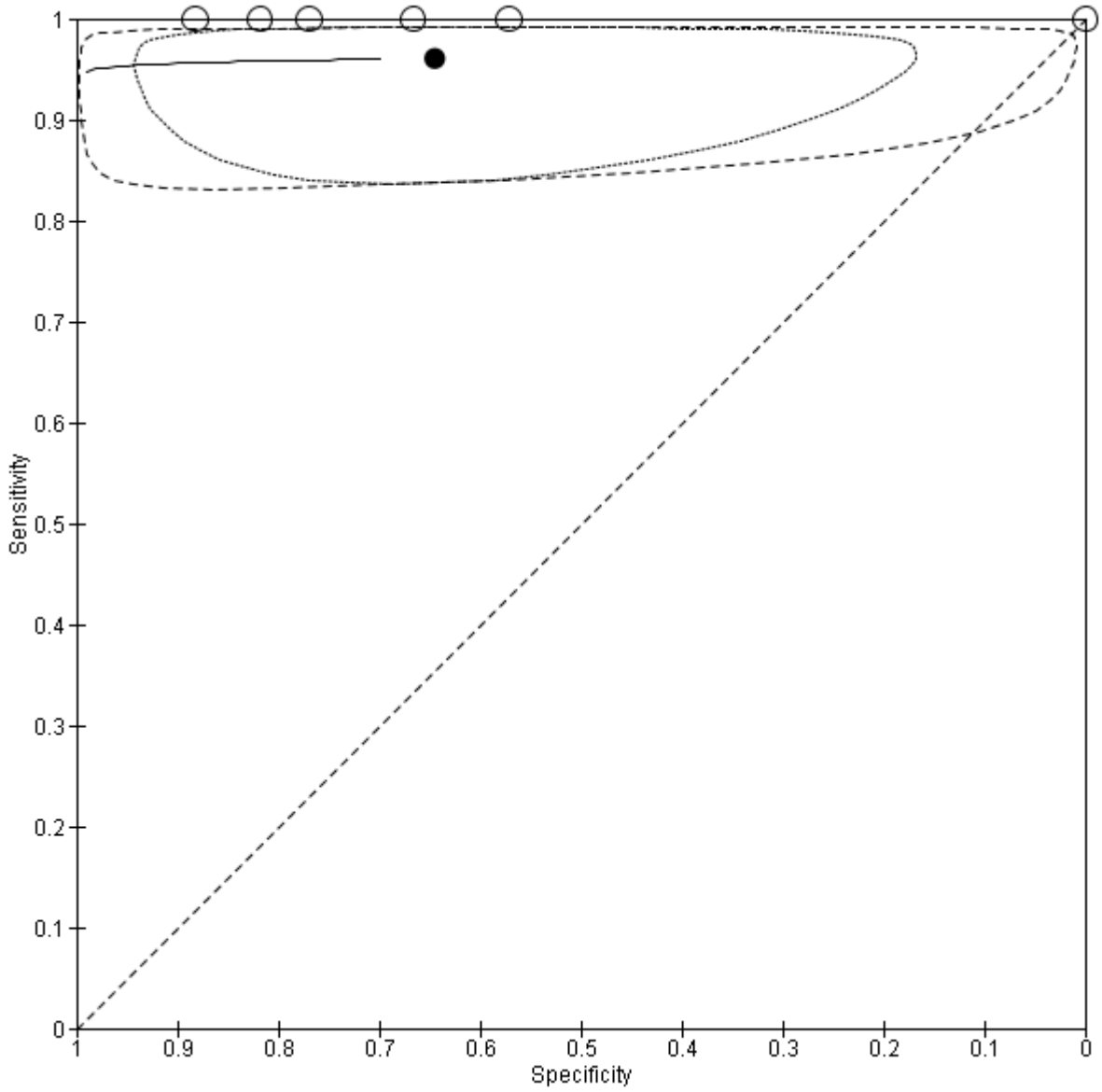


Figure 47: CT for N Staging – forest plots

Study	TP	FP	FN	TN	CT Type	Reference standard	Prior imaging	Sensitivity (95% CI)	Specificity (95% CI)
Klek 2004	10	3	3	54	Helical	Histopathology	na	0.77 [0.46, 0.95]	0.95 [0.85, 0.99]
Mansfield 2008	2	0	3	26	MSCT	Composite	na	0.40 [0.05, 0.85]	1.00 [0.87, 1.00]
Soriano 2004	9	7	15	27	Helical	Composite	US	0.38 [0.19, 0.59]	0.79 [0.62, 0.91]
Furukawa 2008	12	3	26	27	MDCT	Histopathology	na	0.32 [0.18, 0.49]	0.90 [0.73, 0.98]
DeWitt 2004	9	11	23	12	MDCT	Composite	na	0.28 [0.14, 0.47]	0.52 [0.31, 0.73]
Lemke 2004	8	4	23	12	MSCT	Composite	na	0.26 [0.12, 0.45]	0.75 [0.48, 0.93]

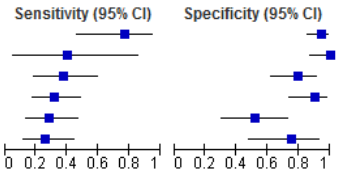


Figure 48: N Staging for other types of imaging - Forest plots

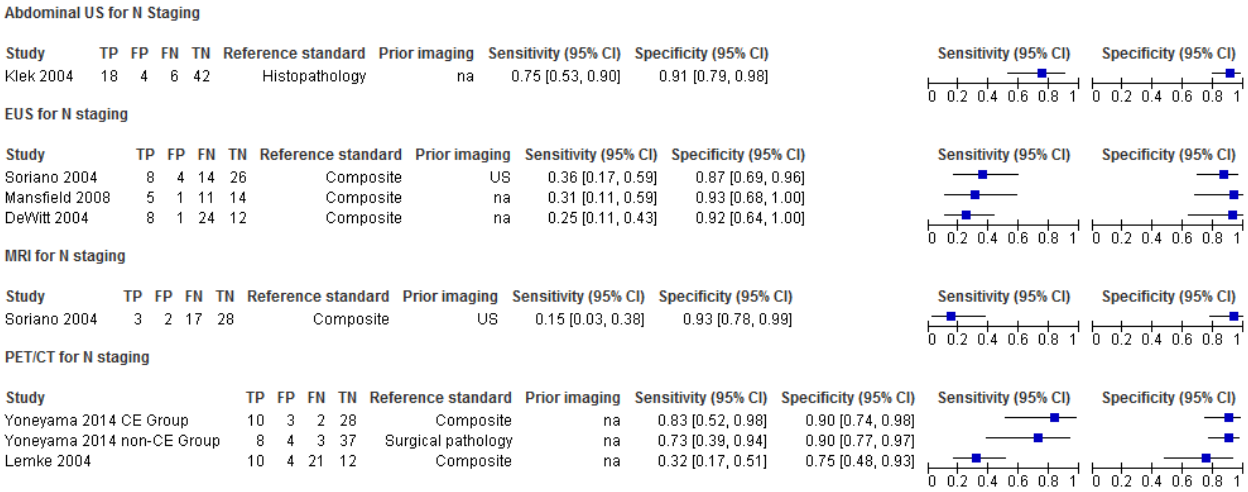


Figure 49: N Staging by number of lymph nodes - forest plot

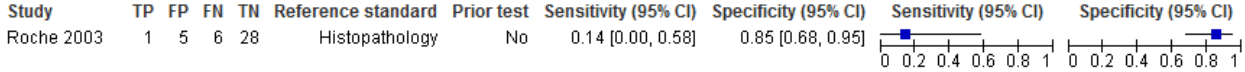
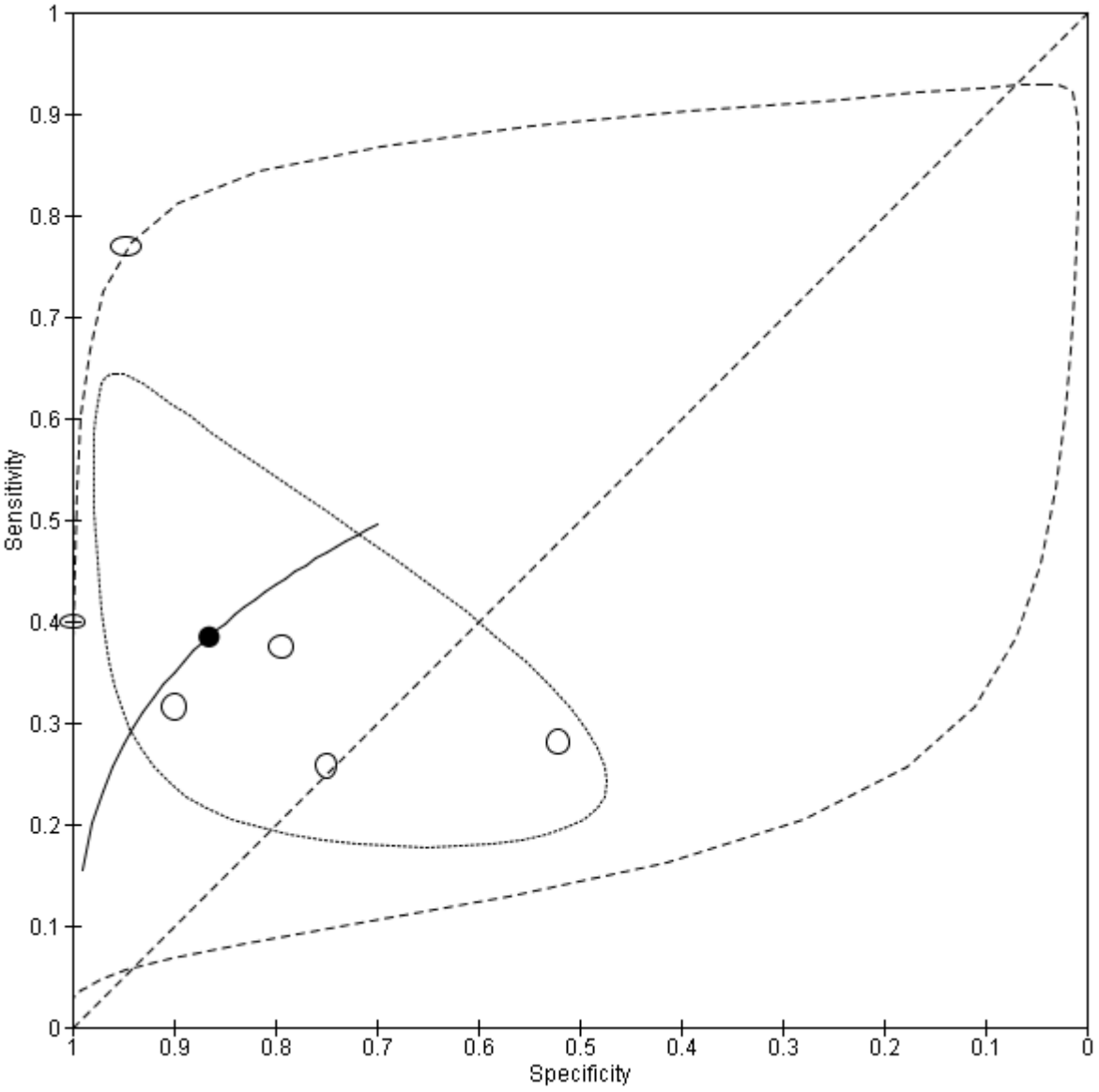


Figure 50: CT for N Staging - Summary ROC curve



1 Figure 51: M Staging - Forest plots

CT for M staging

Study	TP	FP	FN	TN	Reference standard	Prior imaging	Sensitivity (95% CI)	Specificity (95% CI)
Soriano 2004	6	2	5	46	Composite	US	0.55 [0.23, 0.83]	0.96 [0.86, 0.99]
Farma 2008	13	5	10	54	Composite	na	0.57 [0.34, 0.77]	0.92 [0.81, 0.97]

EUS for M staging

Study	TP	FP	FN	TN	Reference standard	Prior imaging	Sensitivity (95% CI)	Specificity (95% CI)
Soriano 2004	0	0	8	44	Composite	US	0.00 [0.00, 0.37]	1.00 [0.92, 1.00]

MRI for M staging

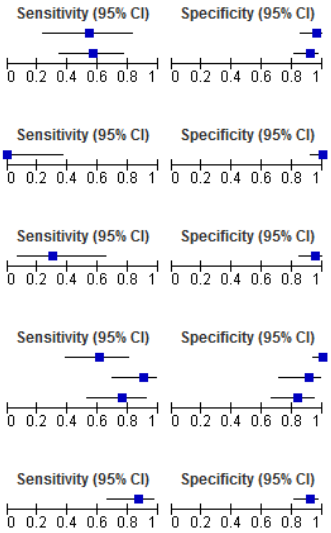
Study	TP	FP	FN	TN	Reference standard	Prior imaging	Sensitivity (95% CI)	Specificity (95% CI)
Soriano 2004	3	2	7	41	Composite	US	0.30 [0.07, 0.65]	0.95 [0.84, 0.99]

PET/CT for M Staging

Study	TP	FP	FN	TN	Reference standard	Prior imaging	Sensitivity (95% CI)	Specificity (95% CI)
Farma 2008	14	0	9	59	Composite	na	0.61 [0.39, 0.80]	1.00 [0.94, 1.00]
Yoneyama 2014 CE Group	19	2	2	20	Composite	na	0.90 [0.70, 0.99]	0.91 [0.71, 0.99]
Yoneyama 2014 non-CE Group	16	5	5	26	Surgical pathology	na	0.76 [0.53, 0.92]	0.84 [0.66, 0.95]

CT + PET/CT for M Staging

Study	TP	FP	FN	TN	Reference standard	Prior imaging	Sensitivity (95% CI)	Specificity (95% CI)
Farma 2008	20	5	3	54	Composite	na	0.87 [0.66, 0.97]	0.92 [0.81, 0.97]



2

3 Figure 52: Vascular invasion - forest plots

CT for vascular invasion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Klauss 2007	7	2	1	18	0.88 [0.47, 1.00]	0.90 [0.68, 0.99]
Tellez-Avila 2012	10	2	8	30	0.56 [0.31, 0.78]	0.94 [0.79, 0.99]
Soriano 2004	16	2	8	33	0.67 [0.45, 0.84]	0.94 [0.81, 0.99]
Klek 2004	51	3	5	67	0.91 [0.80, 0.97]	0.96 [0.88, 0.99]
Lemke 2004	21	0	23	3	0.48 [0.32, 0.63]	1.00 [0.29, 1.00]

EUS for vascular invasion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Tellez-Avila 2012	11	3	7	27	0.61 [0.36, 0.83]	0.90 [0.73, 0.98]
Soriano 2004	8	1	11	32	0.42 [0.20, 0.67]	0.97 [0.84, 1.00]

MRI for vascular invasion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Soriano 2004	13	5	9	26	0.59 [0.36, 0.79]	0.84 [0.66, 0.95]

Abdominal US for vascular invasion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Klek 2004	50	3	5	68	0.91 [0.80, 0.97]	0.96 [0.88, 0.99]

PET/CT for vascular invasion

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Lemke 2004	30	1	14	2	0.68 [0.52, 0.81]	0.67 [0.09, 0.99]

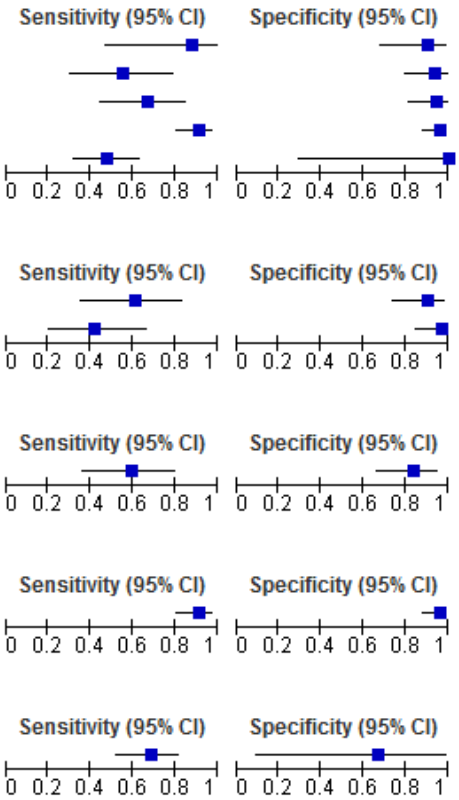


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Figure 53: CT for vascular invasion - Summary ROC curve

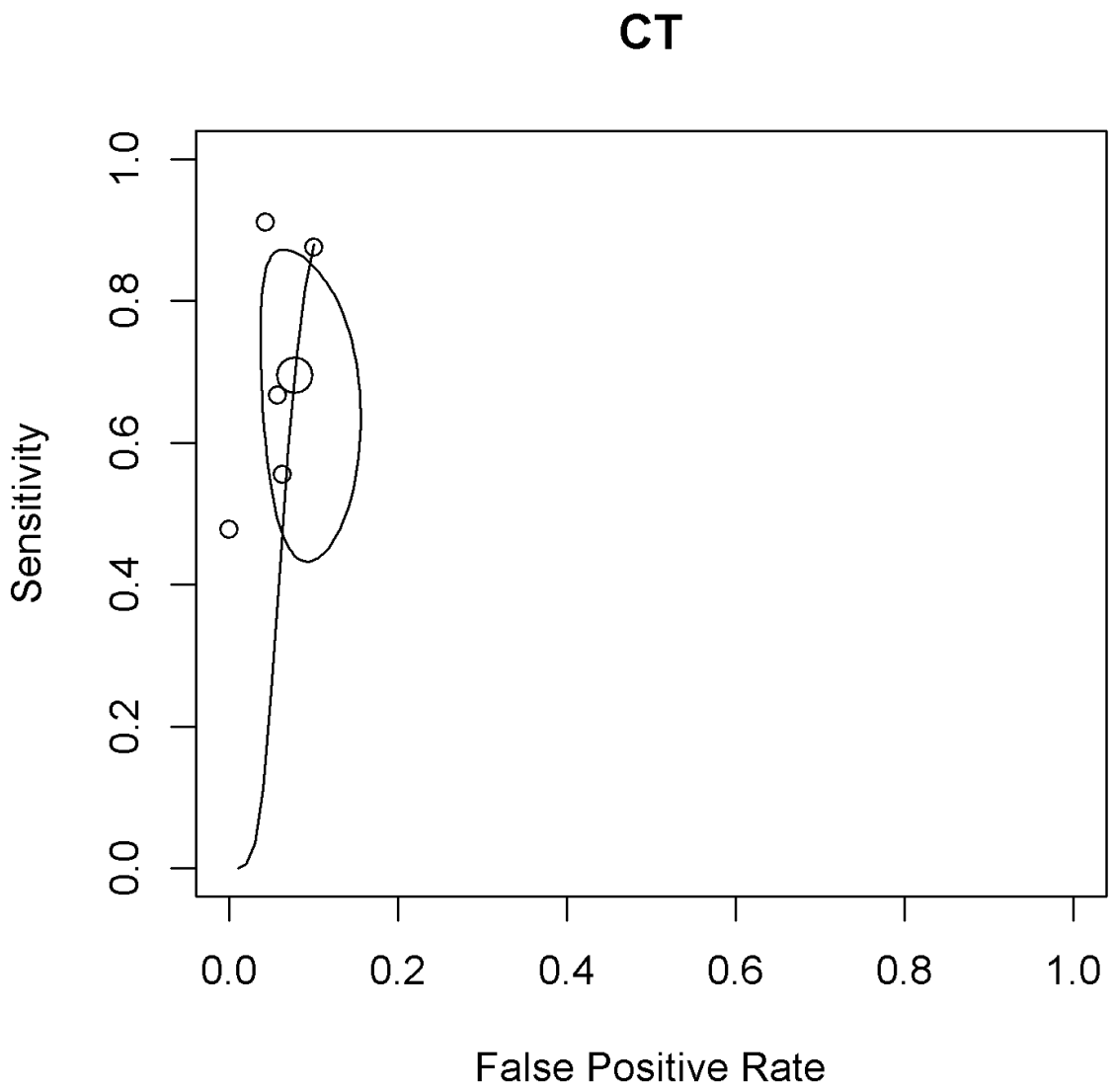
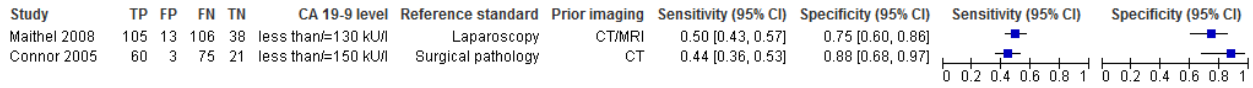


Figure 54: CA 19-9 for improving staging laparoscopy – forest plots



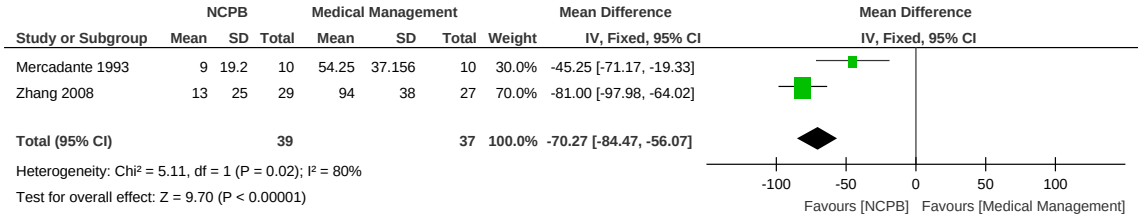
H.76 Psychological support needs

Not applicable for this review.

H.8 1 Pain

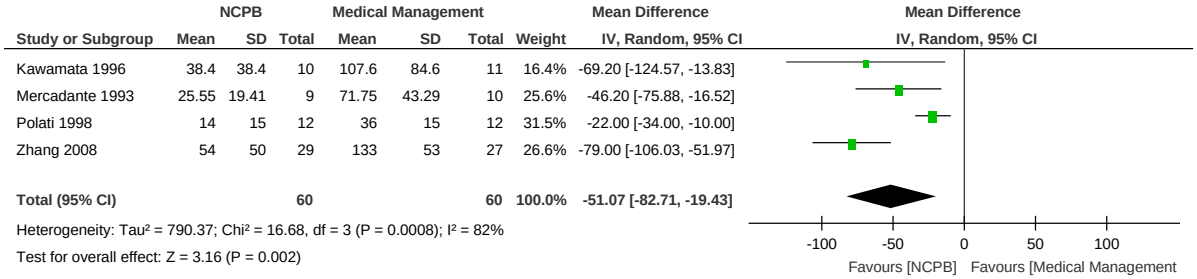
H.8.1 2 NCPB versus medical management alone

3 Figure 55: Opioid use at 2 weeks



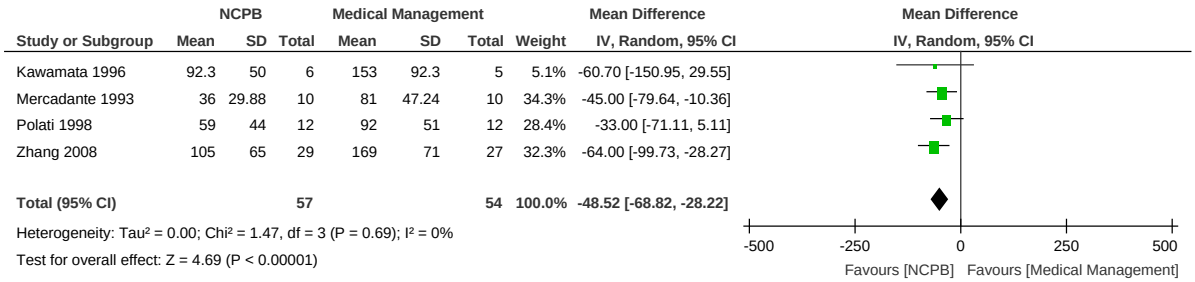
4

5 Figure 56: Opioid use at 4 weeks



6

7 Figure 57: Opioid use the day before to death



8

Figure 58: Percentage change in analgesic medications use and 3 months

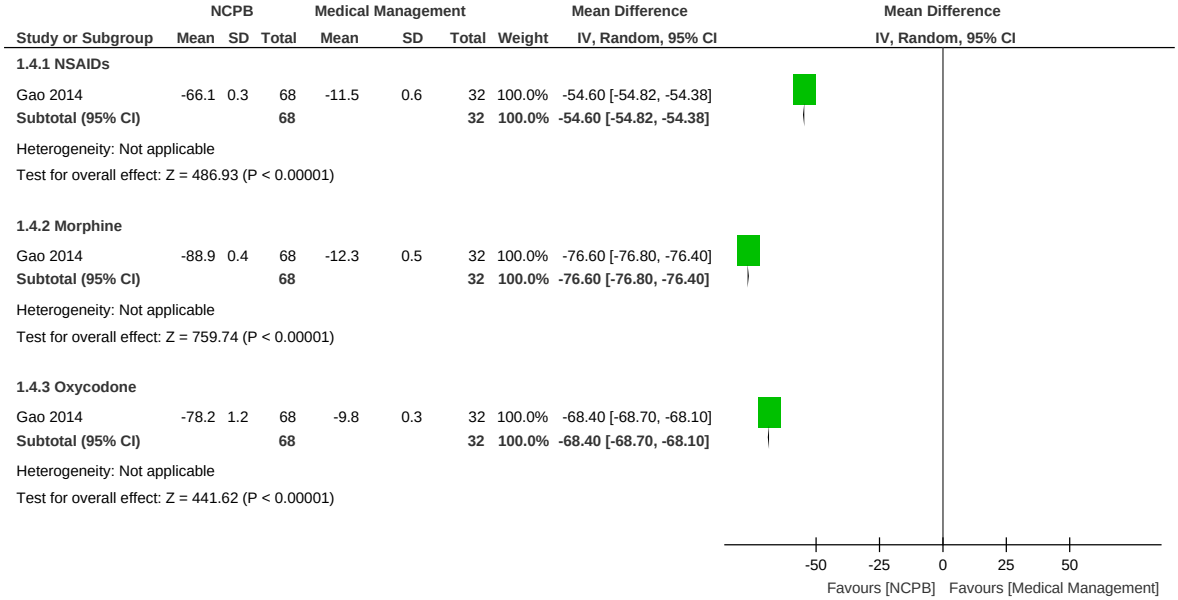


Figure 59: Reduction in opioid medication: Absolute change in morphine use at 1 and 3 months

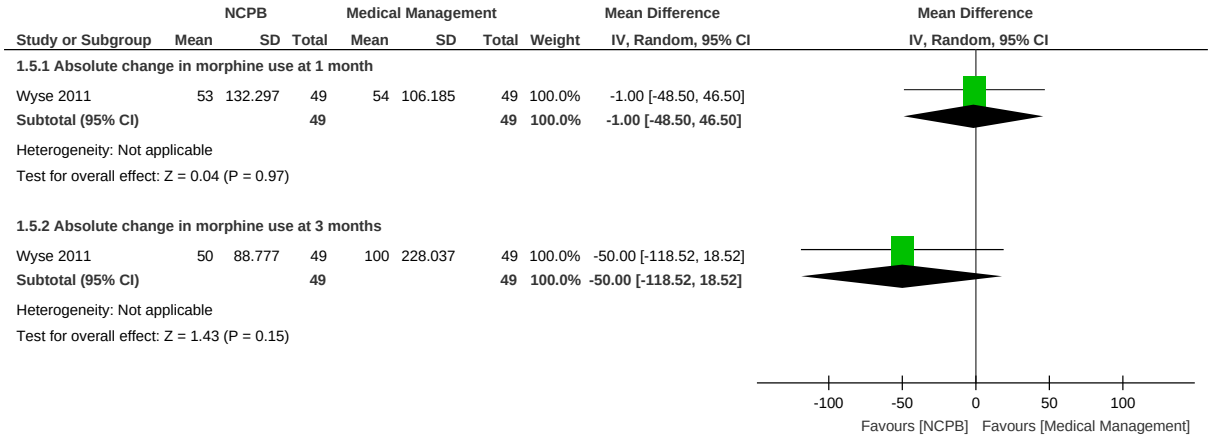


Figure 60: Pain scores at 2 weeks

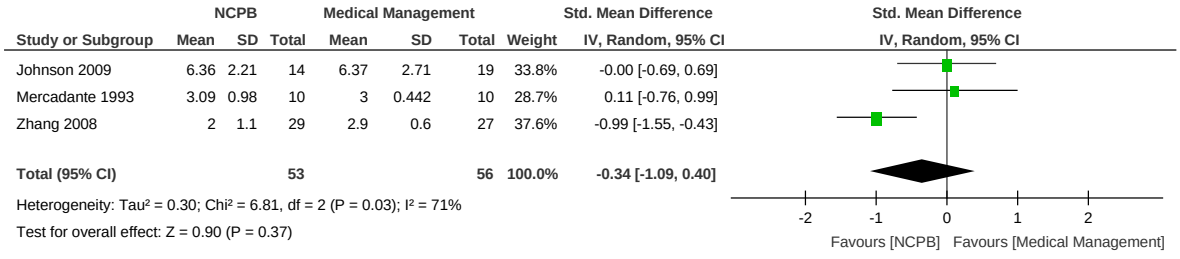


Figure 61: Pain scores at 4 weeks

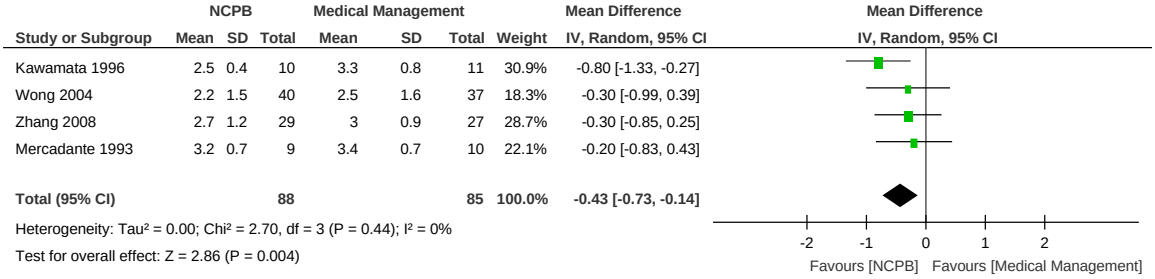


Figure 62: Pain scores at 8 weeks

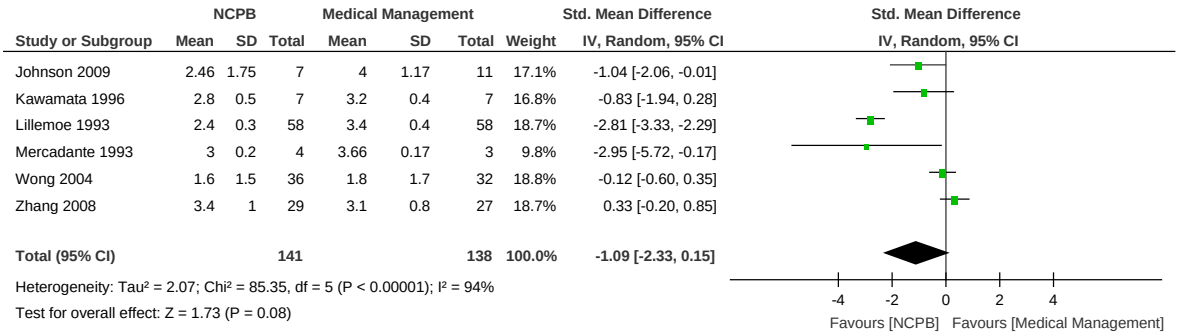


Figure 63: Patients reporting effective pain management at 2 and 8 weeks

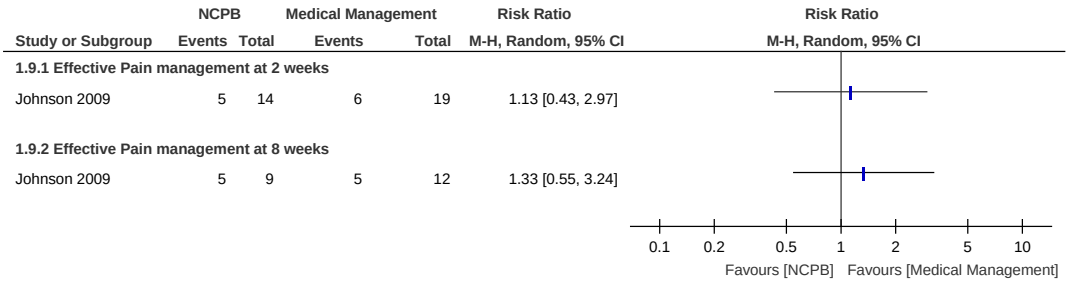


Figure 64: Absolute Change in Pain score at 1 and 3 months

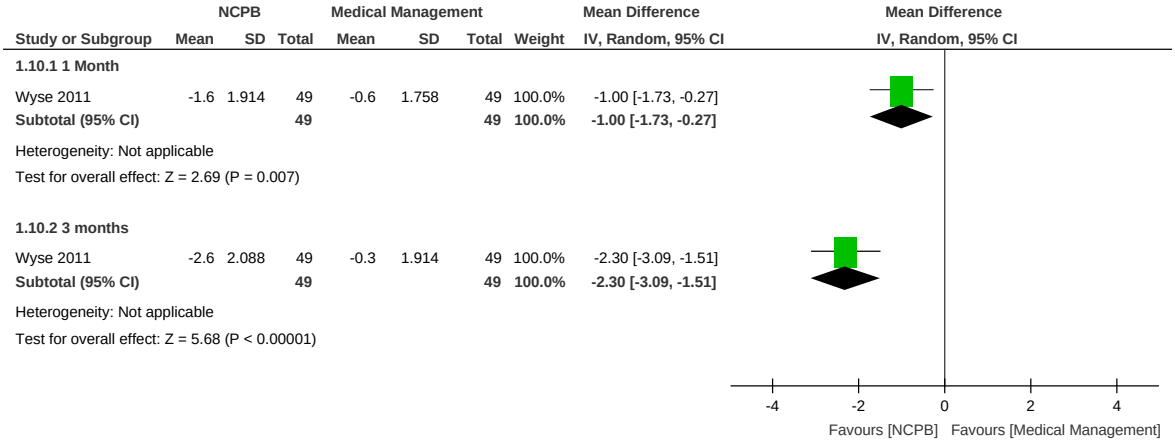


Figure 65: Adverse effects – constipation

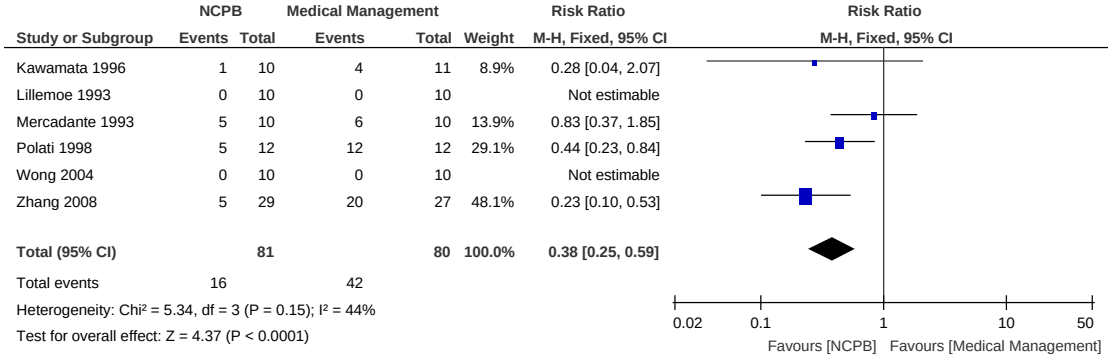


Figure 66: Adverse effects: diarrhoea

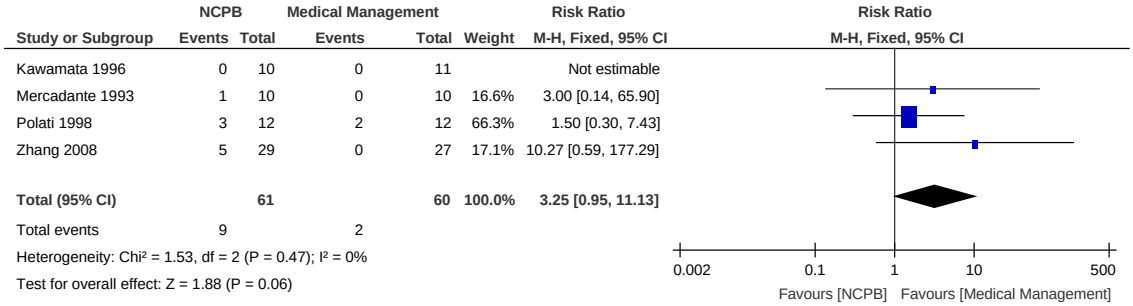


Figure 67: QOL scores (as interference with appetite, sleep, communication) at 1 month

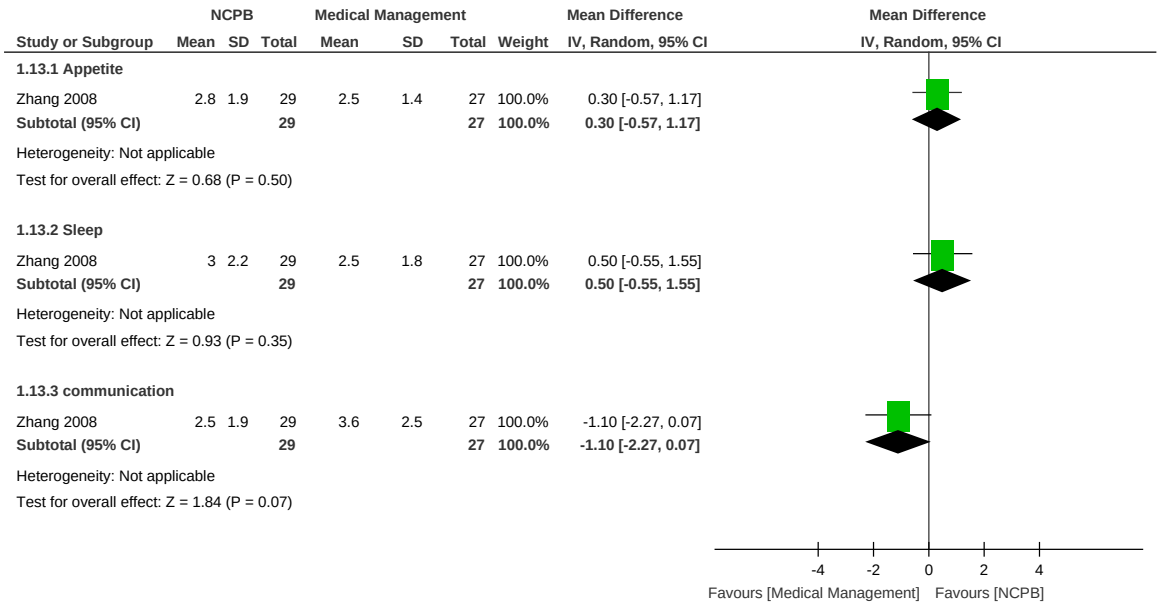


Figure 68: QOL scores (as interference with appetite, sleep, communication) 3 months

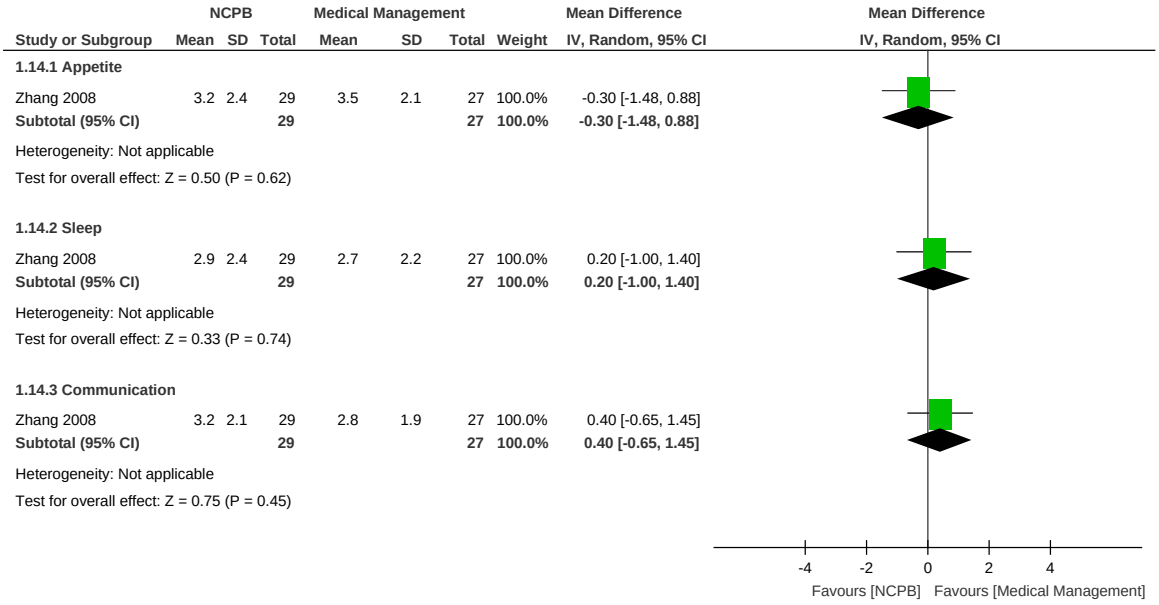


Figure 69: QOL scores (Functional scales: physical; role; emotional; cognitive and social) at 3 months

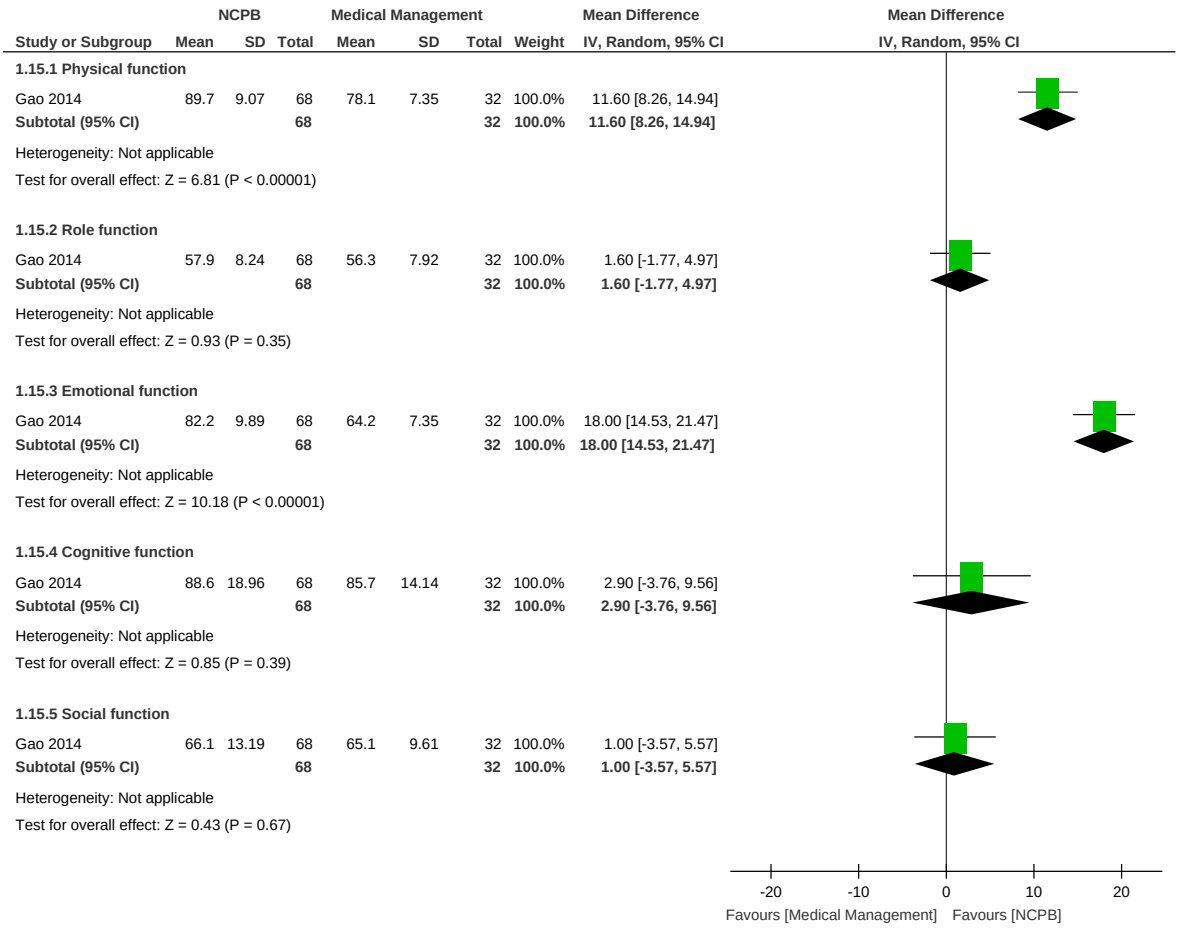


Figure 70: QOL scores - Digestive Disease questionnaire-15: Percentage change at 1 and 3 months

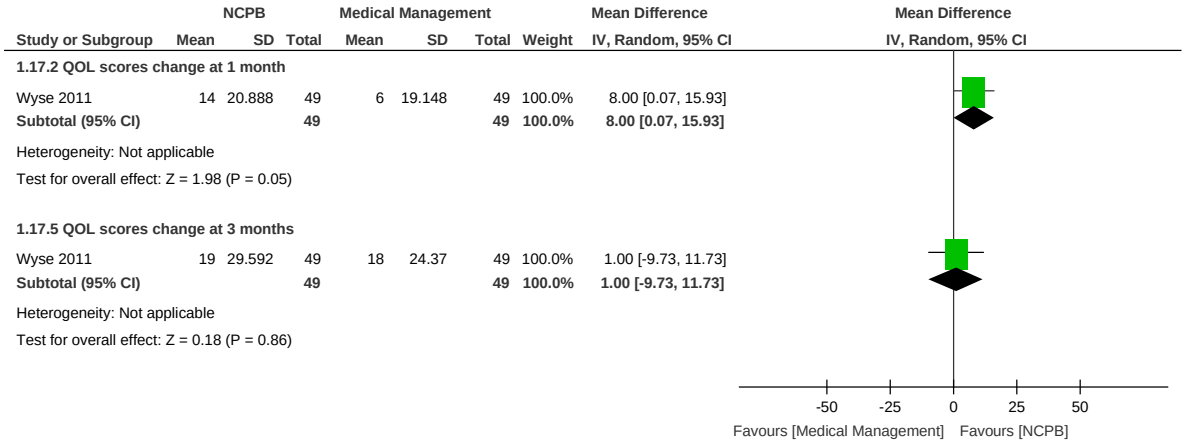


Figure 71: QOL scores – Global quality of life at 3 month

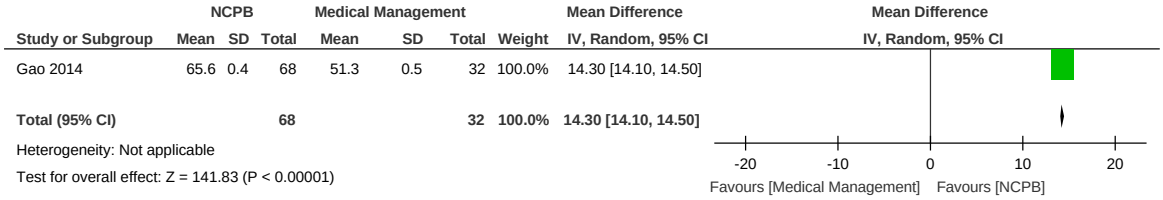


Figure 72: QOL scores – Symptom (Fatigue; Nausea/vomiting; Pain; Dyspnea; Insomnia; Appetite loss; Constipation and financial difficulties) at 3 months

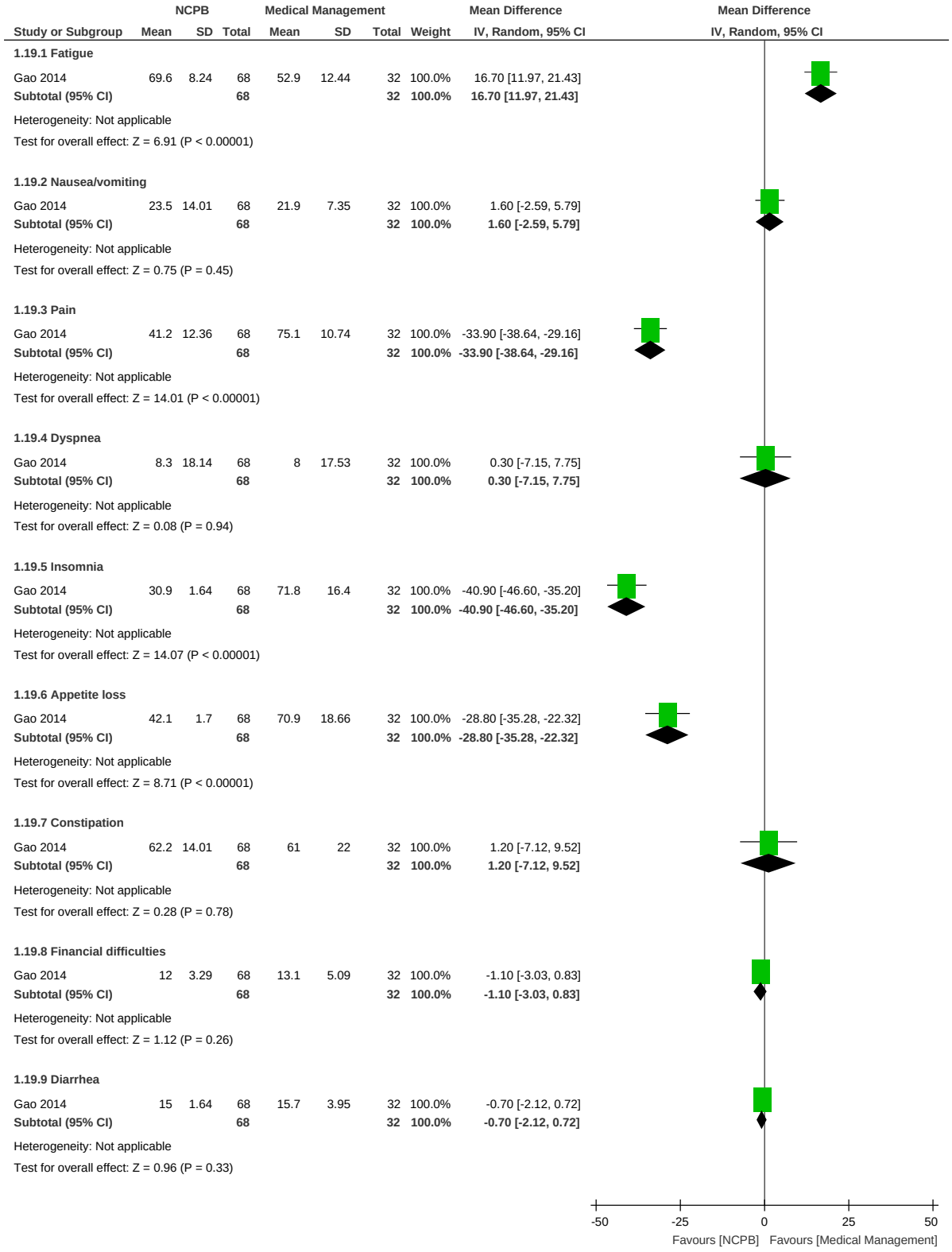
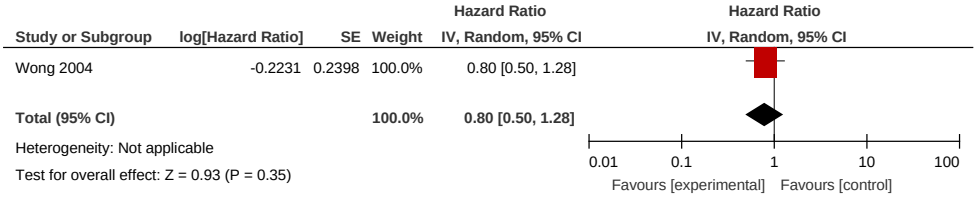


Figure 73: Overall survival



H.8.23 Early NCPB versus late NCPB

Figure 74: Oral morphine use at 16 and 24 weeks follow-up

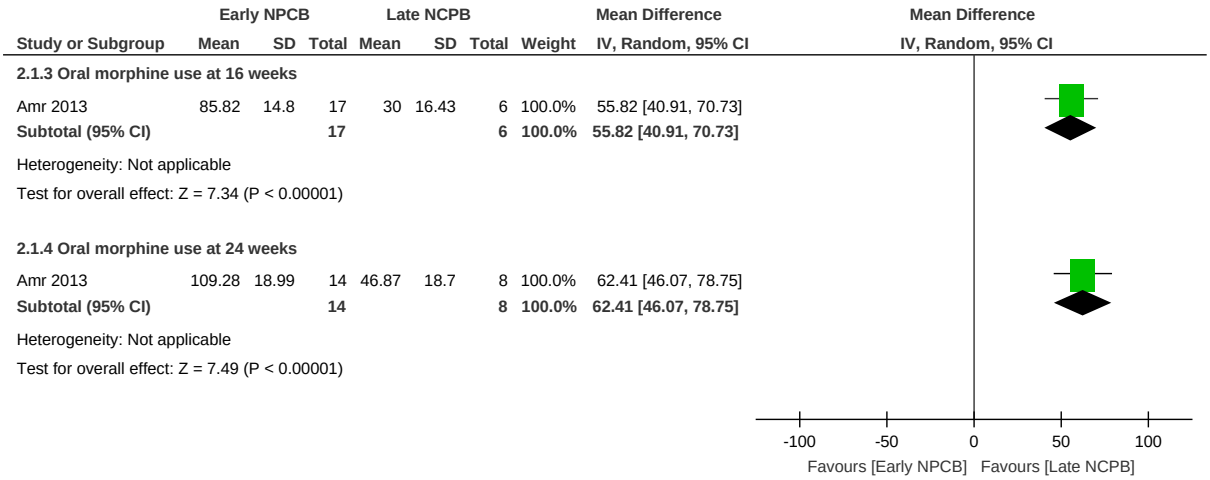


Figure 75: Oral Tramodol Hydrochloride use at 16 and 24 weeks follow-up.

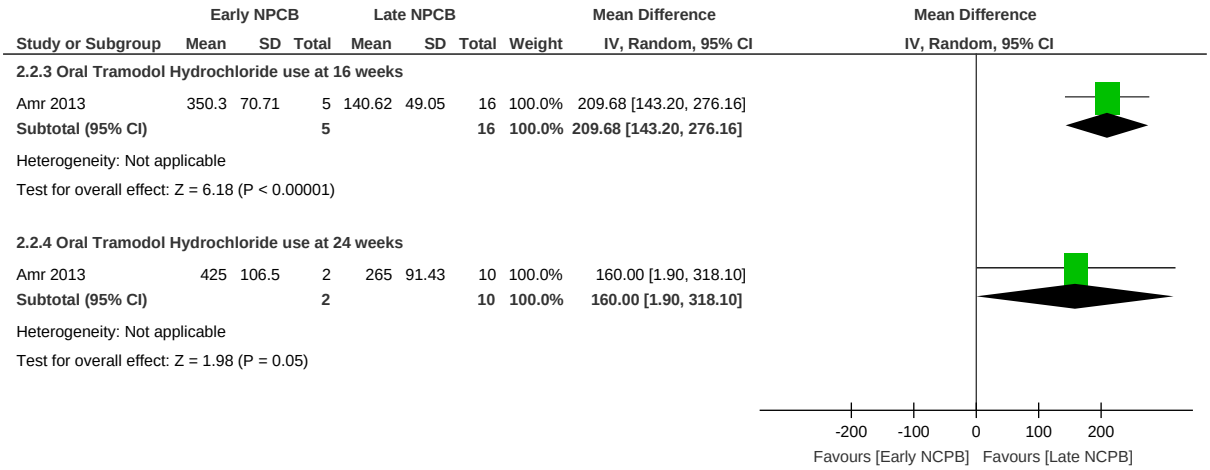


Figure 76: Pain scores at 16 and 24 weeks follow-up.

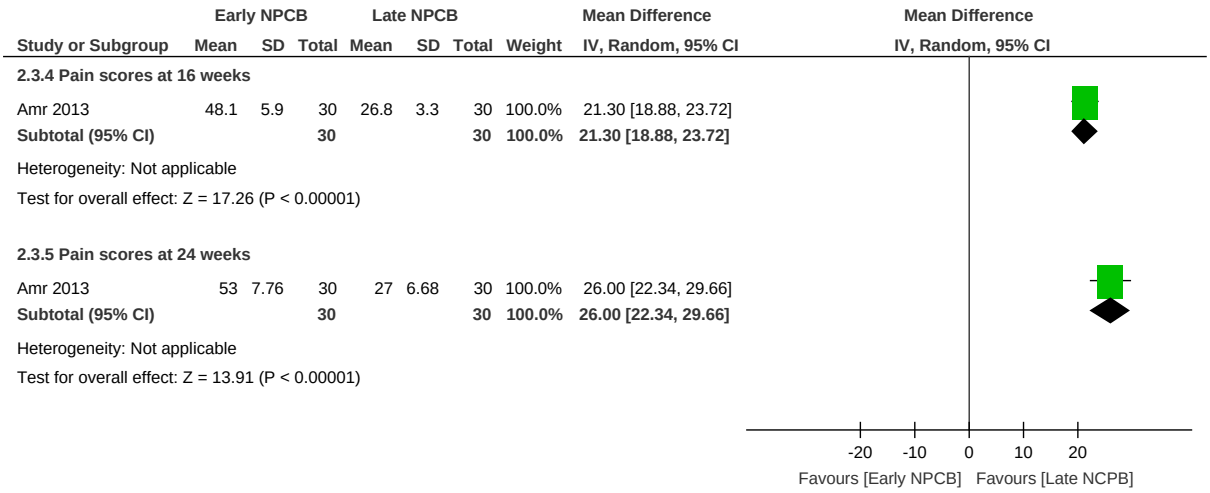
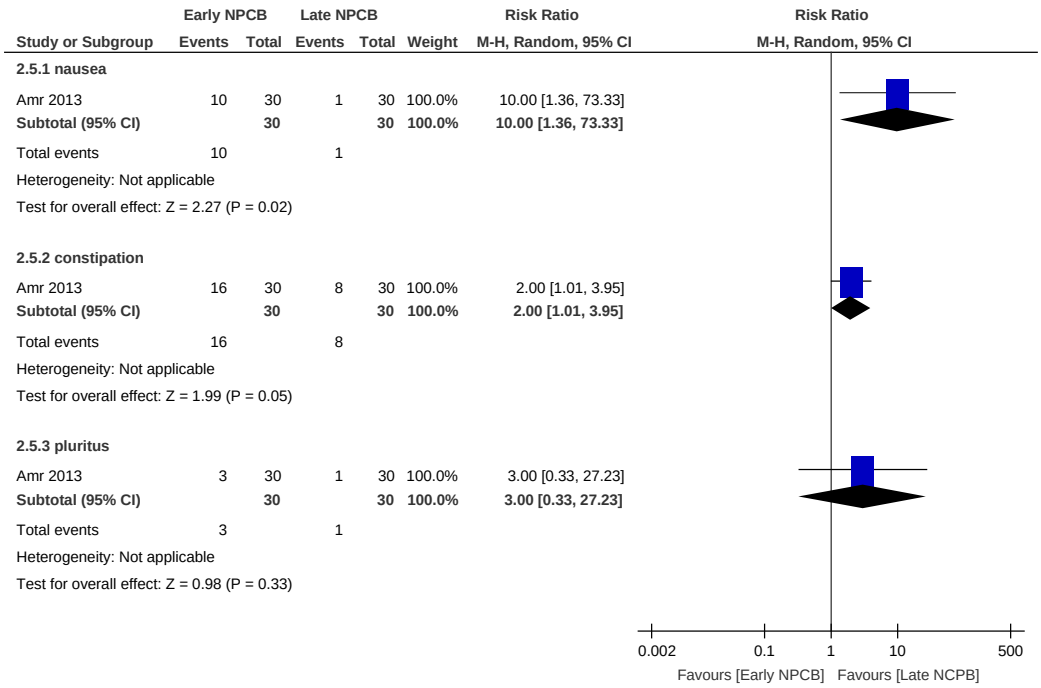


Figure 77: Adverse effects - nausea, constipation, pluritus



H.8.3 NCPB plus medical management versus thoracic splanchnicectomy plus medical management

Figure 78: Pain scores at 2 and 8 weeks

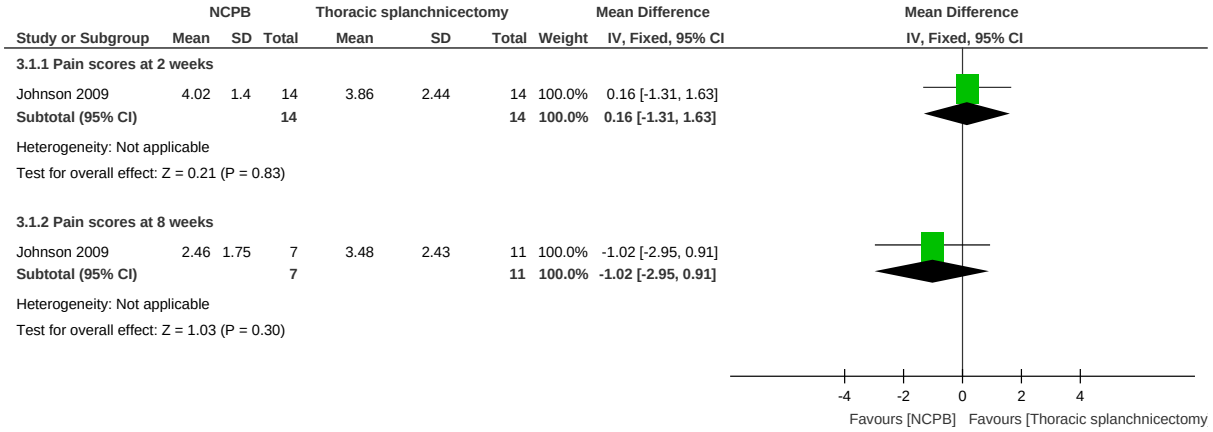
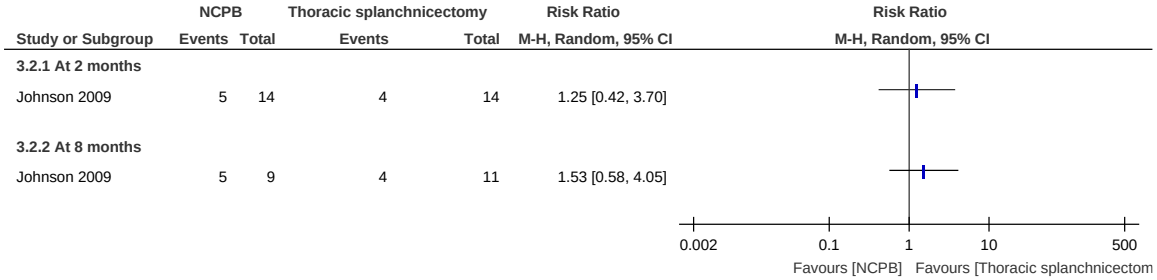


Figure 79: Patients reporting effective pain management at 2 and 8 weeks



H.8.4 Thoracic splanchnicectomy + medical management versus medical management alone

Figure 80: Pain scores at 2 and 8 weeks

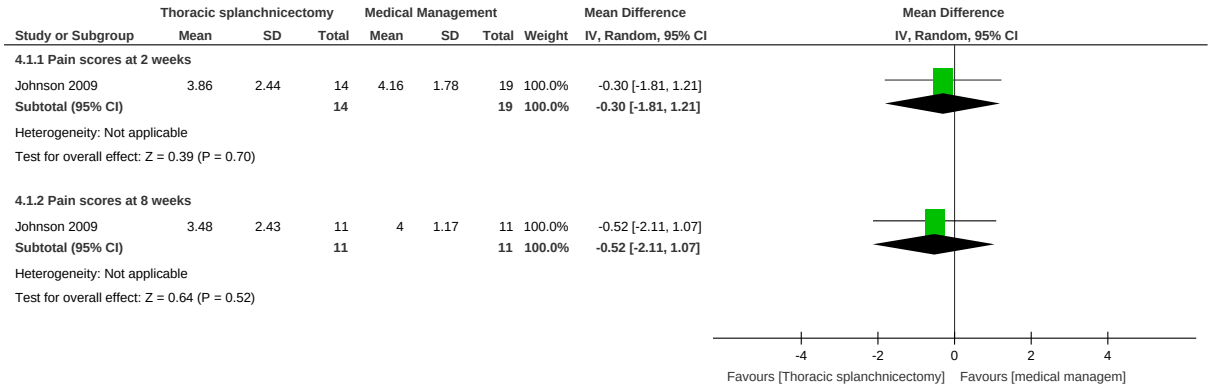
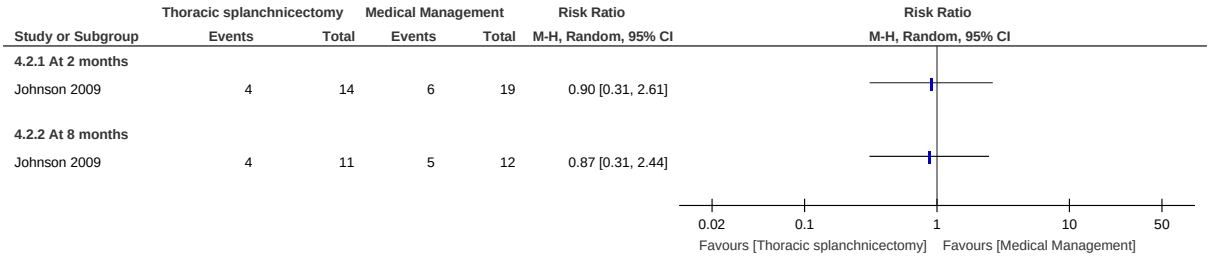


Figure 81: Patients reporting effective pain management at 2 and 8 weeks



H.8.5 EUS- guided NCPB: 1 injection versus EUS- guided NCPB: 2 injections

Figure 82: Reduction in pain medication

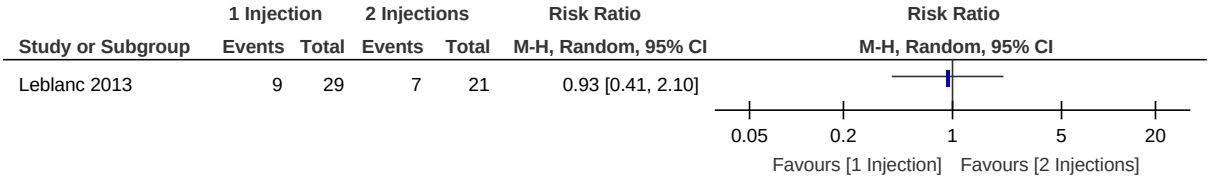


Figure 29: Patients with pain relief

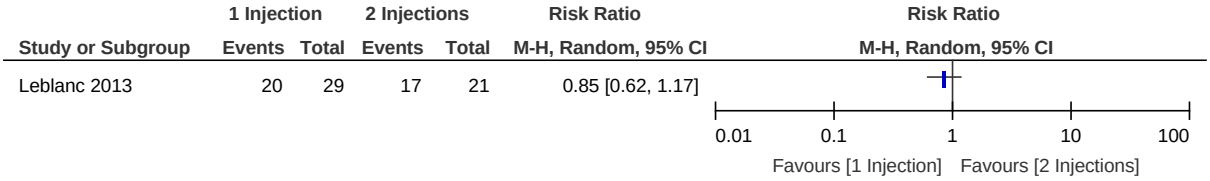


Figure 83: Patients with a complete pain relief

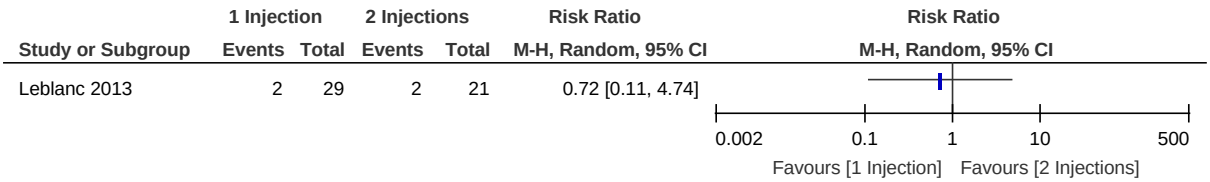
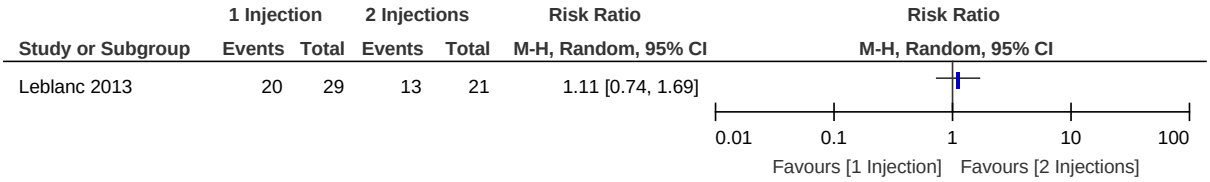


Figure 84: Patients reporting a block effective (subjective)



H.8.6 NCPB versus splanchnic nerve blocks

None

H.9 Nutritional Interventions

H.9.1 Standard Enteral nutrition versus enteral immunonutrition before and after surgery

Figure 85: Treatment related morbidity - postoperative complications

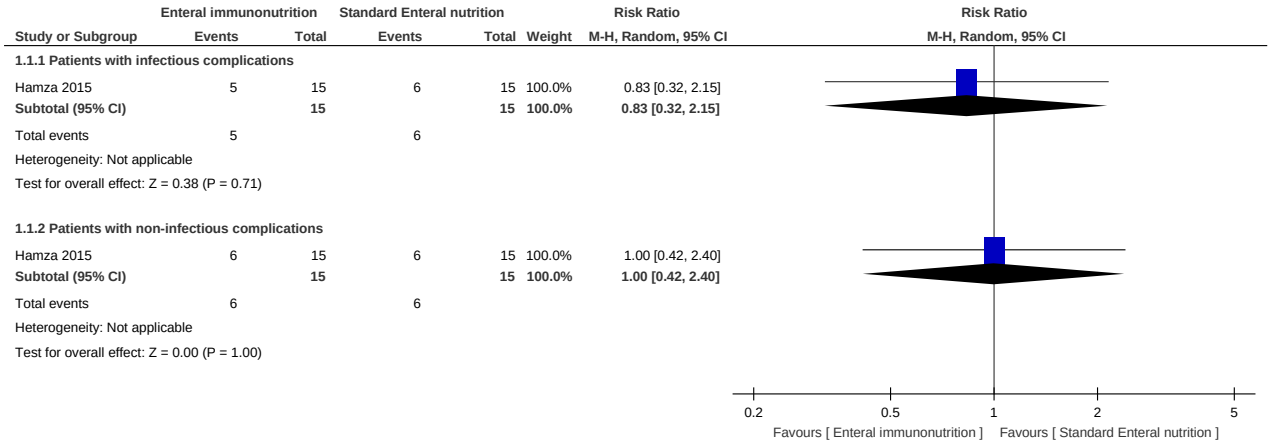


Figure 86: Health Related Quality of Life - Karnofsky score at 2 weeks after surgery, change from baseline

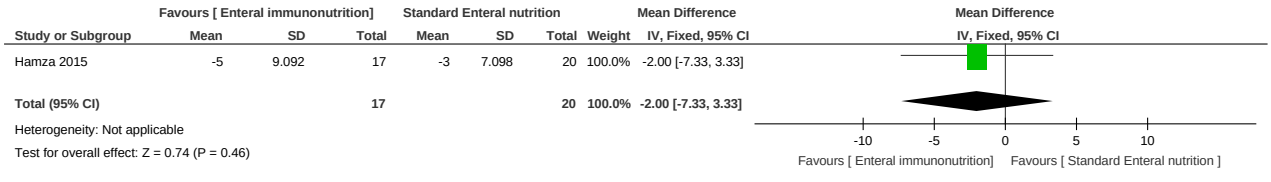


Figure 87: Nutritional status at 2 weeks after surgery - BMI (kg/m2), change from baseline

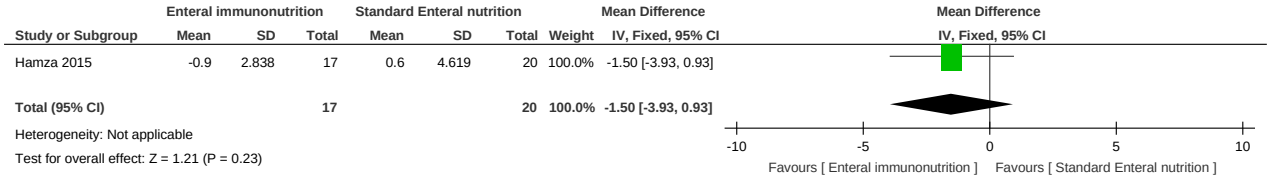


Figure 88: Nutritional status at 2 weeks after surgery - mid-arm circumference (cm), change from baseline

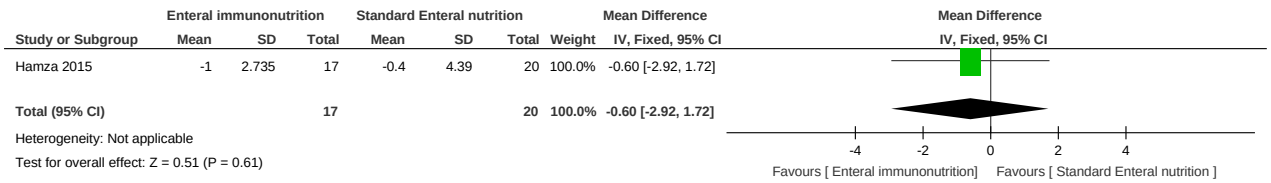
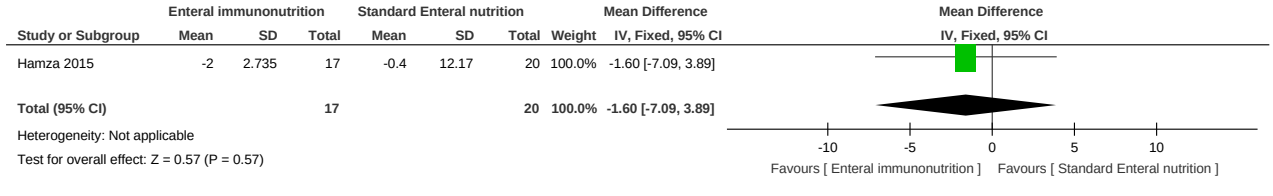


Figure 89: Nutritional status at 2 weeks after surgery - corrected arm muscle area (cm2), change from baseline



H.9.24 Standard Enteral nutrition (versus enteral immunonutrition after surgery

Figure 90: Treatment related morbidity - postoperative complications

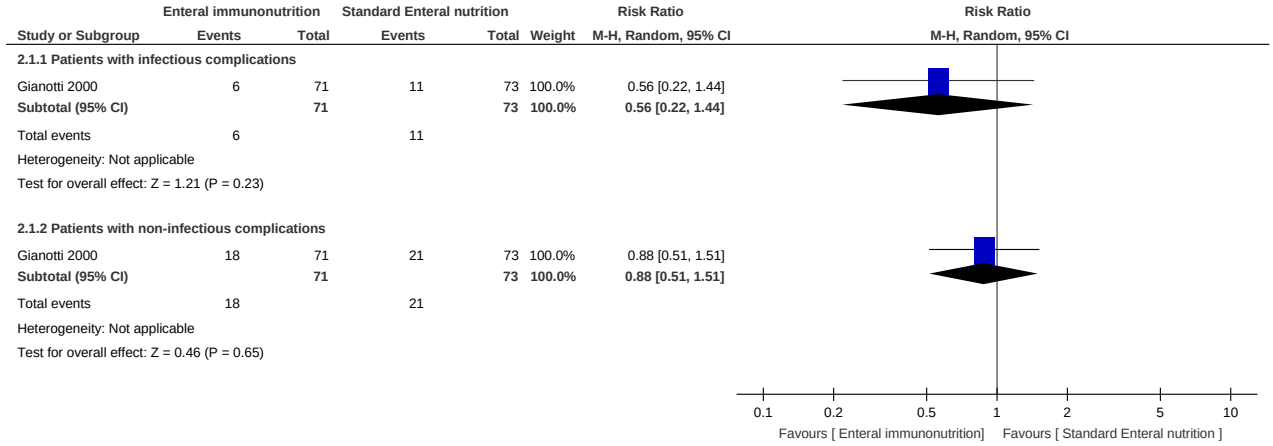


Figure 91: Treatment related morbidity - postoperative mortality

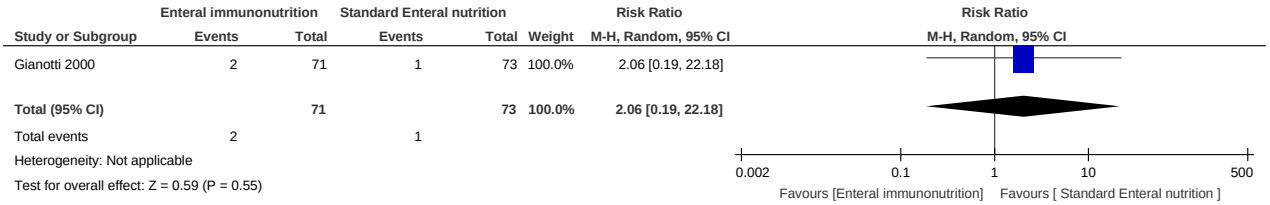
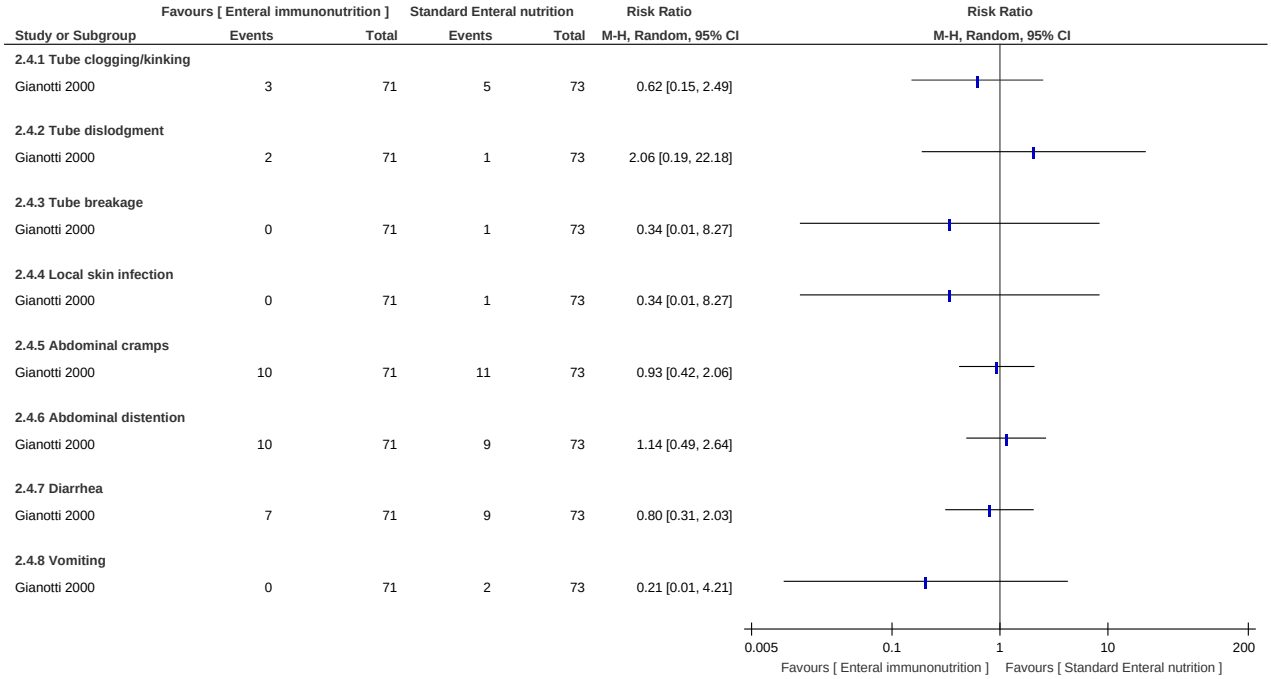


Figure 92: Treatment related morbidity - Jejunostomy and enteral nutritional related complications



H.9.34 Enteral immunonutrition versus Standard nutrition (no intervention)

Figure 93: Nutritional status at 30 days after surgery - Absolute change in weight (kg) from baseline

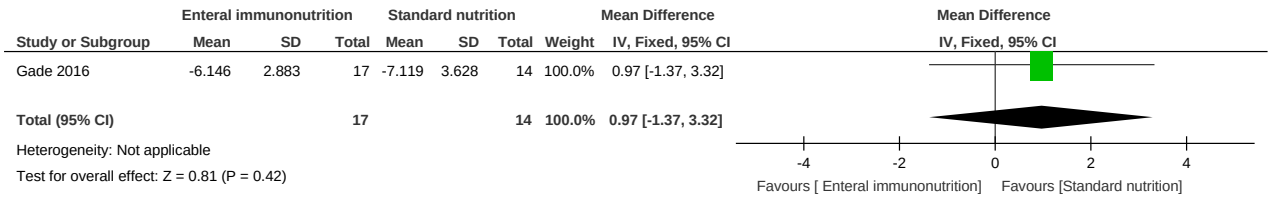
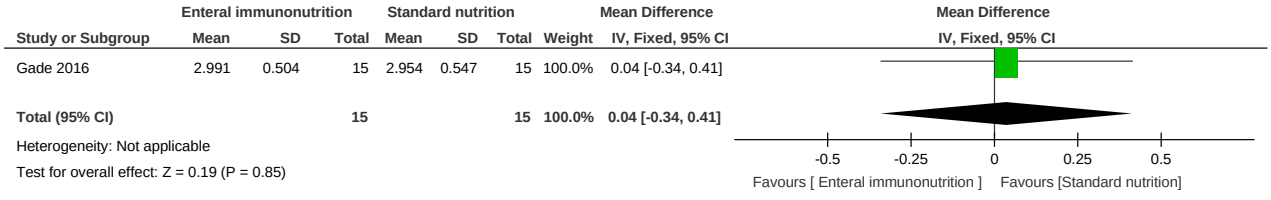


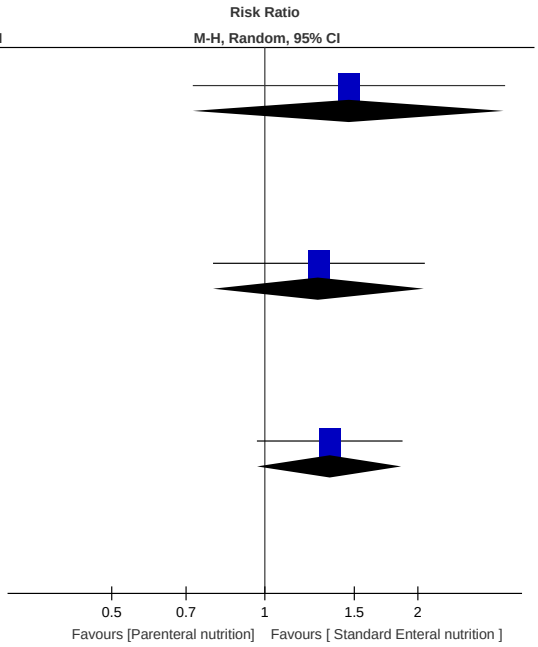
Figure 10: PROMS - Satisfaction with nutritional treatment at 1 month after surgery



H.9.41 Parenteral nutrition versus standard enteral nutrition after surgery

2 Figure 94: Treatment related morbidity - postoperative complications

Study or Subgroup	Parenteral nutrition Events	Total	Standard Enteral nutrition Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
4.1.1 Patients with infectious complications						
Gianotti 2000	15	68	11	73	100.0%	1.46 [0.72, 2.96]
Subtotal (95% CI)		**68**		**73**	**100.0%**	**1.46 [0.72, 2.96]**
Total events	15		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.06 (P = 0.29)						
4.1.2 Patients with non-infectious complications						
Gianotti 2000	25	68	21	73	100.0%	1.28 [0.79, 2.06]
Subtotal (95% CI)		**68**		**73**	**100.0%**	**1.28 [0.79, 2.06]**
Total events	25		21			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.01 (P = 0.31)						
4.1.3 Total patients with complications (infectious+ non-infectious)						
Gianotti 2000	40	68	32	73	100.0%	1.34 [0.97, 1.86]
Subtotal (95% CI)		**68**		**73**	**100.0%**	**1.34 [0.97, 1.86]**
Total events	40		32			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.76 (P = 0.08)						



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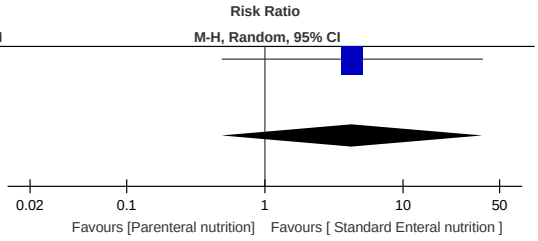
4 Figure 95: Treatment related morbidity - postoperative mortality

Study or Subgroup	Parenteral nutrition Events	Total	Standard Enteral nutrition Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Gianotti 2000	4	68	1	73	100.0%	4.29 [0.49, 37.47]
Liu 2011	0	30	0	28		Not estimable
Total (95% CI)		**98**		**101**	**100.0%**	**4.29 [0.49, 37.47]**
Total events	4		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.32 (P = 0.19)						



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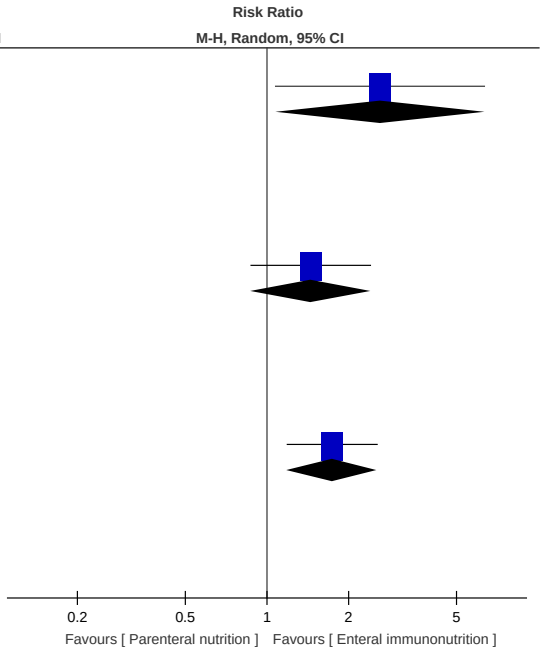
H.9.5 Parenteral nutrition versus enteral immunonutrition after surgery

Figure 96: Treatment related morbidity - postoperative complications

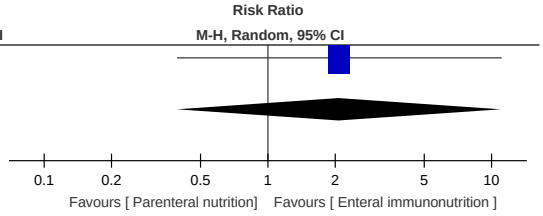
Study or Subgroup	Parenteral nutrition Events	Total	Enteral immunonutrition Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
5.1.1 Patients with infectious complications						
Gianotti 2000	15	68	6	71	100.0%	2.61 [1.08, 6.33]
Subtotal (95% CI)		**68**		**71**	**100.0%**	**2.61 [1.08, 6.33]**
Total events	15		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.12 (P = 0.03)						
5.1.2 Patients with non-infectious complications						
Gianotti 2000	25	68	18	71	100.0%	1.45 [0.87, 2.41]
Subtotal (95% CI)		**68**		**71**	**100.0%**	**1.45 [0.87, 2.41]**
Total events	25		18			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.44 (P = 0.15)						
5.1.3 Total patients with complications (infectious+ non-infectious)						
Gianotti 2000	40	68	24	71	100.0%	1.74 [1.19, 2.55]
Subtotal (95% CI)		**68**		**71**	**100.0%**	**1.74 [1.19, 2.55]**
Total events	40		24			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.85 (P = 0.004)						



Test for subgroup differences: Chi² = 1.29, df = 2 (P = 0.52), I² = 0%

Figure 97: Treatment related morbidity - postoperative mortality

Study or Subgroup	Parenteral nutrition Events	Total	Enteral immunonutrition Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Gianotti 2000	4	68	2	71	100.0%	2.09 [0.40, 11.03]
Total (95% CI)		**68**		**71**	**100.0%**	**2.09 [0.40, 11.03]**
Total events	4		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.87 (P = 0.39)						



H.9.61 Parenteral nutrition versus no intervention after surgery

2 Figure 98: Treatment related morbidity - major complications

Study or Subgroup	Parenteral nutrition Events	Total	No intervention Events	Total	Risk Ratio M-H, Random, 95% CI
6.1.1 Deep infection					
Brennan 1994	4	60	4	57	0.95 [0.25, 3.62]
6.1.2 Fistula					
Brennan 1994	8	60	5	57	1.52 [0.53, 4.37]
6.1.3 Abscess					
Brennan 1994	12	60	2	57	5.70 [1.33, 24.36]
6.1.4 Peritonitis					
Brennan 1994	7	60	2	57	3.33 [0.72, 15.34]
6.1.5 Hemorrhage					
Brennan 1994	1	60	2	57	0.47 [0.04, 5.10]
6.1.6 Intestinal obstruction					
Brennan 1994	4	60	0	57	8.56 [0.47, 155.45]
6.1.7 Anastomotic breakdown					
Brennan 1994	7	60	3	57	2.22 [0.60, 8.16]
6.1.8 Aspiration					
Brennan 1994	0	60	1	57	0.32 [0.01, 7.62]
6.1.9 Pneumonia					
Brennan 1994	5	60	6	57	0.79 [0.26, 2.45]
6.1.10 Pulmonary embolus					
Brennan 1994	0	60	1	57	0.32 [0.01, 7.62]
6.1.11 Myocardial infarction					
Brennan 1994	2	60	1	57	1.90 [0.18, 20.38]
6.1.12 Reoperation					
Brennan 1994	6	60	3	57	1.90 [0.50, 7.24]
6.1.13 Total major complications (excluding death)					
Brennan 1994	23	60	12	57	1.82 [1.00, 3.31]

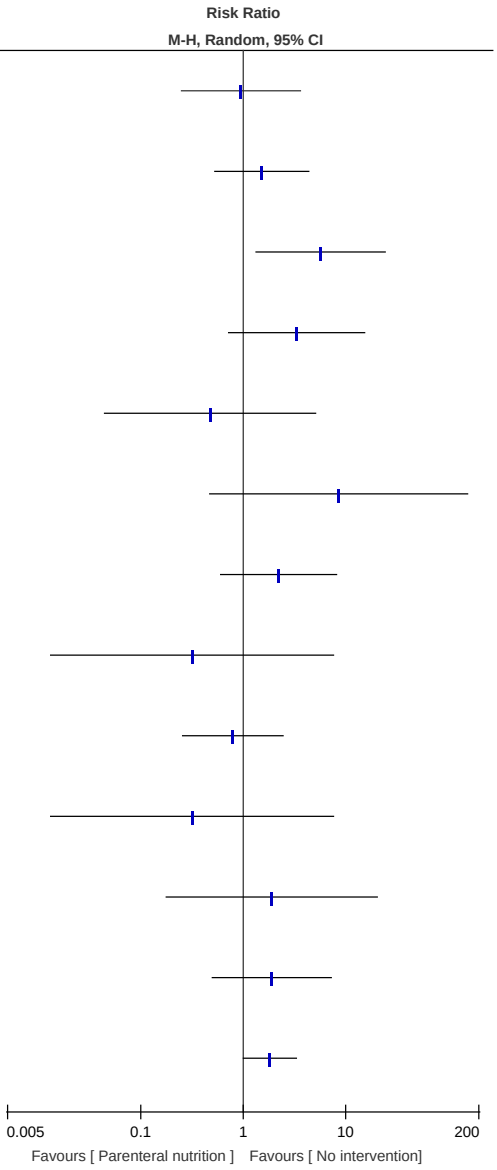


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Figure 99: Treatment related morbidity - minor complications

Study or Subgroup	Parenteral nutrition Events	Total	no intervention Events	Total	Risk Ratio M-H, Random, 95% CI
6.2.1 Superficial wound infection					
Brennan 1994	5	60	1	57	4.75 [0.57, 39.42]
6.2.2 Cellulitis					
Brennan 1994	1	60	0	57	2.85 [0.12, 68.62]
6.2.3 Prolonged ileus					
Brennan 1994	13	60	5	57	2.47 [0.94, 6.49]
6.2.4 Gastric atony					
Brennan 1994	2	60	1	57	1.90 [0.18, 20.38]
6.2.5 Atelectasis					
Brennan 1994	15	60	12	57	1.19 [0.61, 2.31]
6.2.6 Pleural effusion					
Brennan 1994	12	60	13	57	0.88 [0.44, 1.76]
6.2.7 Catheter sepsis					
Brennan 1994	5	60	1	57	4.75 [0.57, 39.42]
6.2.8 Urinary tract infection					
Brennan 1994	4	60	6	57	0.63 [0.19, 2.13]
6.2.9 PN related complication					
Brennan 1994	2	60	0	57	4.75 [0.23, 96.93]
6.2.10 Liver function abnormality					
Brennan 1994	0	60	0	57	Not estimable
6.2.11 Total minor complications					
Brennan 1994	32	60	24	57	1.27 [0.86, 1.86]

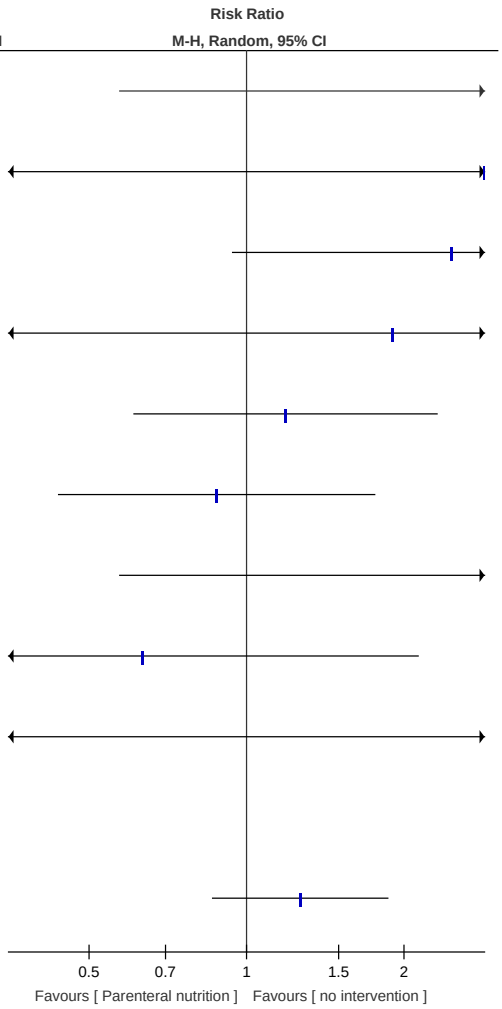
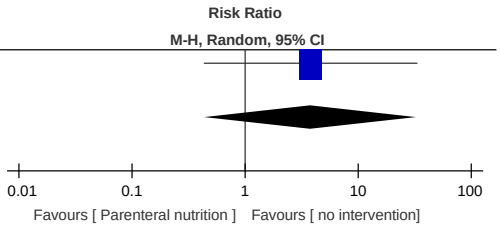


Figure 100: Treatment related morbidity - postoperative mortality

Study or Subgroup	Parenteral nutrition Events	Total	no intervention Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Brennan 1994	4	60	1	57	100.0%	3.80 [0.44, 32.99]
Total (95% CI)		**60**		**57**	**100.0%**	**3.80 [0.44, 32.99]**
Total events	4		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.21 (P = 0.23)						



H.9.7 Oral nutritional supplements (n-3 fatty acids) versus isocaloric-isonitrogenous supplement (without n-3 fatty acids)

Figure 101: Nutritional status - Change in weight (kg/month) at 8 weeks

Study or Subgroup	n-3 fatty acids Mean	SD	Total	without n-3 fatty acids Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Fearon 2003	-0.25	0.4173	50	-0.37	0.6867	60	100.0%	0.12 [-0.09, 0.33]
Total (95% CI)			**50**			**60**	**100.0%**	**0.12 [-0.09, 0.33]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.13 (P = 0.26)								

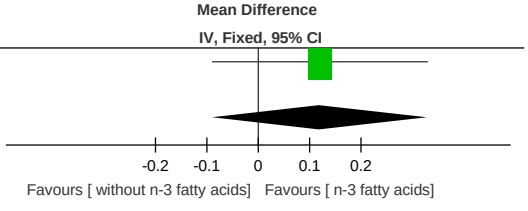


Figure 102: Nutritional status - Change in lean body mass (kg) at 8 weeks

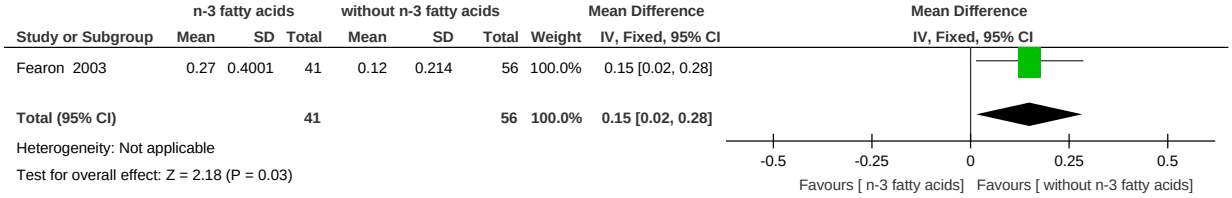


Figure 103: Change in resting energy expenditure at 8 weeks

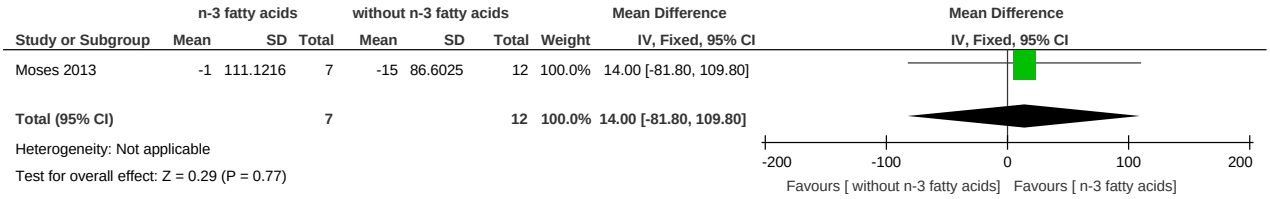


Figure 104: Change in total energy expenditure at 8 weeks

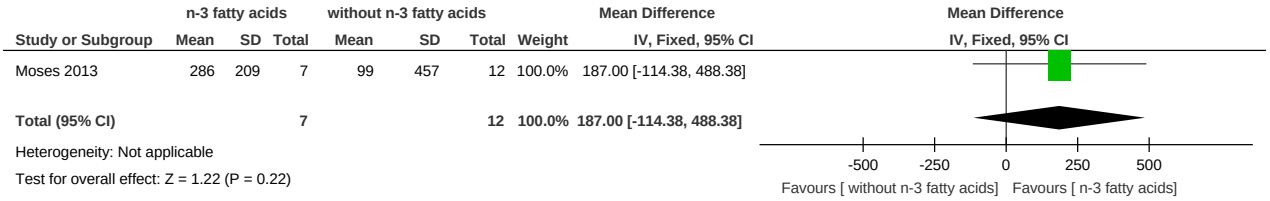
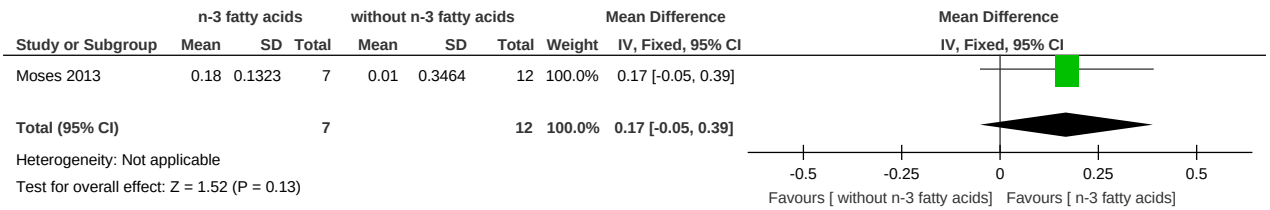
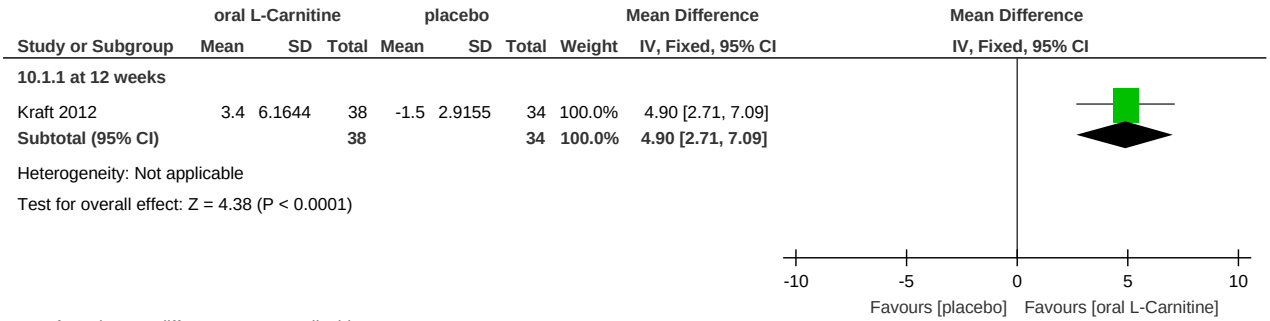


Figure 105: Change in physical activity level at 8 weeks



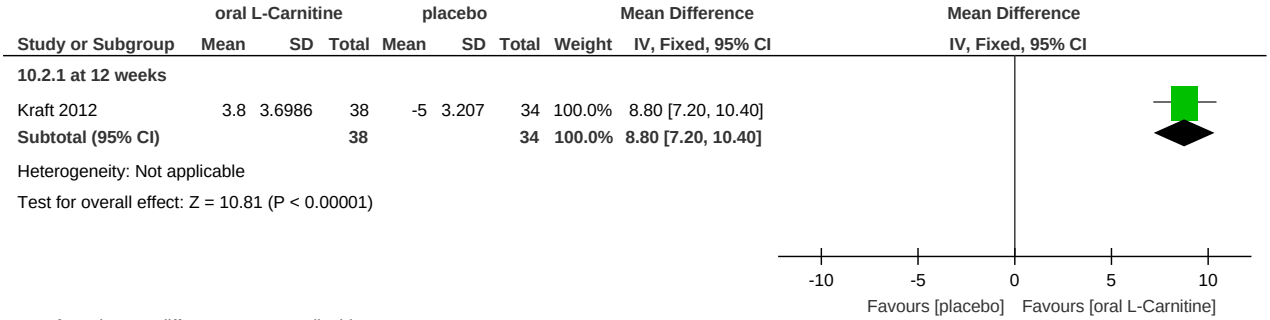
H.9.89 Oral nutritional supplements (oral L-Carnitine therapy) versus placebo

Figure 106: Nutritional status - % change of BMI at 12 weeks



Test for subgroup differences: Not applicable

Figure 107: Nutritional status - % change of body fat and BCM at 12 weeks



Test for subgroup differences: Not applicable

H.9.93 Pancreatic enzyme replacement therapy (PERT) versus placebo

Figure 108: Nutritional status - Percentage change in body weight (%) at 8 weeks follow-up

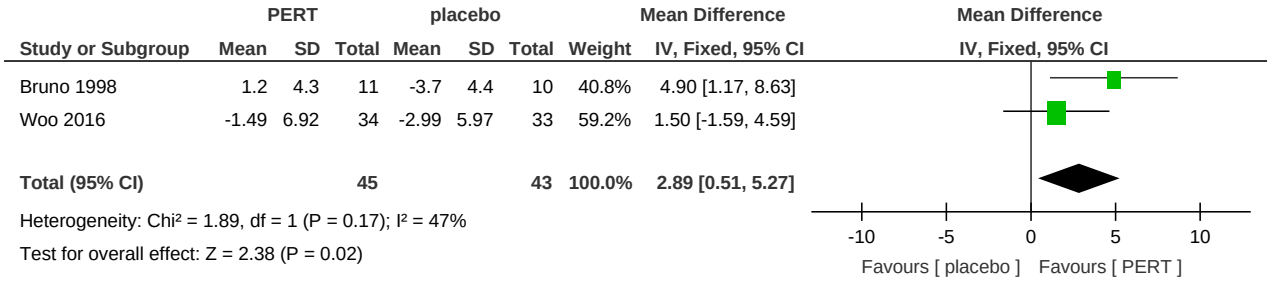


Figure 109: Nutritional status - Absolute change in body weight (Kg) at 8 weeks follow-up

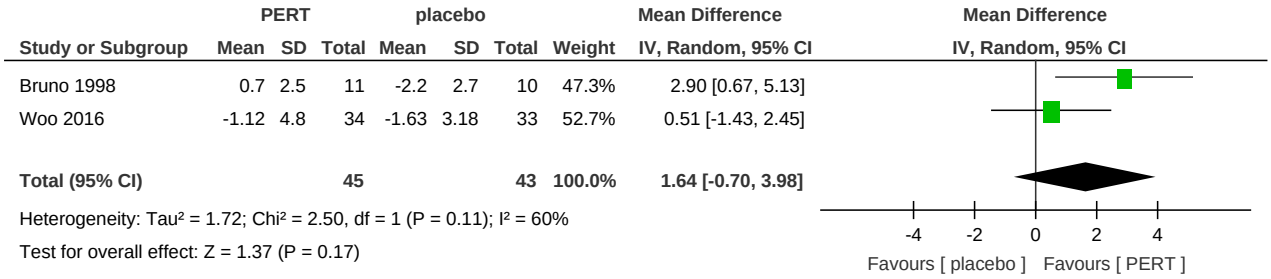
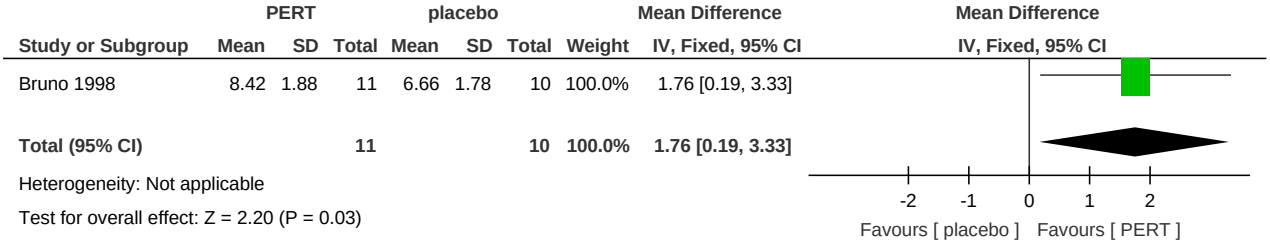
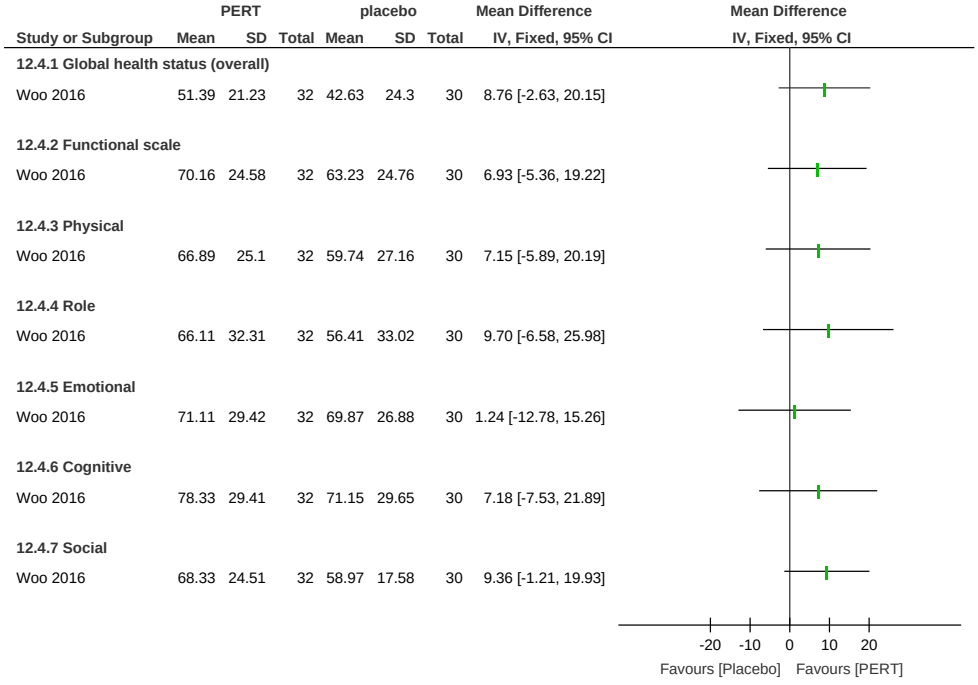


Figure 110: Nutritional status - Daily dietary intake of total calories at 8 weeks follow-up

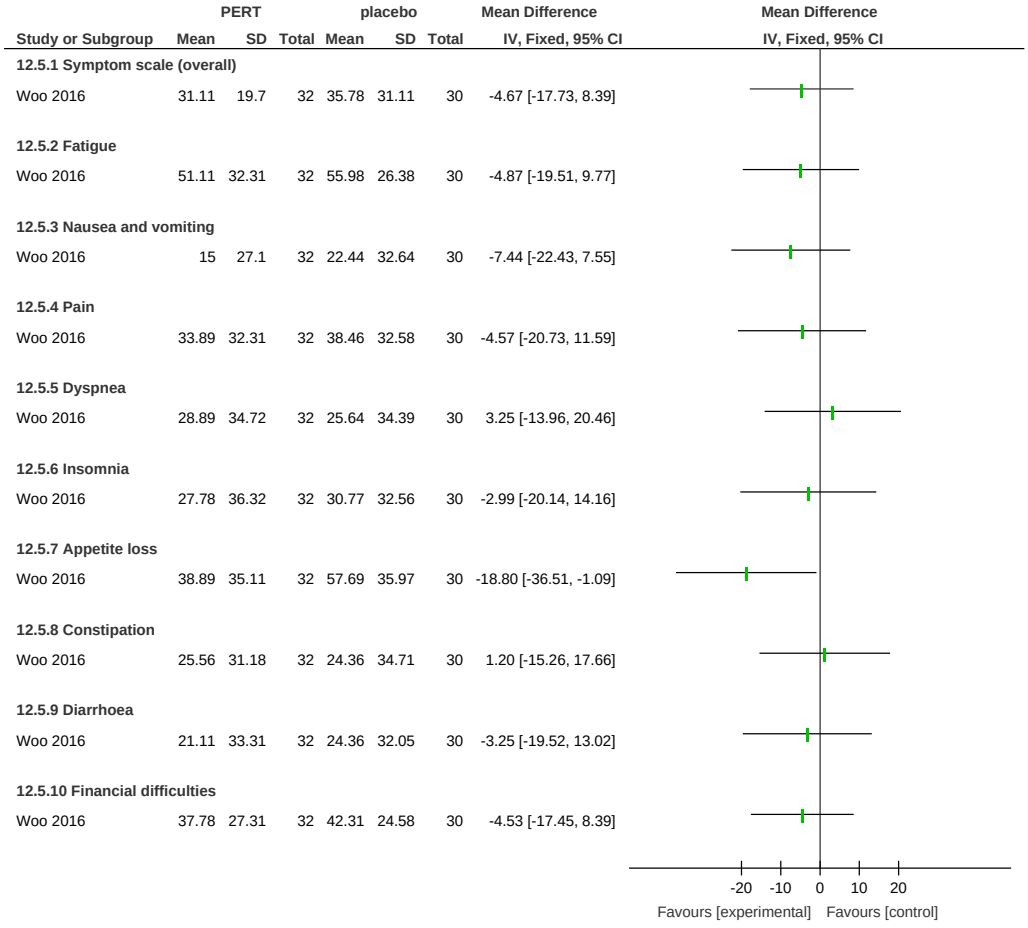


1 Figure 111: Health related quality of life - Global Health status at 8 weeks follow-up



2

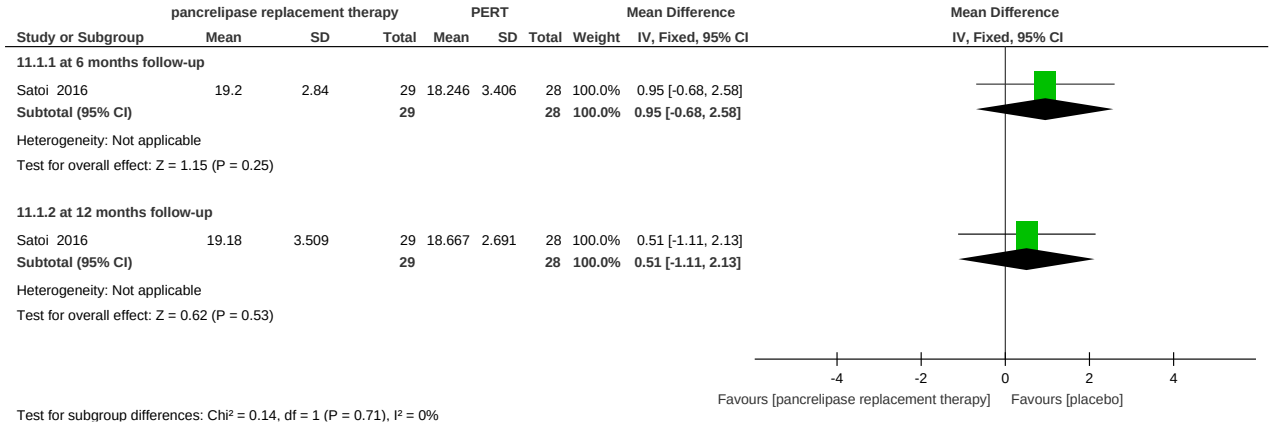
3 Figure 112: Health related quality of life - Symptom scale at 8 weeks follow-up



4

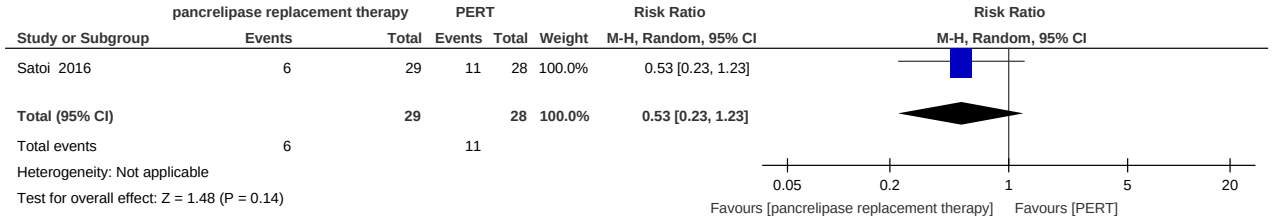
H.9.101 PERT versus pancrelipase replacement therapy

2 Figure 113: Nutritional status - BMI (kg/m2) at 6 and 12 months follow-up



3 Test for subgroup differences: Chi² = 0.14, df = 1 (P = 0.71), I² = 0%

4 Figure 114: Treatment related morbidity - NAFLD at 1 year follow-up



5
6

H.107 Biliary obstruction

H.10.18 Plastic stent versus self-expanding metal stent in adults with pancreatic 9 cancer

Figure 115: Treatment-related mortality

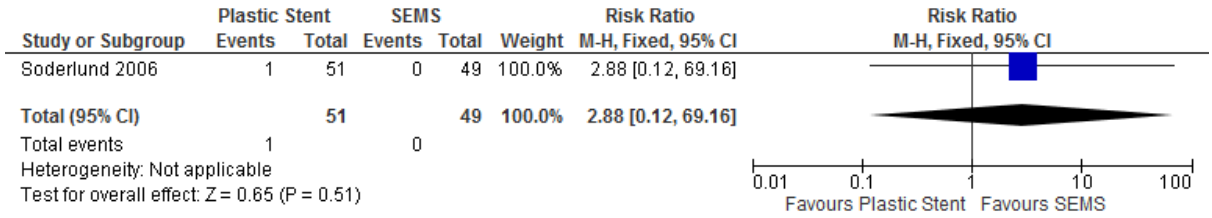


Figure 116: Overall survival

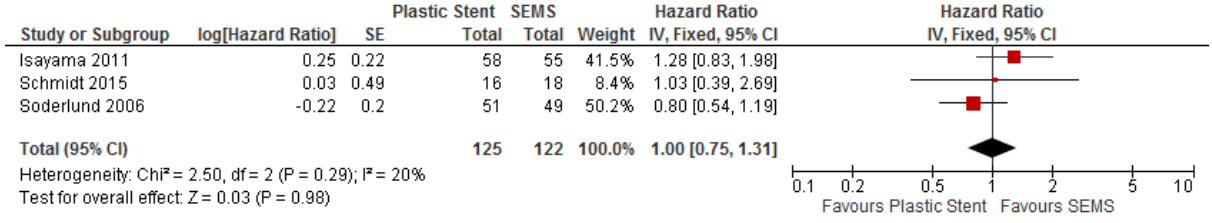


Figure 117: Time to stent dysfunction – primary and/or secondary stent

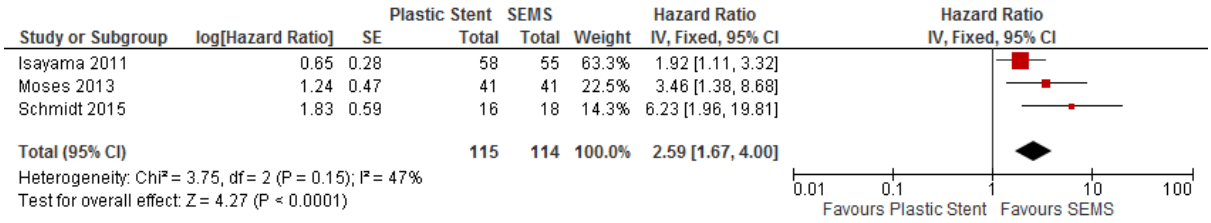


Figure 118: Time to stent dysfunction – primary stent subgroup analysis by covered status

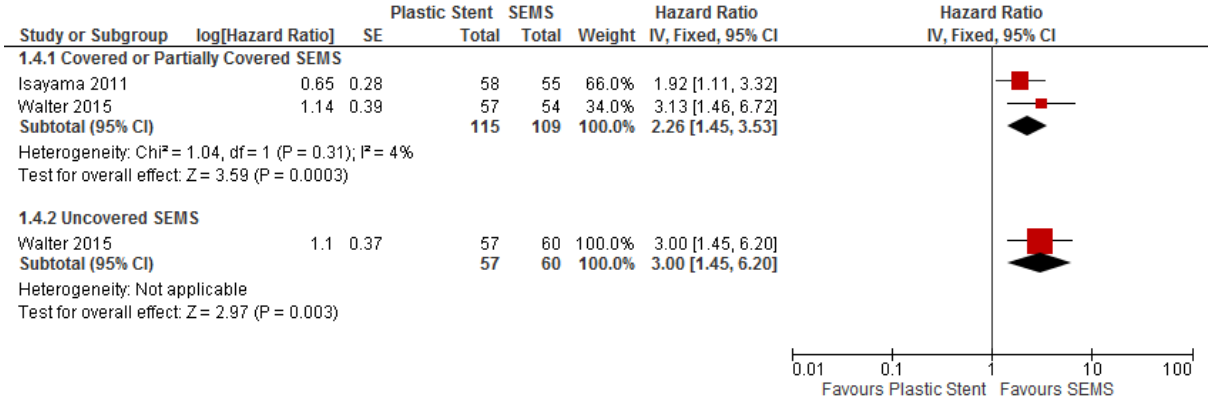


Figure 119: Time to stent dysfunction – secondary stent subgroup analysis by covered status

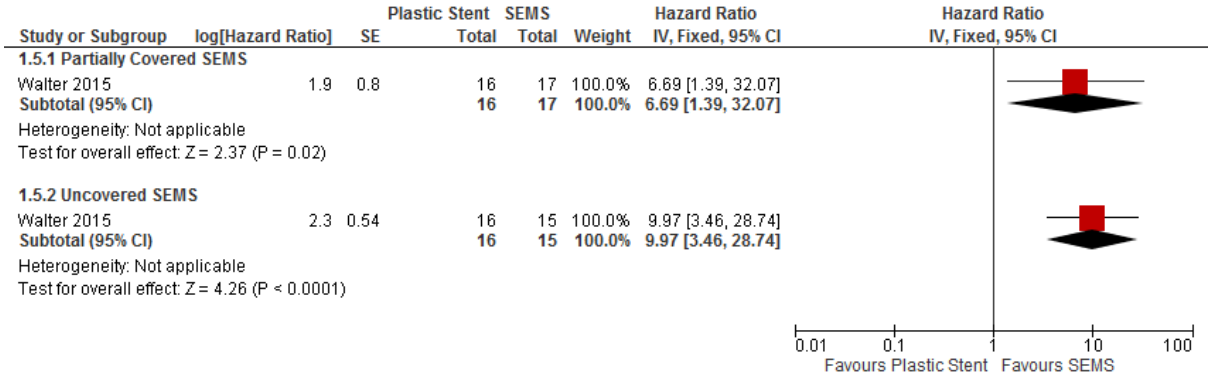


Figure 120: Number of patients with stent dysfunction

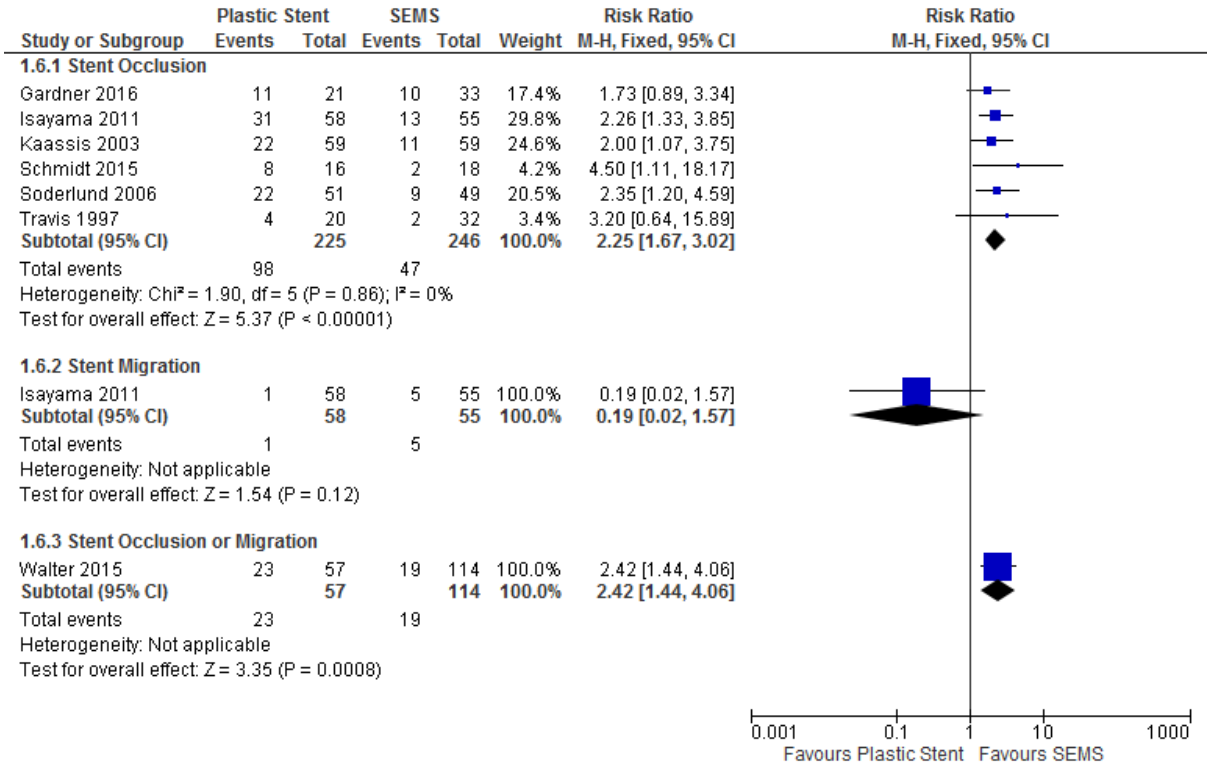


Figure 121: Number of patients with stent occlusion – subgroup analysis by covered status

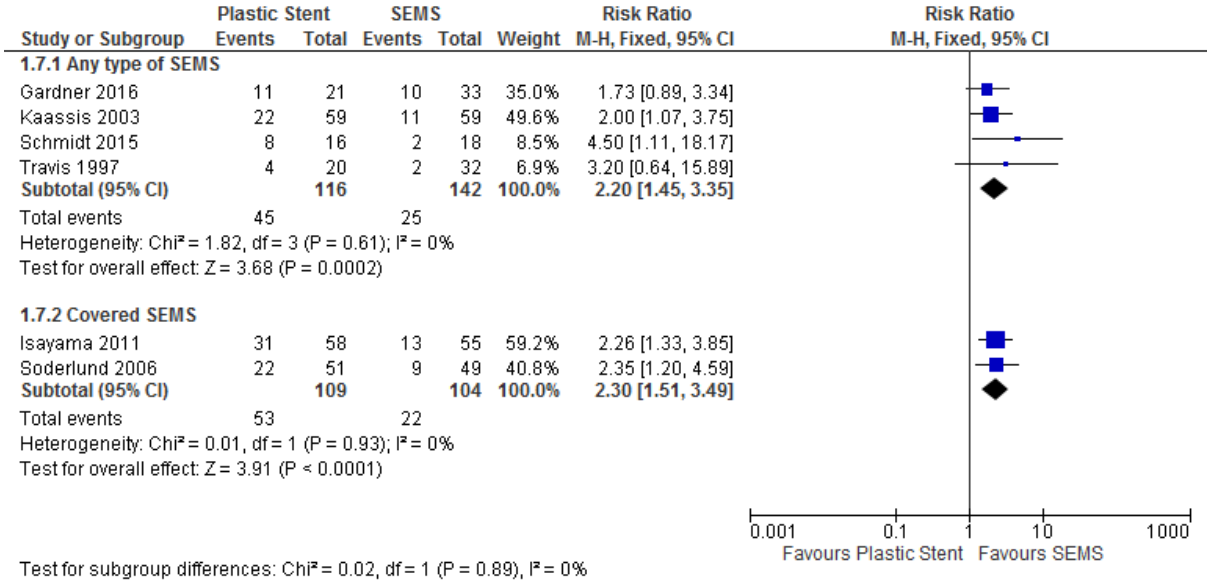


Figure 122: Number of patients with stent occlusion – subgroup analysis by resectability status

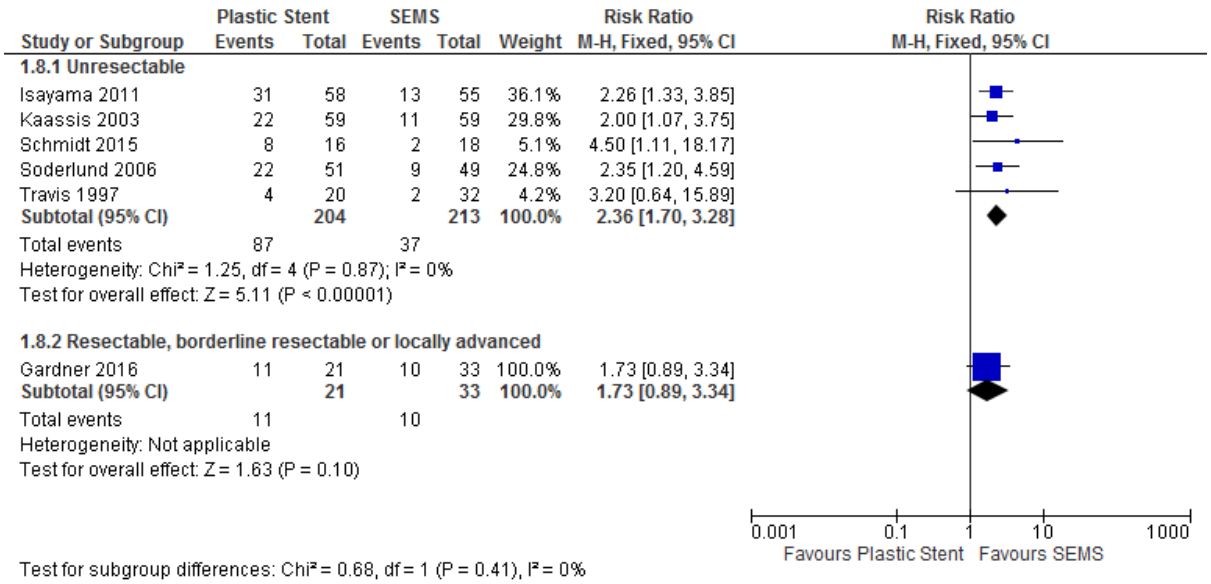


Figure 123: Number of patients with pancreatitis

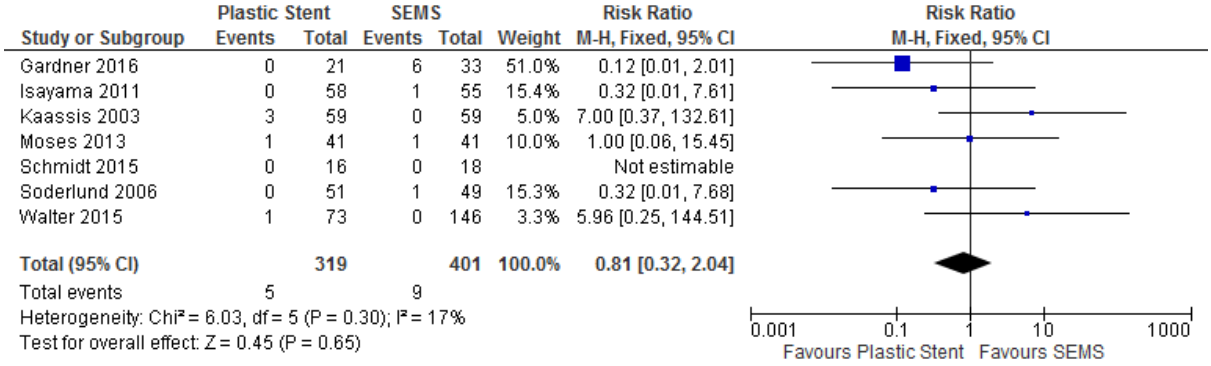


Figure 124: Number of patients with pancreatitis – subgroup analysis by covered status

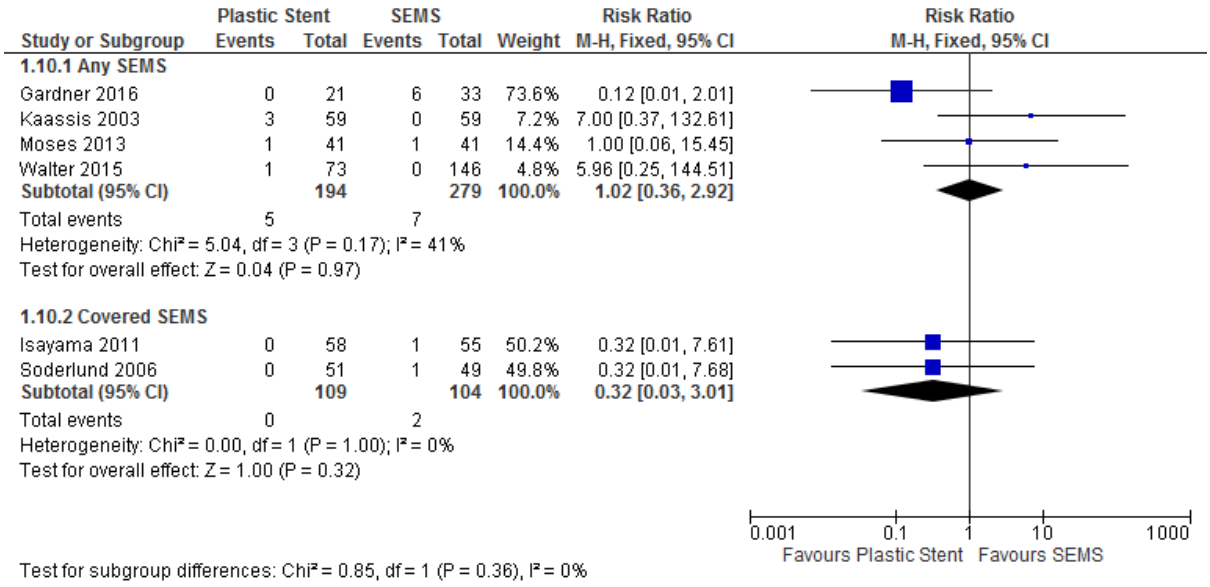


Figure 125: Number of patients with pancreatitis – subgroup analysis by resectability status

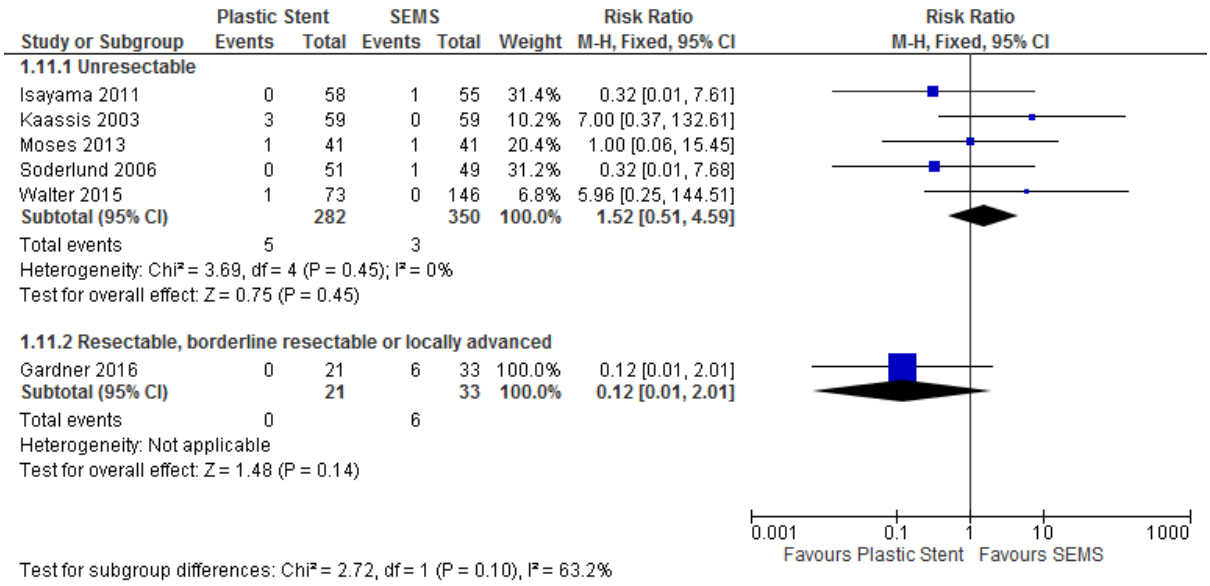


Figure 126: Number of patients with cholangitis – unresectable patients

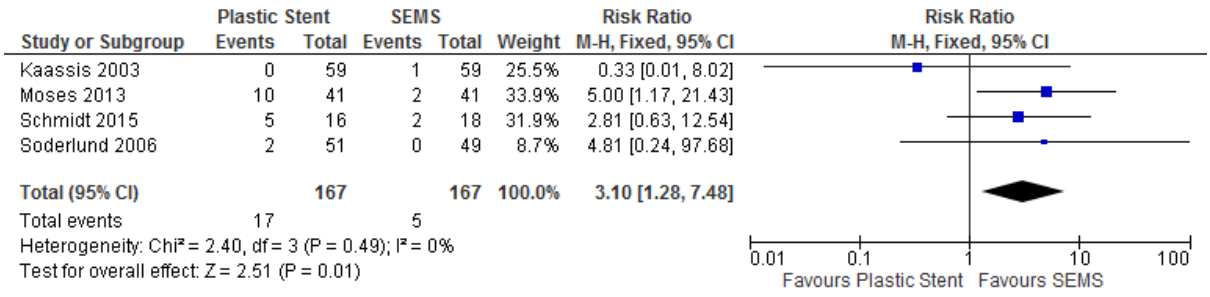


Figure 127: Number of patients with cholangitis – subgroup analysis by covered status

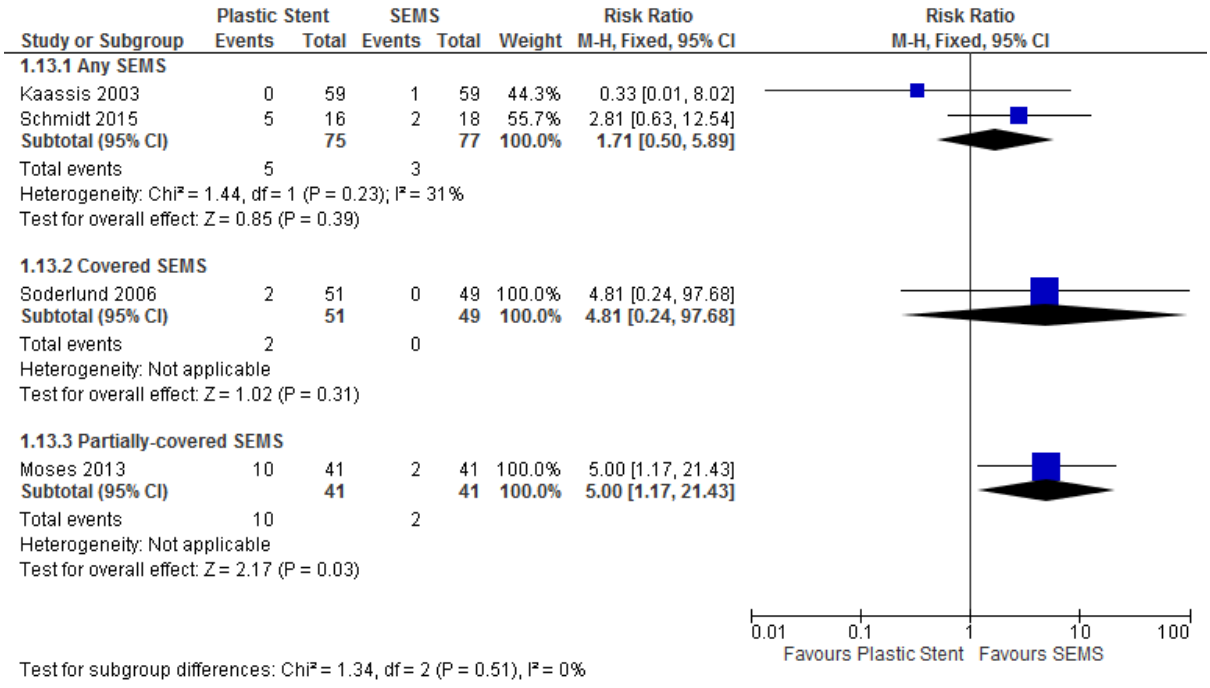


Figure 128: Number of patients with cholecystitis – unresectable patients

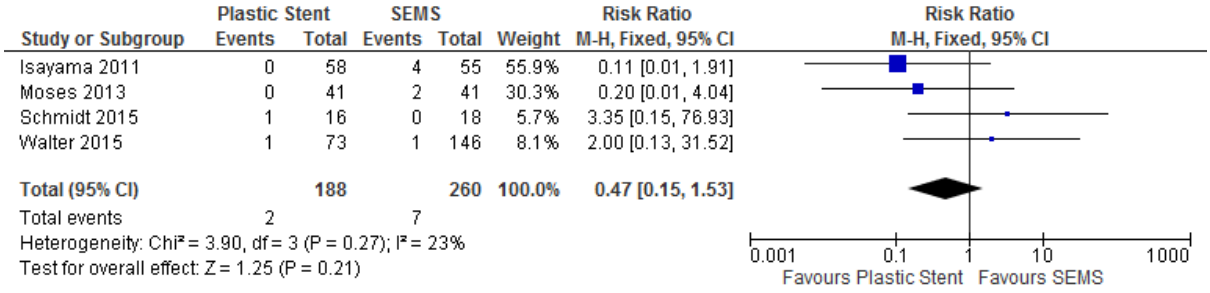


Figure 129: Number of patients with cholecystitis – subgroup analysis by covered status

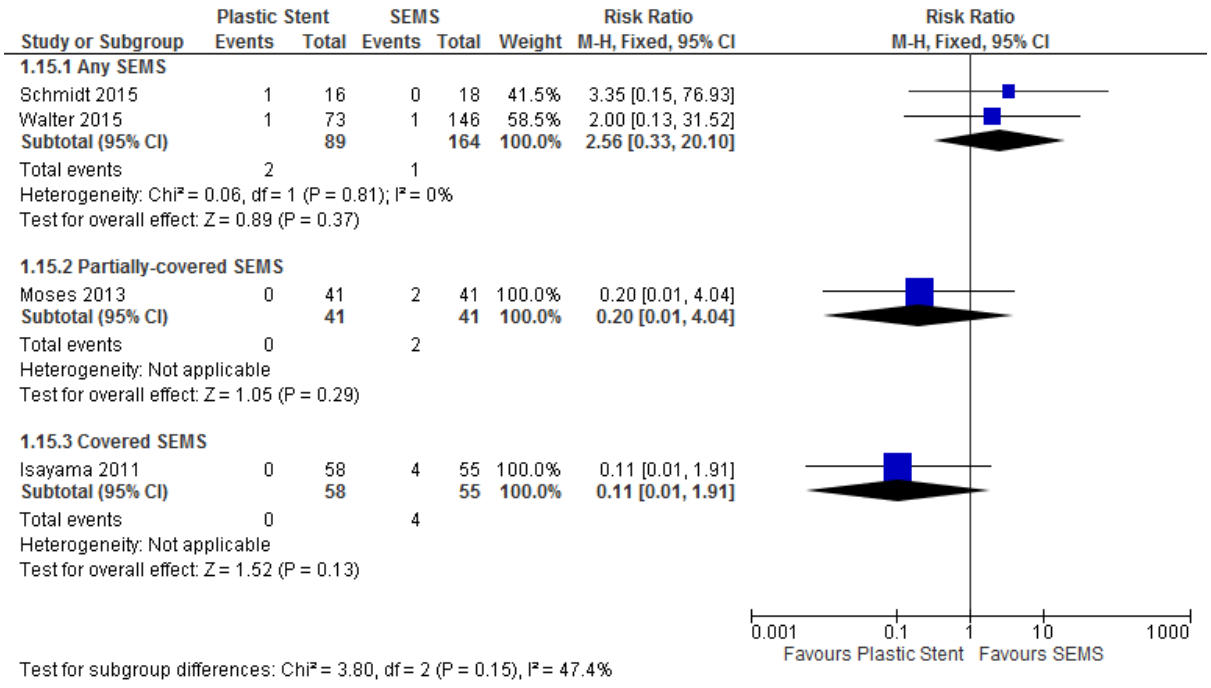


Figure 130: Number of patients with cholestatic symptoms to 2-year follow up

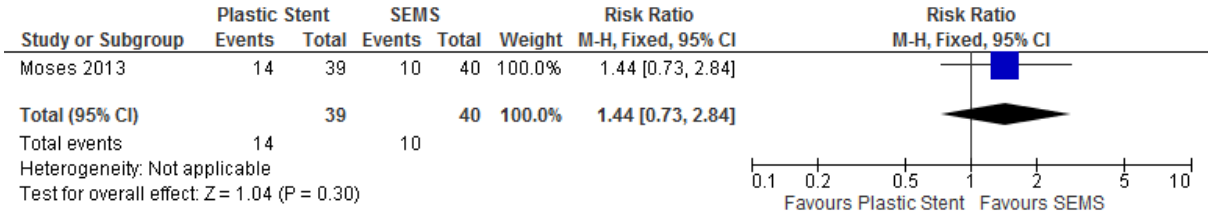


Figure 131: Number of patients with post-endoscopic sphincterotomy haemorrhage

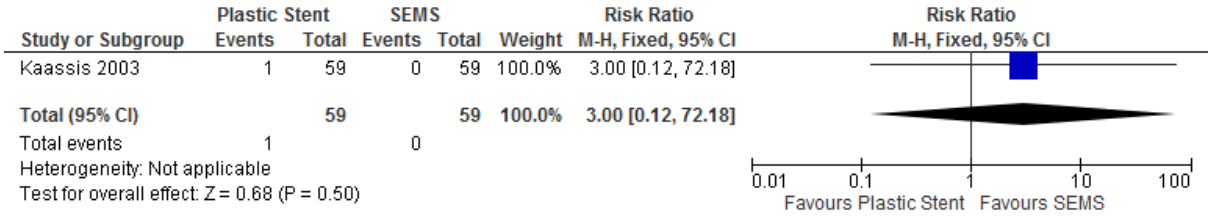


Figure 132: Number of days hospitalised

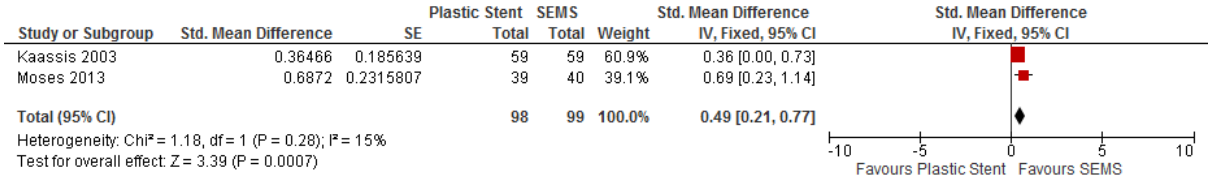


Figure 133: Number of patients with ≥30% decrease in total serum bilirubin

Figure 134: Percentage reduction in total serum bilirubin

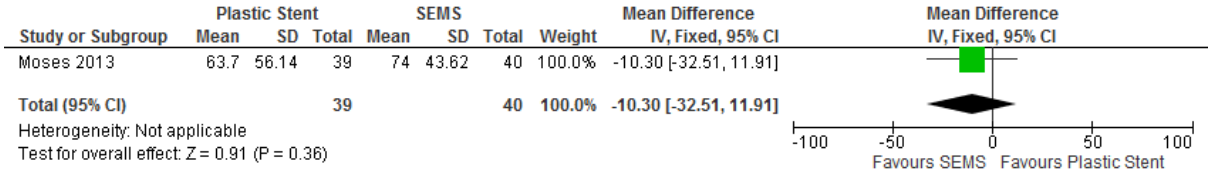
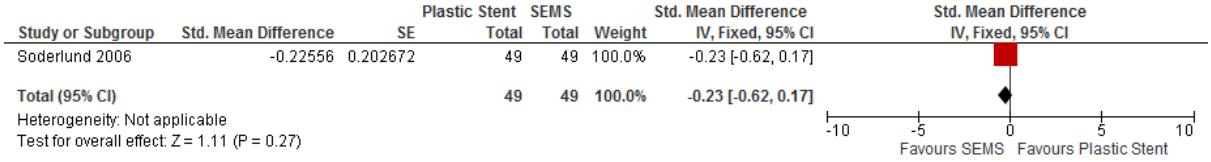


Figure 135: Total serum bilirubin – rate of change



H.10.21 2 Covered self-expanding metal stent versus uncovered self-expanding metal stent

Figure 136: Stent dysfunction

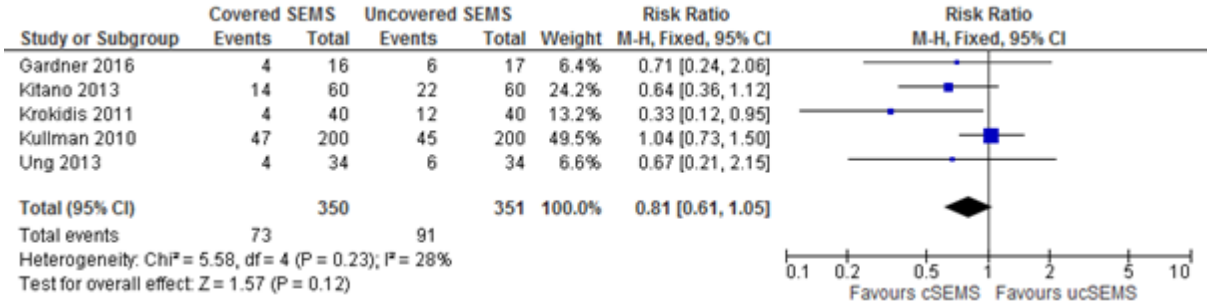


Figure 137: Stent dysfunction by cause

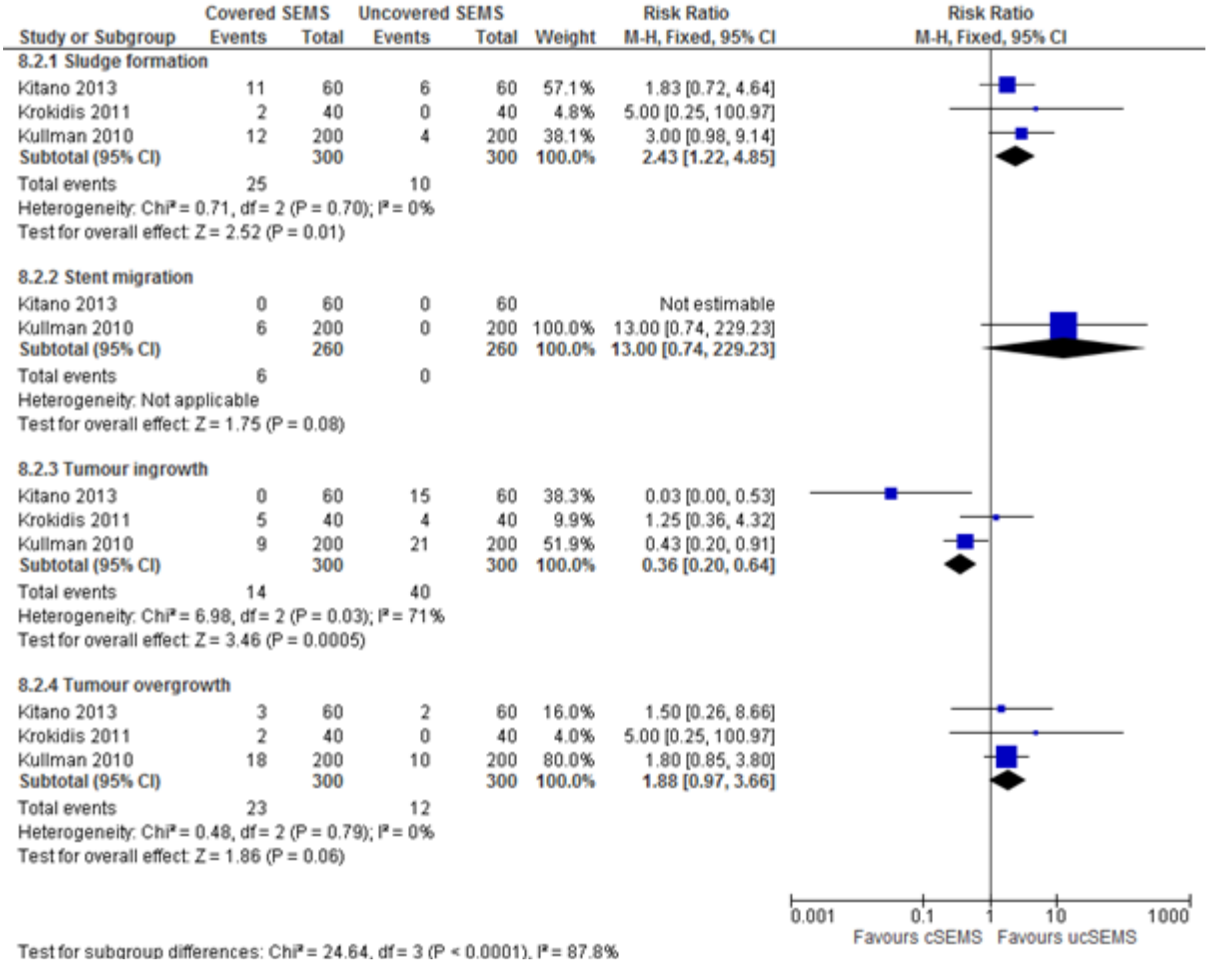
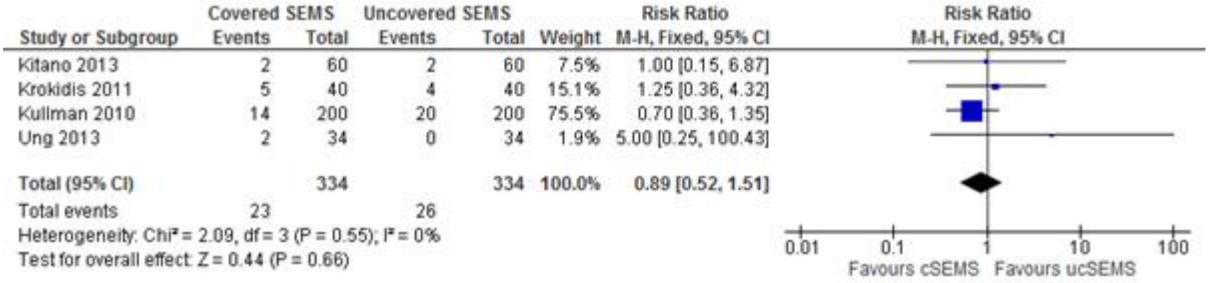


Figure 138: Adverse events



H.10.3 Partially covered self-expanding metal stent versus uncovered self-expanding metal stent

Figure 139: Stent dysfunction

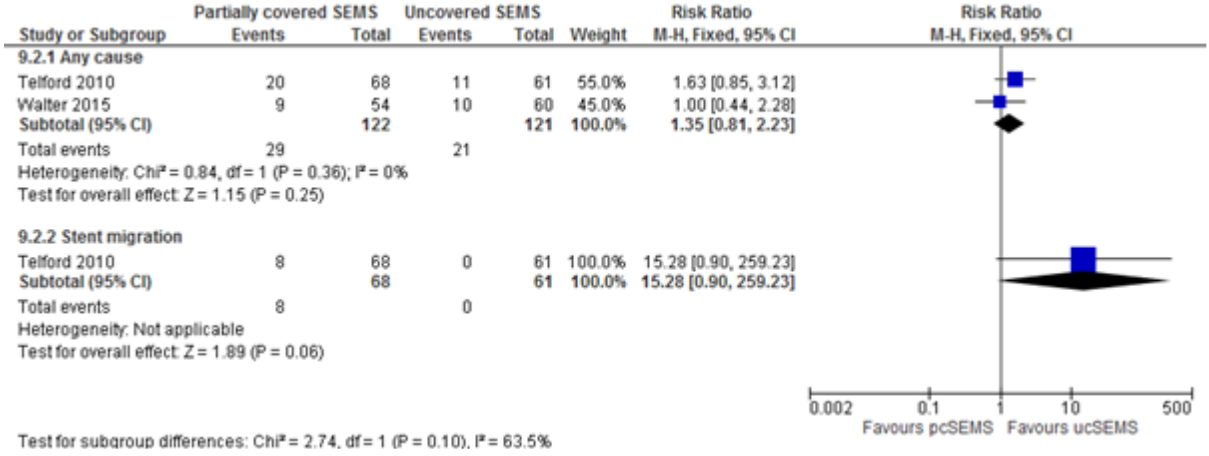
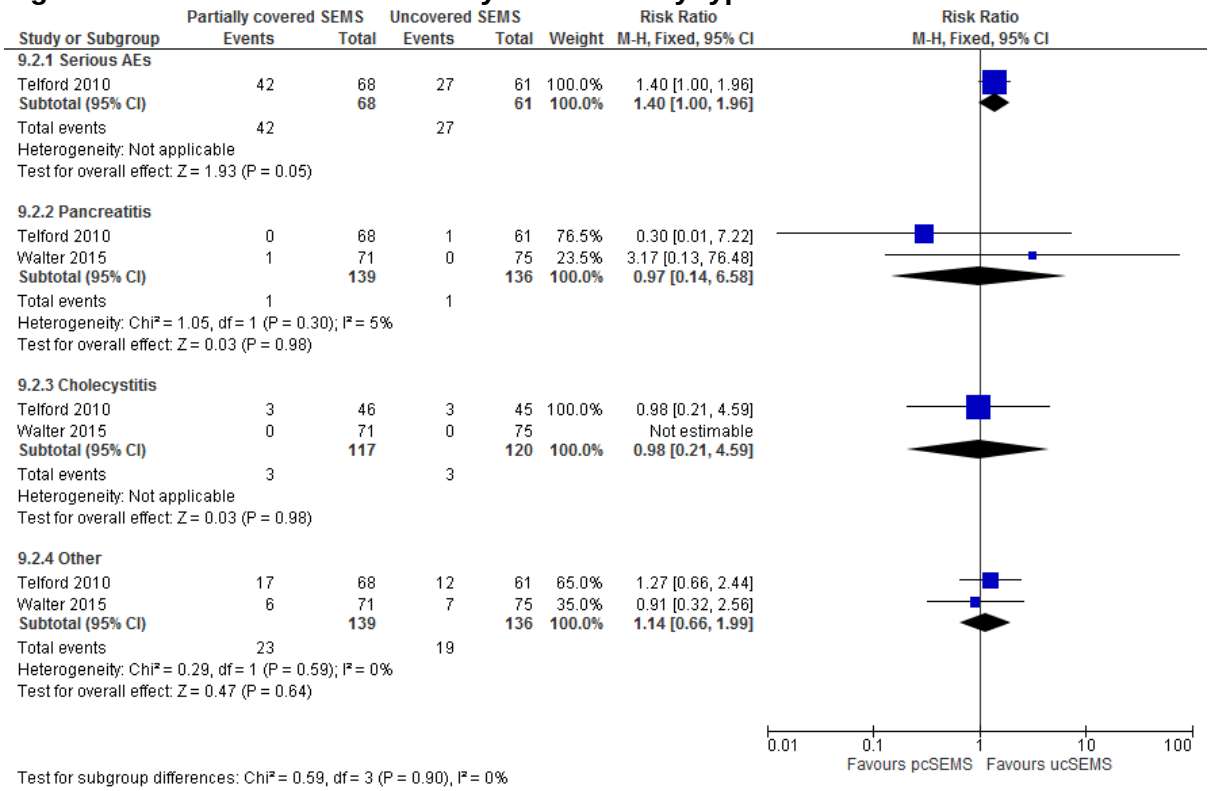


Figure 140: Adverse events – any cause and by type



H.10.4 Paclitaxel-eluting self-expanding metal stent versus covered SEMS in adults with unresectable distal malignant biliary obstruction

Figure 141: Time to stent dysfunction

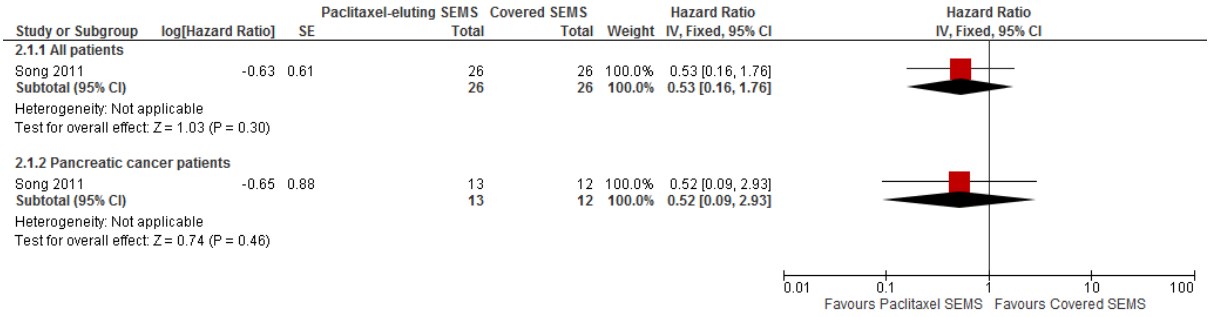


Figure 142: Overall survival

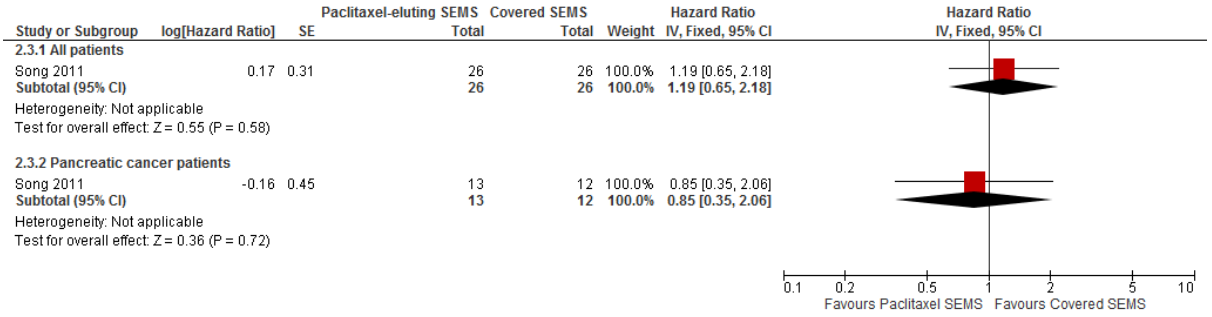


Figure 143: Stent dysfunction

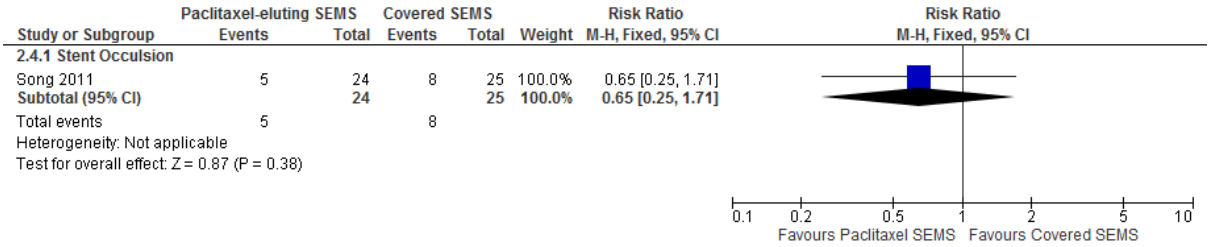


Figure 144: Cholangitis symptoms

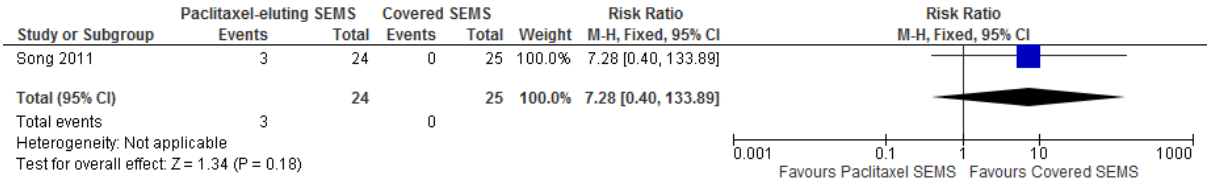
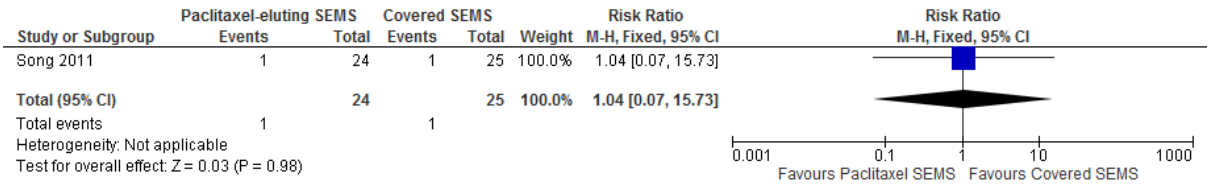


Figure 145: Pancreatitis



H.10.5 Preoperative endoscopic biliary drainage then surgery versus surgery in adults with suspected pancreatic cancer

Figure 146: Mortality at 120 days

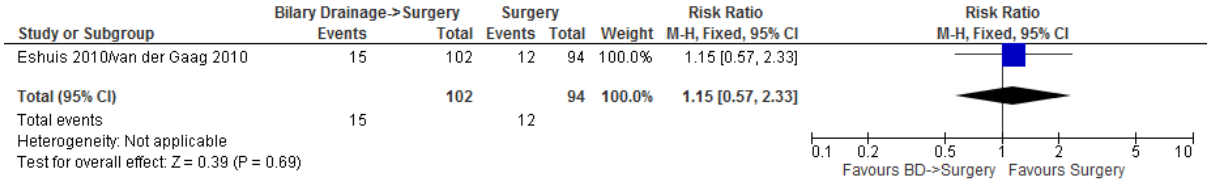


Figure 147: Mortality at 2 years

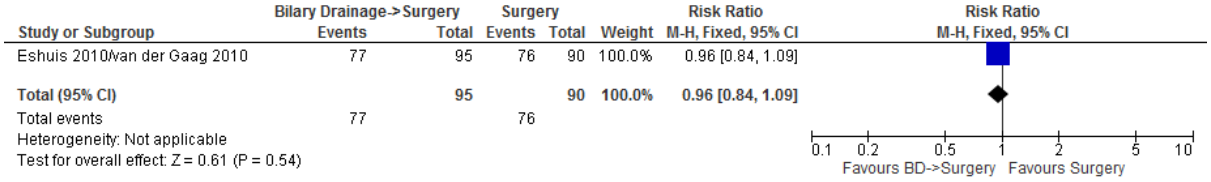


Figure 148: Treatment-related mortality

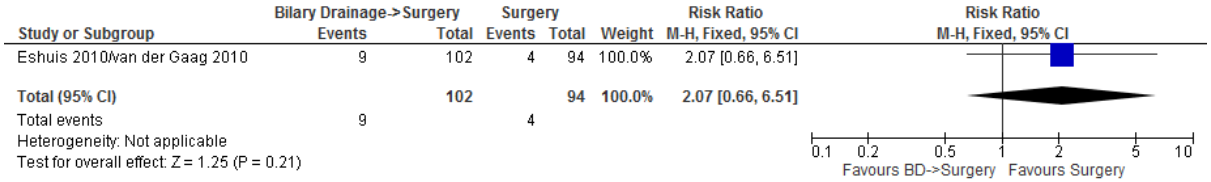


Figure 149: Overall survival at 2 years

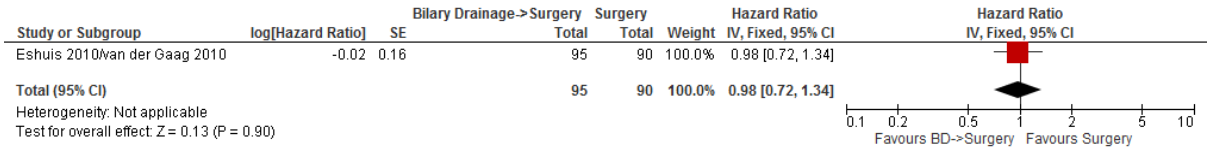


Figure 150: Overall survival at 2 years – subgroup analysis by type of surgery

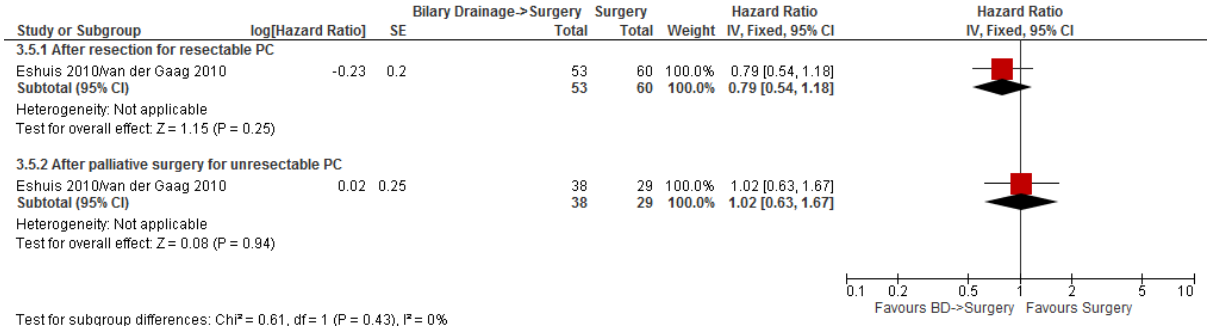


Figure 151: Delay to surgery (weeks)

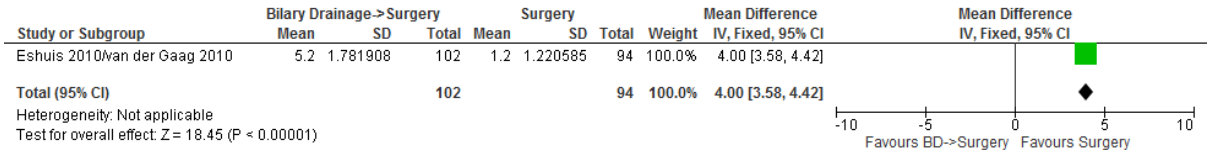


Figure 152: Hospitalisation due to protocol-specific complications

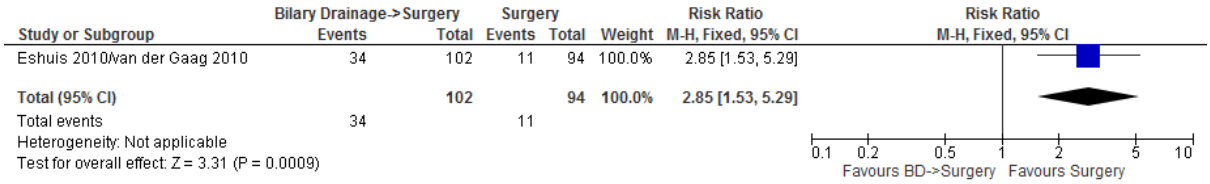


Figure 153: Rate of serious complications (<120 days after randomisation)

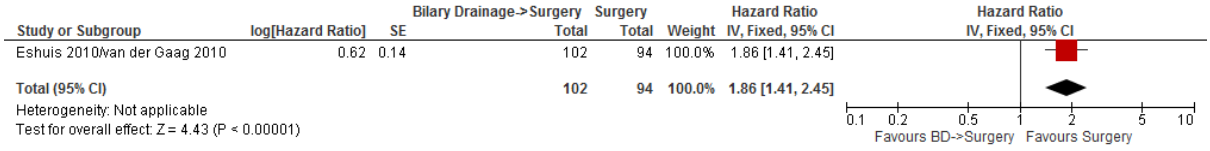


Figure 154: Total number of patients with protocol-specific complications

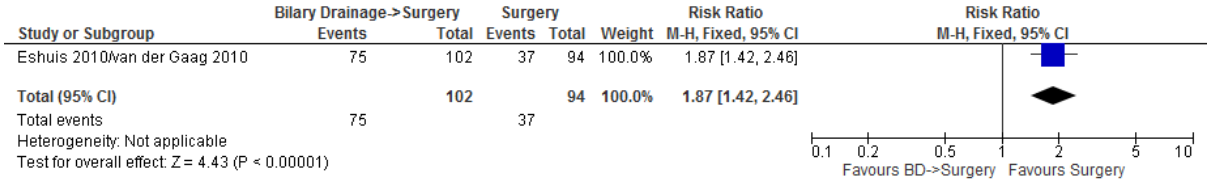


Figure 155: Total number of patients with stent dysfunction

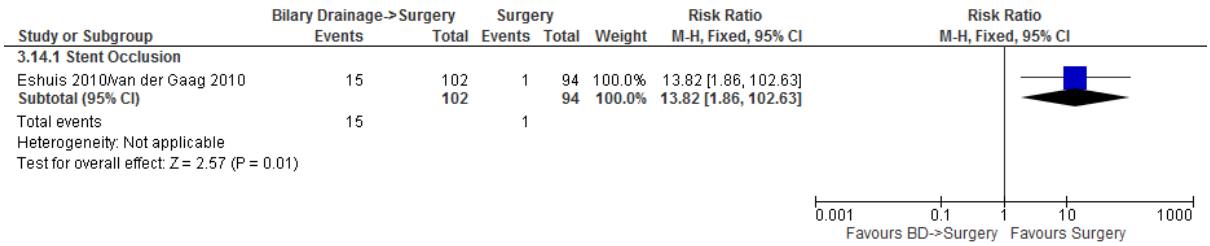


Figure 156: Total number of patients with surgery-related complications

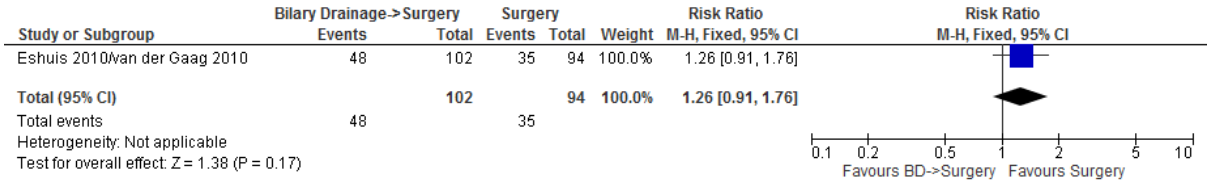


Figure 157: Total number of patients with surgery-related complications – after palliative bypass

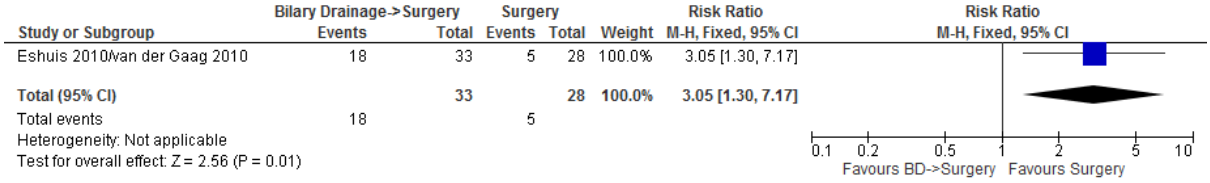
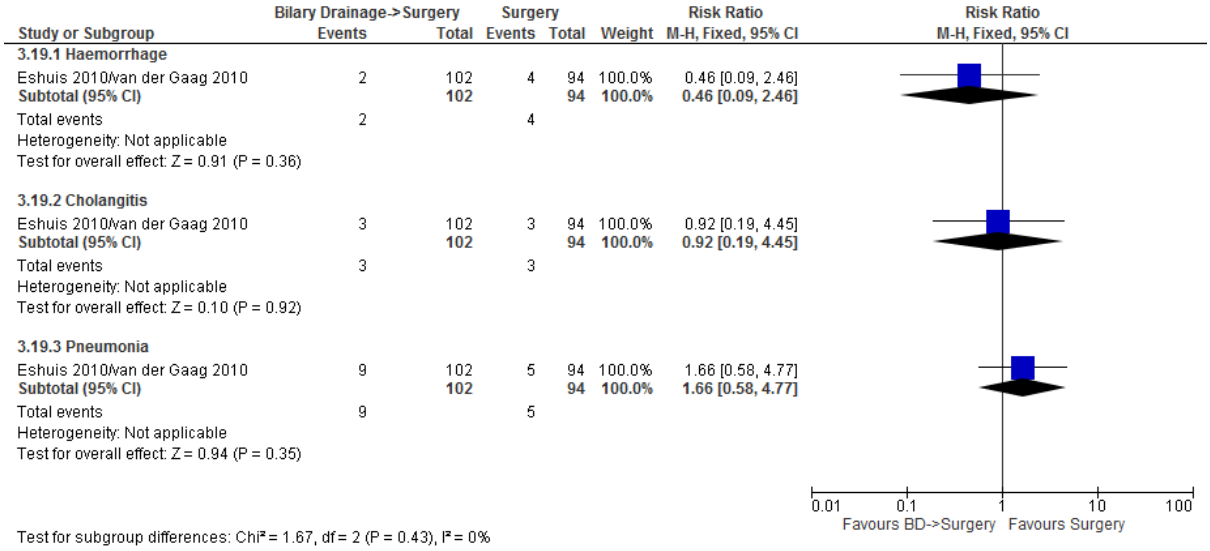


Figure 158: Surgery-related adverse events



H.10.61 Endoscopic sphincterotomy then stent versus stent in adults with 2 unresectable pancreatic cancer

Figure 159: Deaths due to progression of pancreatic cancer

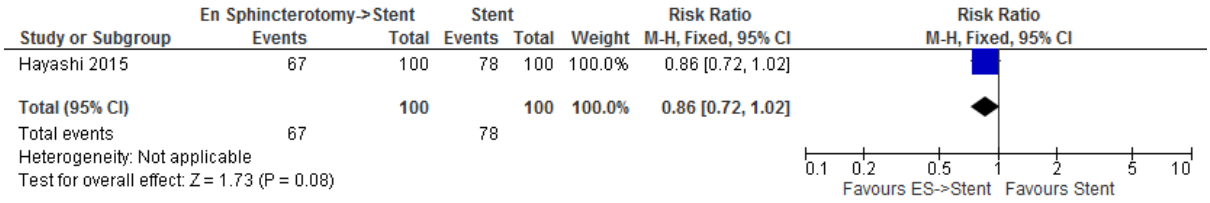


Figure 160: Number of patients with stent dysfunction by type

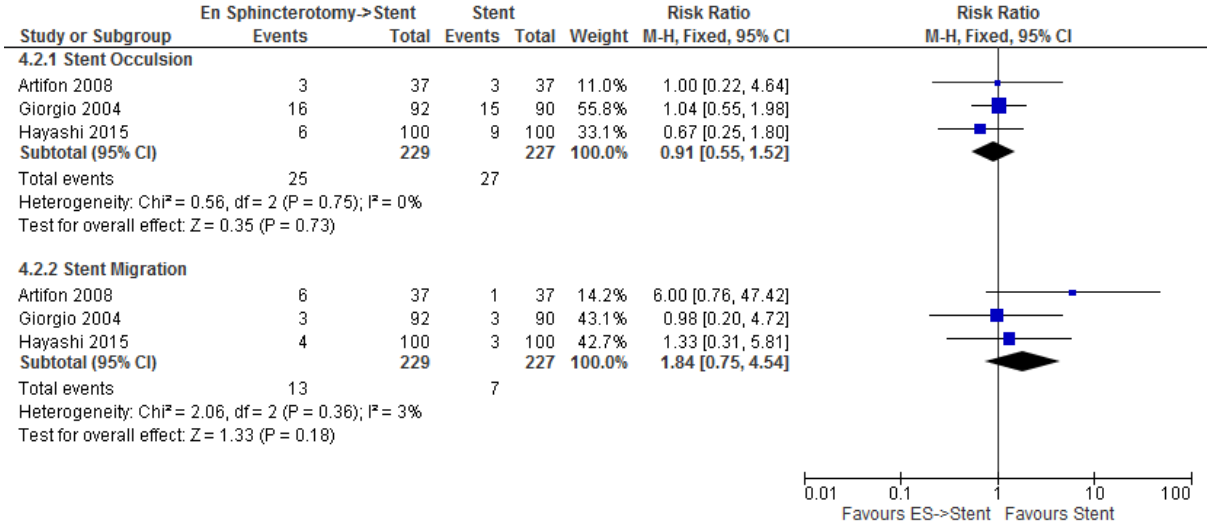


Figure 161: Number of patients with early complications (≤30 days)

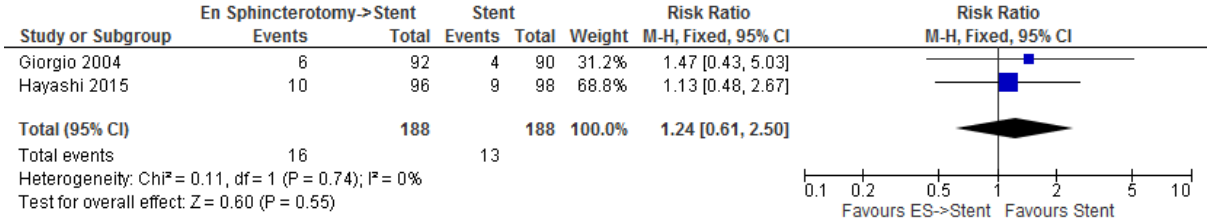


Figure 162: Number of patients with stent-related early complications (≤30 days)

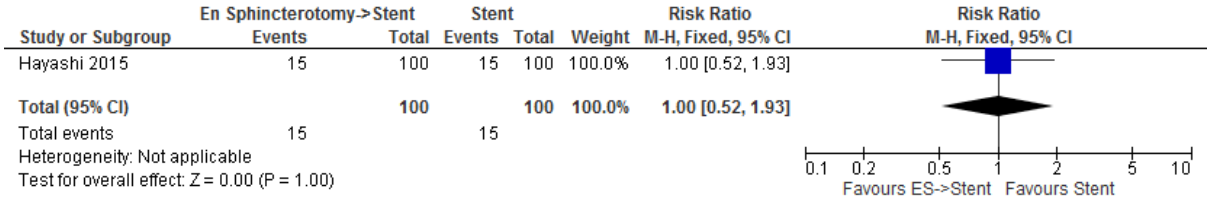


Figure 163: Number of patients with pancreatitis (≤30 days)

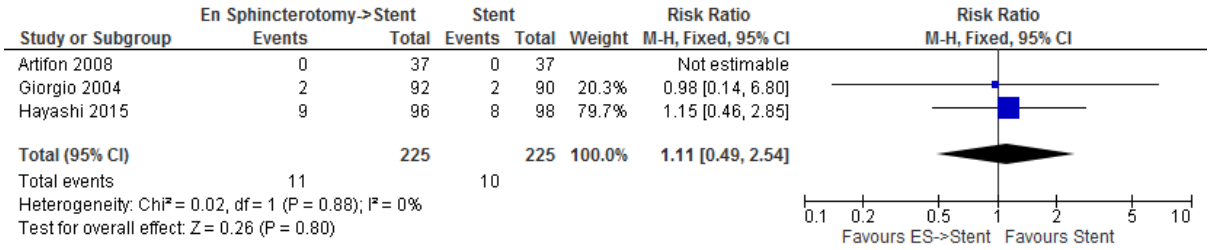


Figure 164: Number of patients with stent-related pancreatitis (≤30 days)

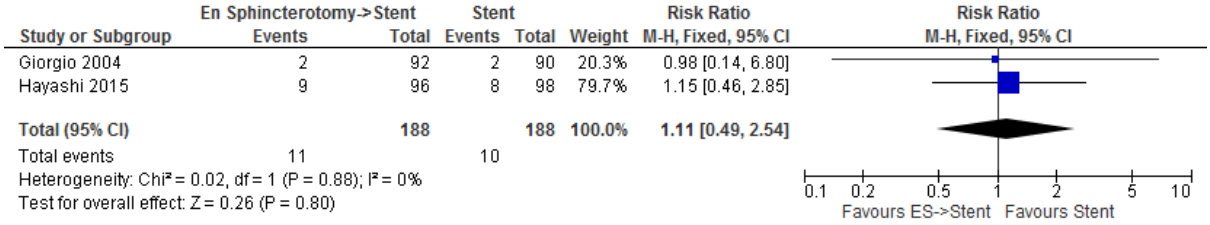


Figure 165: Number of patients with perforation (≤30 days)

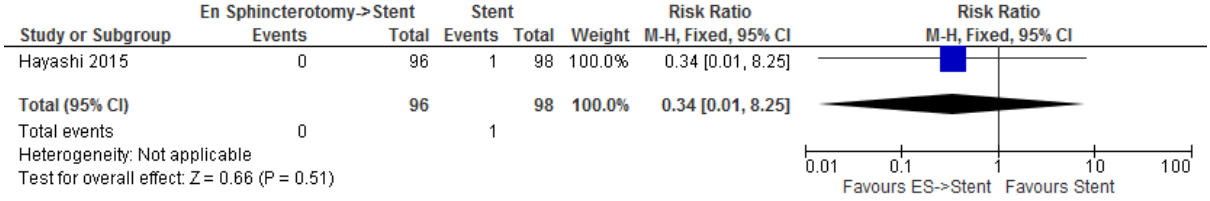


Figure 166: Number of patients with cholecystitis (≤30 days)

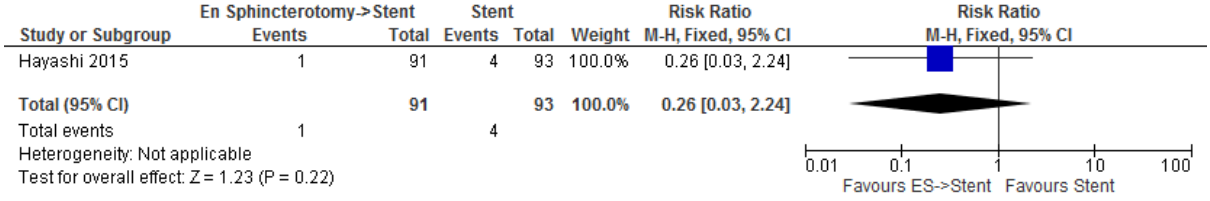


Figure 167: Number of patients with stent-related late complications (>30 days)

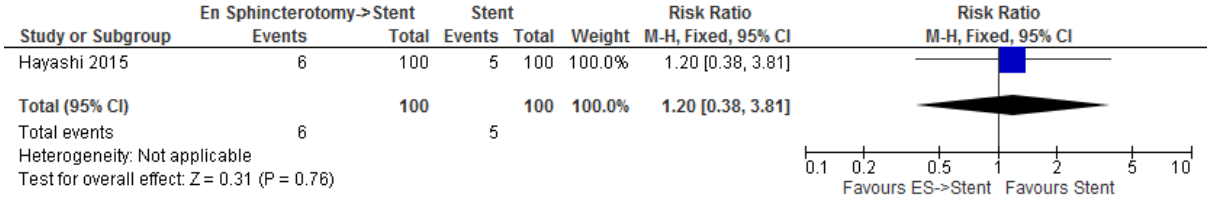


Figure 168: Number of patients with cholangitis (>30 days)

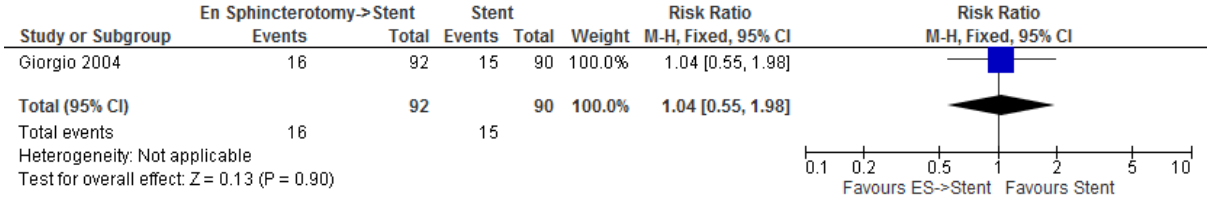
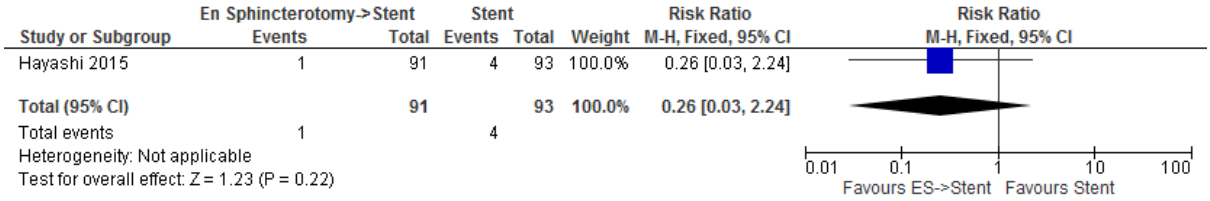


Figure 169: Number of patients with cholecystitis (>30 days)



H.10.71 Endoscopic sphincterotomy then stent versus surgical bypass in adults with 2 unresectable pancreatic cancer

Figure 170: Relief of biliary obstruction

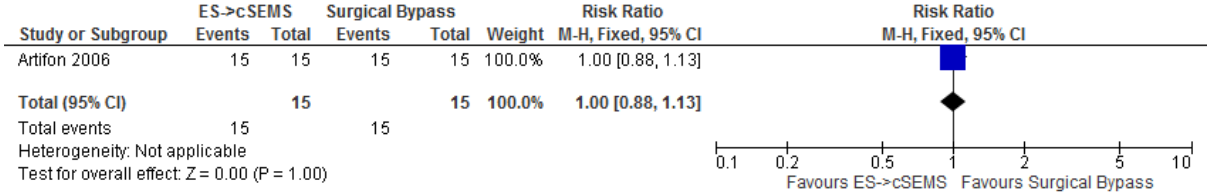


Figure 171: Treatment-related morbidity

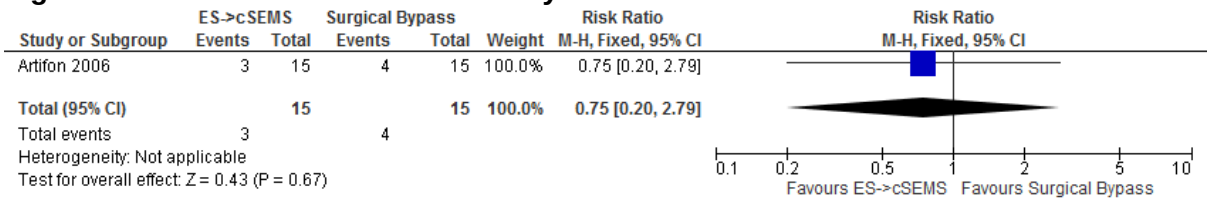


Figure 172: Treatment-related hospitalisation

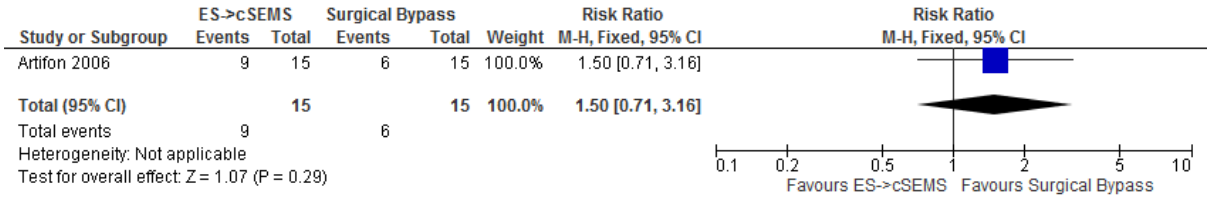


Figure 173: Number of patients with bilirubin level <2.5 mg/dL at day 30

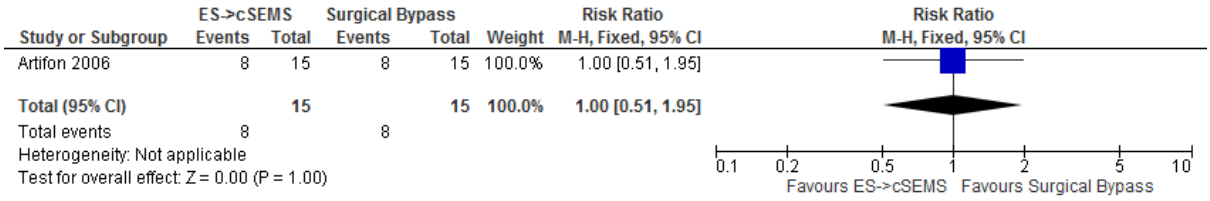


Figure 174: Serum bilirubin level at 30 days

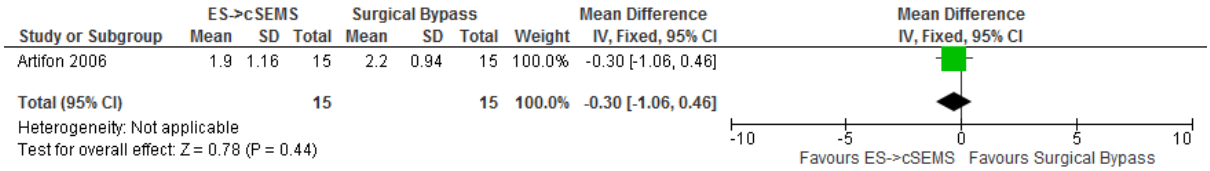


Figure 175: Number of patients with stent-related complications

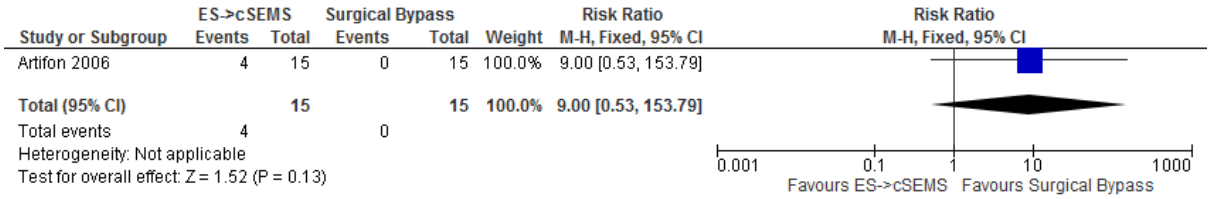


Figure 176: Treatment-related early complications

Figure 177: Treatment-related late complications

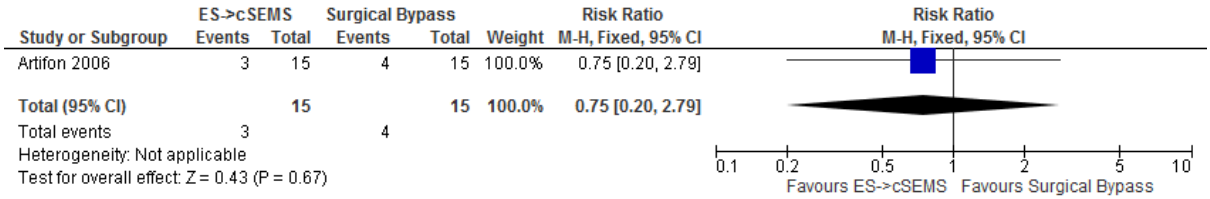


Figure 178: Post-operative complications

Figure 179: Number of patients with pneumonia

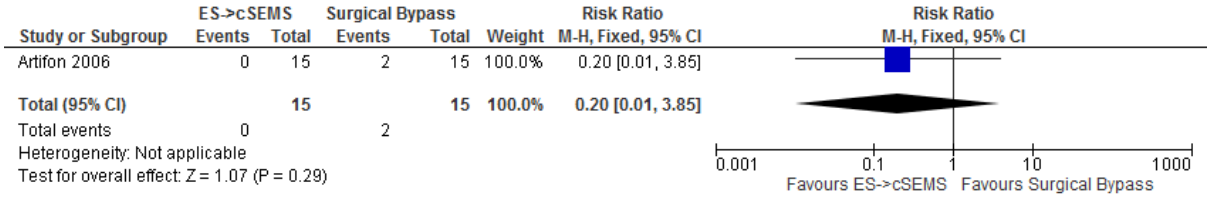


Figure 180: Number of patients with post-ERCP pancreatitis

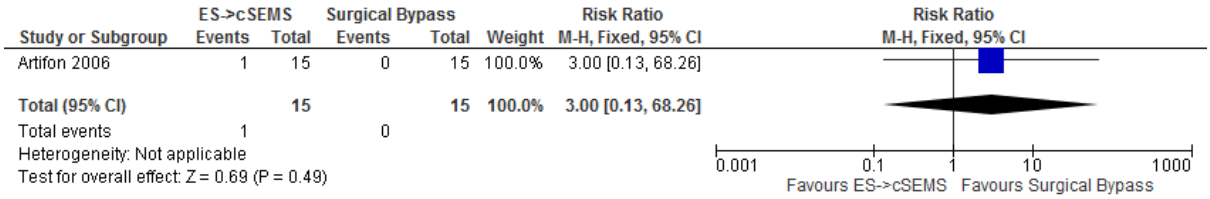
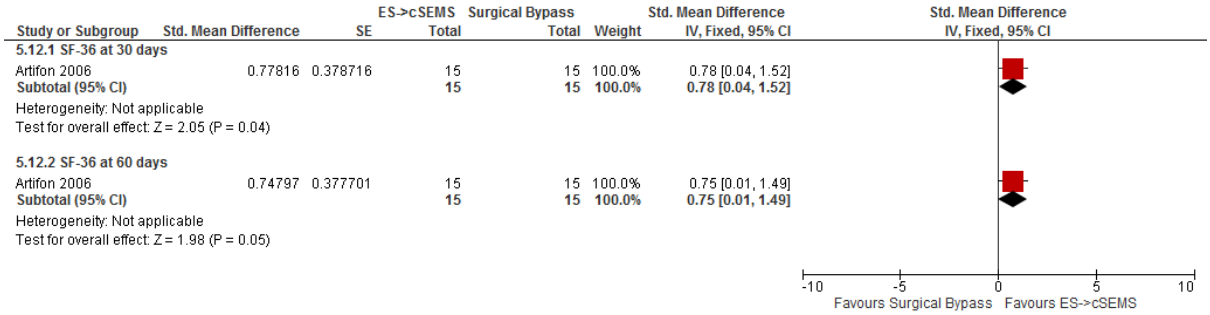


Figure 181: SF-36 Total (Quality of life) at 30 and 60 days



H.10.8 Endoscopic ultrasound-guided choledochoduodenostomy and stent versus percutaneous transhepatic biliary drainage in adults with an unresectable malignant biliary obstruction where either ERCP or EUS-guided transpapillary rendezvous has failed

Figure 182: Total serum bilirubin at 7 and 30 days

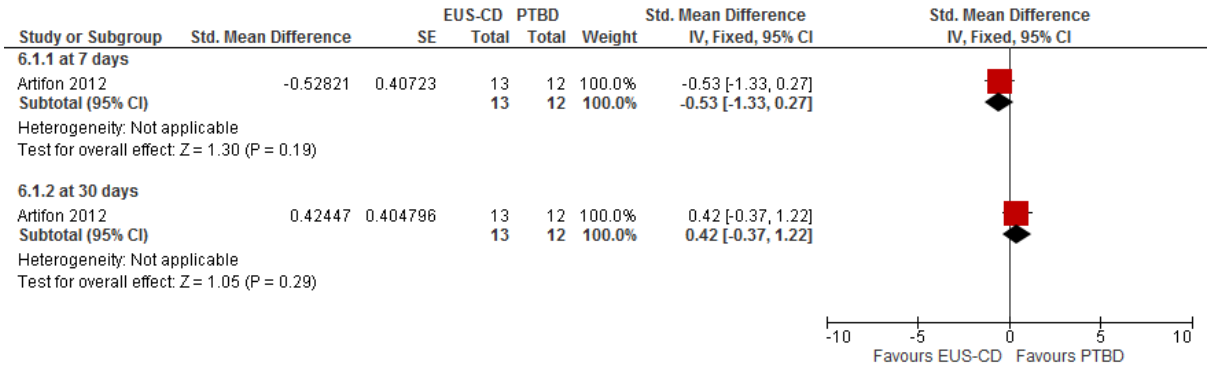


Figure 183: Treatment-related complications

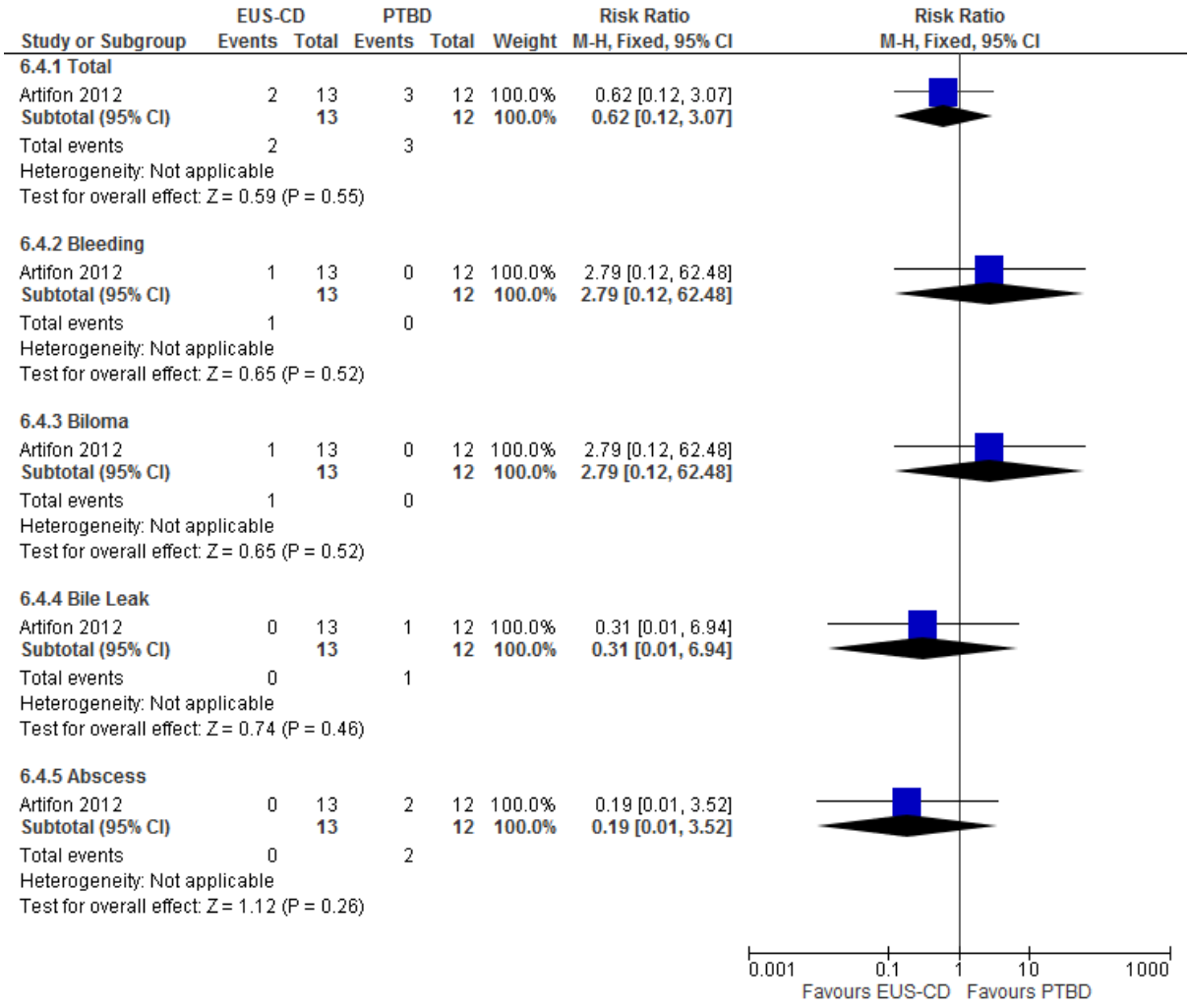
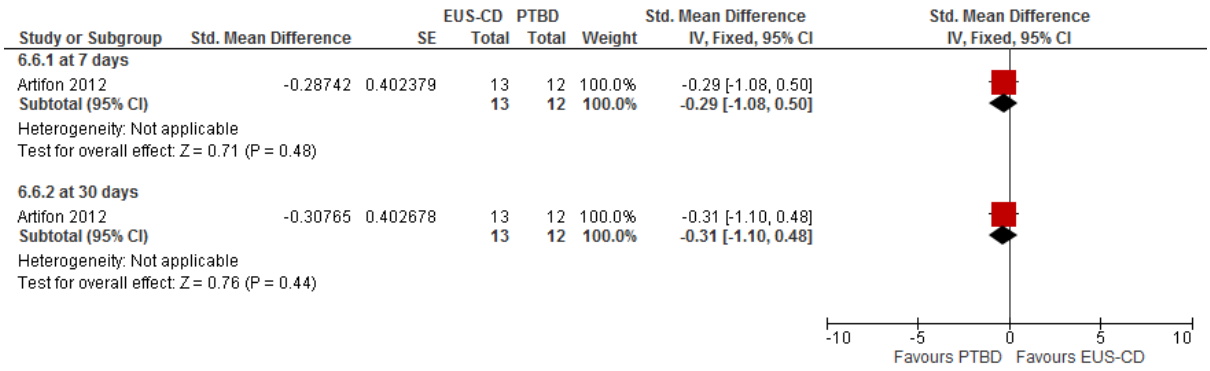


Figure 184: SF-36 Total (Quality of life)



H.10.9 Endoscopic ultrasound-guided choledochoduodenostomy and stent versus surgical bypass in adults with an unresectable malignant biliary obstruction where ERCP has failed

Figure 185: Number of patients with ≥50% reduction in total serum bilirubin after 7 days

Figure 186: Total serum bilirubin at 7, 30, 60 and 90 days

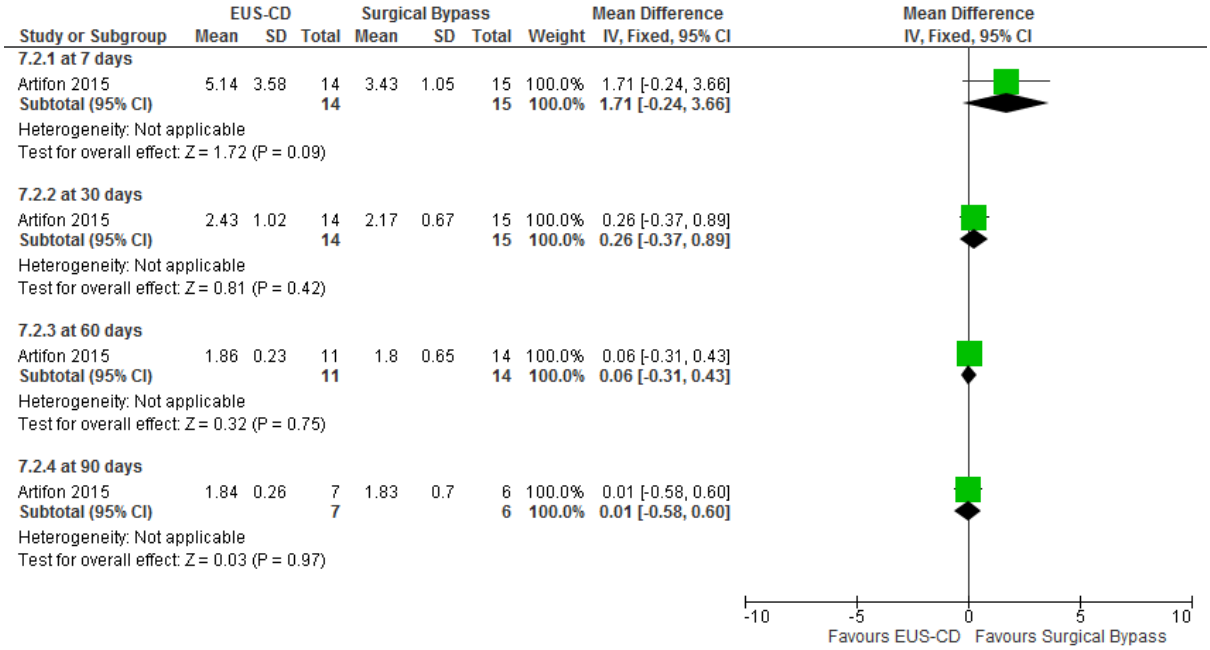


Figure 187: Treatment-related complications

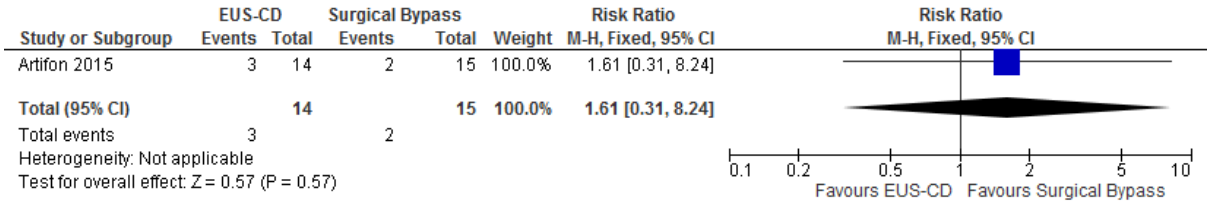


Figure 188: Overall survival 90 days after surgery

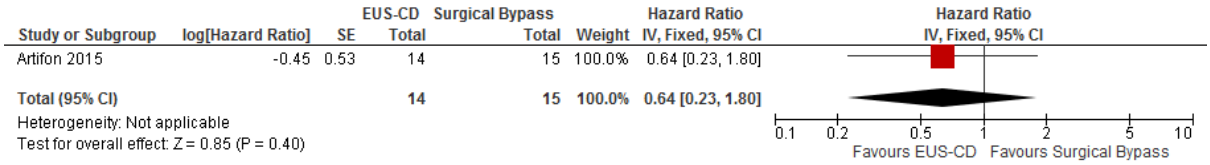


Figure 189: SF-36 Functional capacity at 7, 30, 60 and 90 days

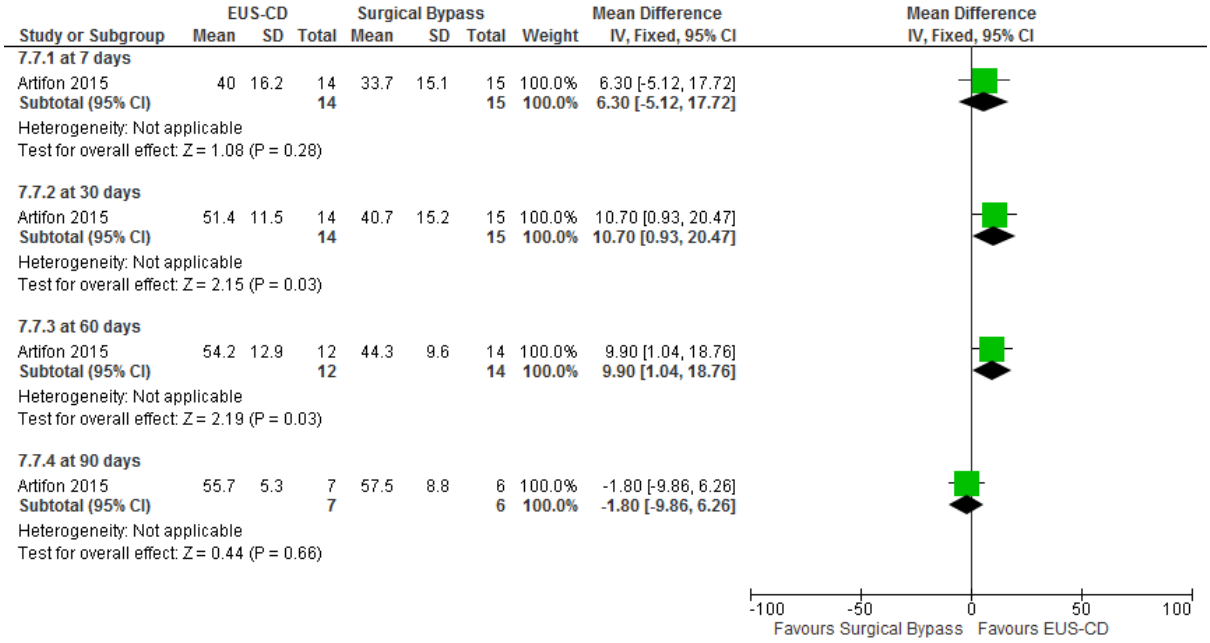


Figure 190: SF-36 Physical health at 7, 30, 60 and 90 days

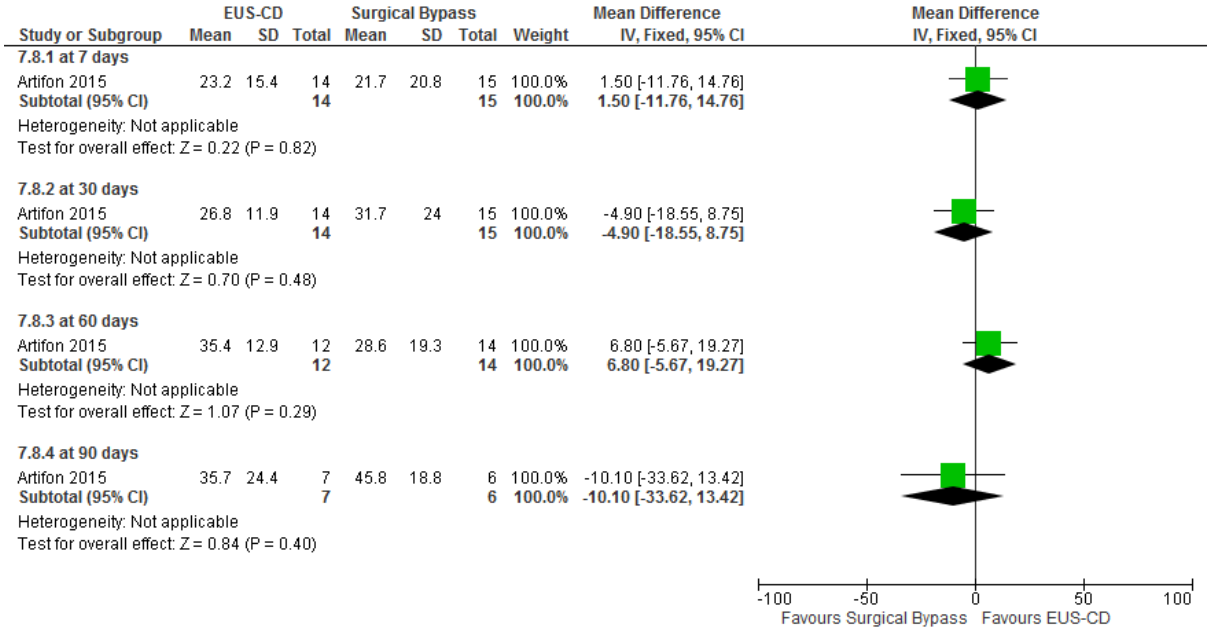


Figure 191: SF-36 Pain at 7, 30, 60 and 90 days

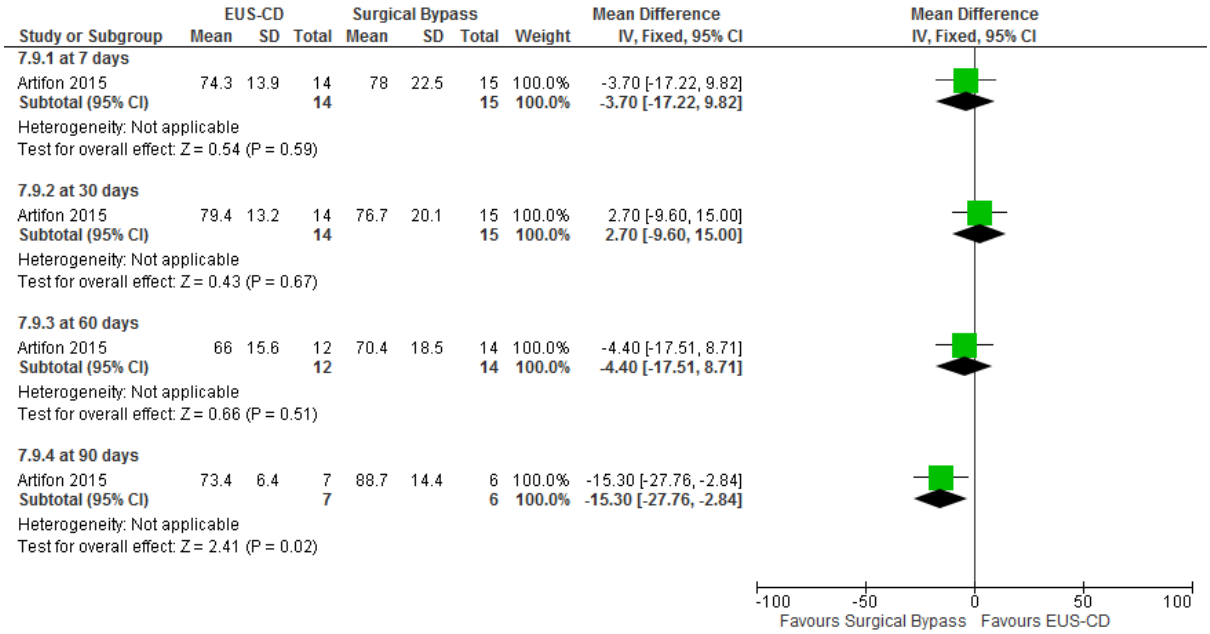


Figure 192: SF-36 General health at 7, 30, 60 and 90 days

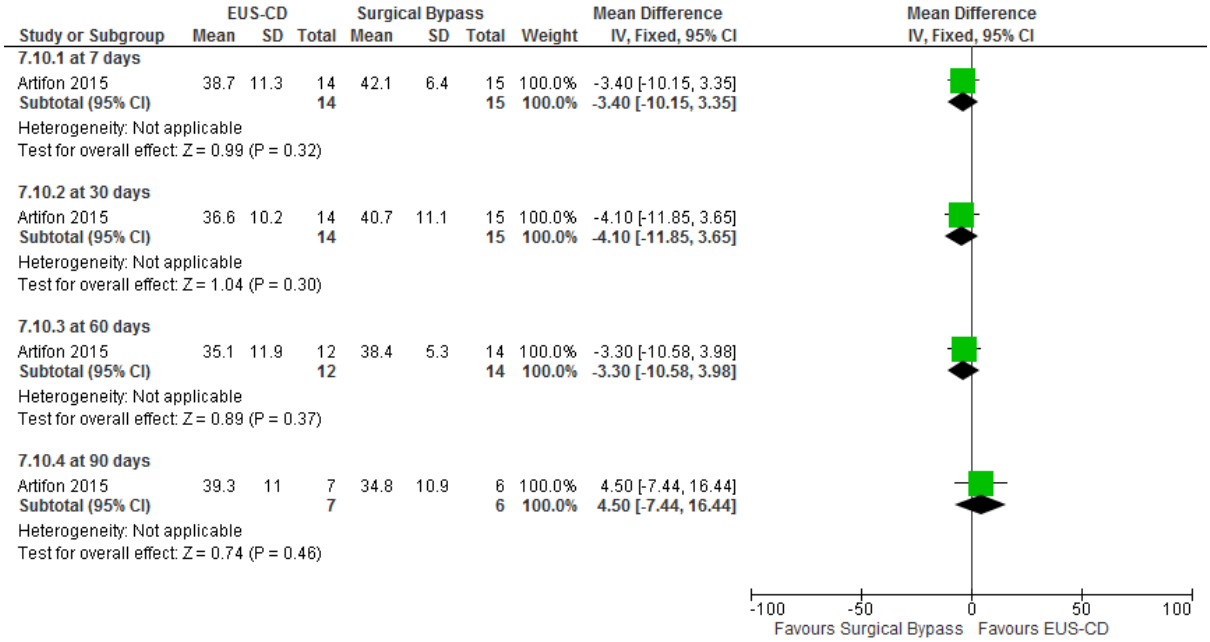


Figure 193: SF-36 Vitality at 7, 30, 60 and 90 days

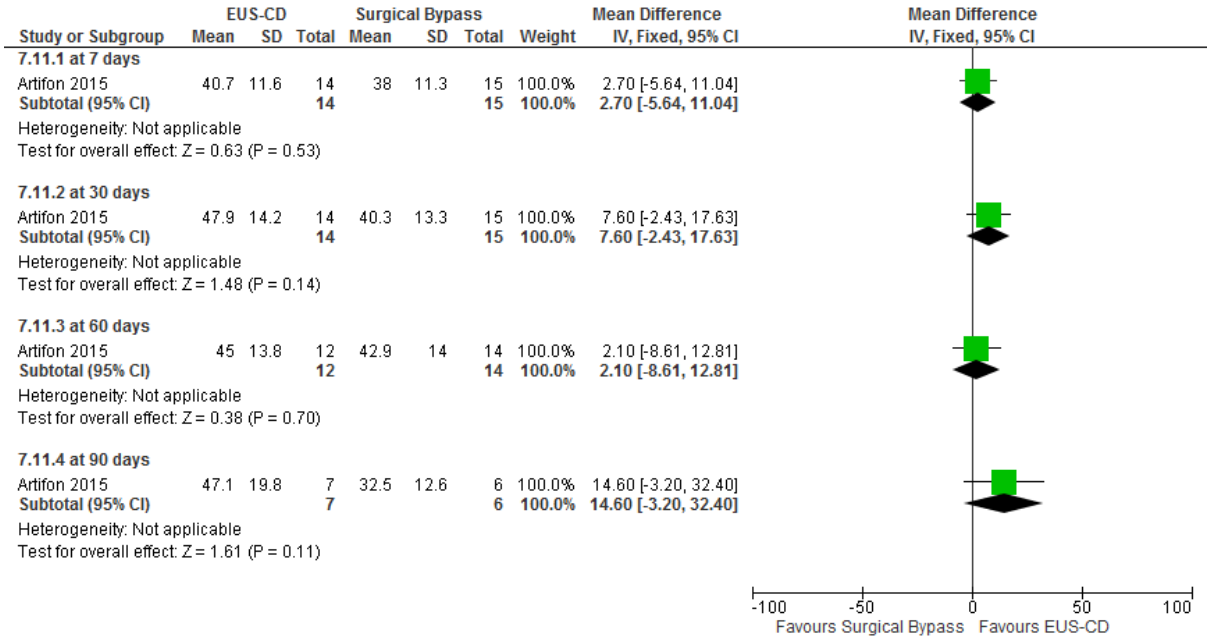


Figure 194: SF-36 Social role functioning at 7, 30, 60 and 90 days

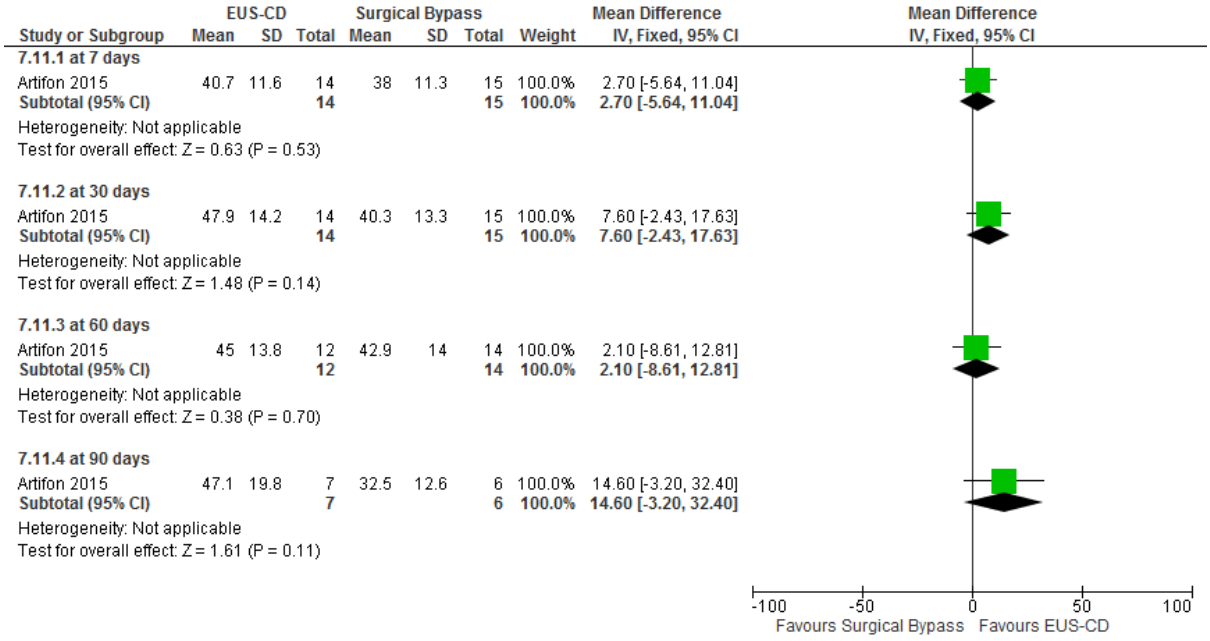


Figure 195: SF-36 Emotional role functioning at 7, 30, 60 and 90 days

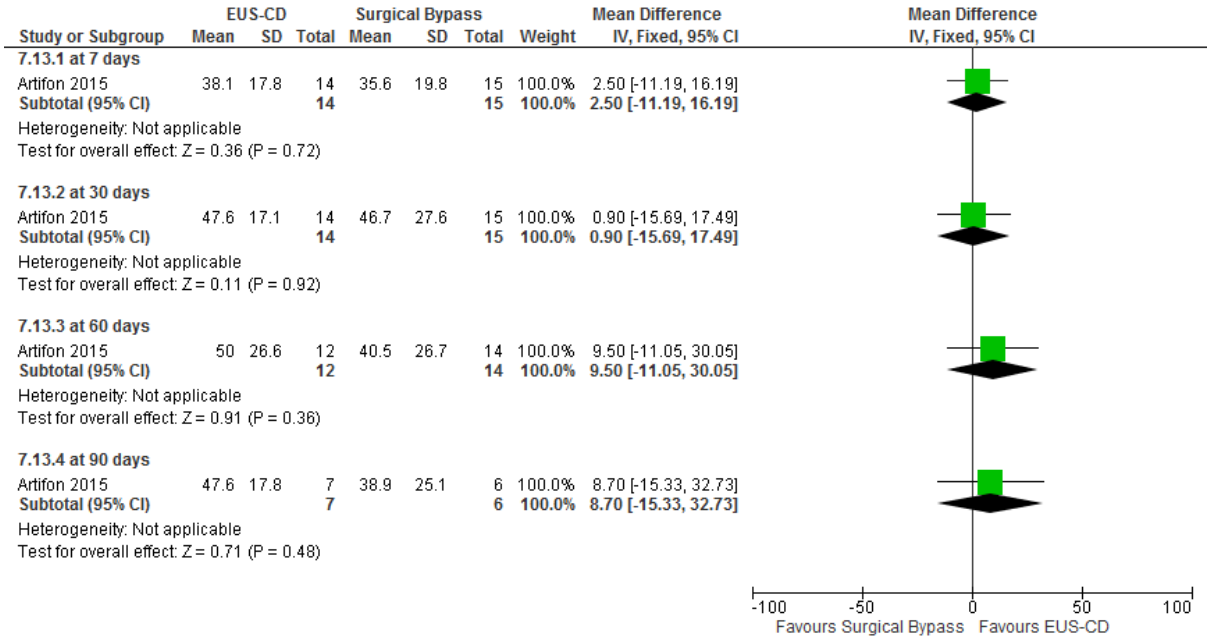
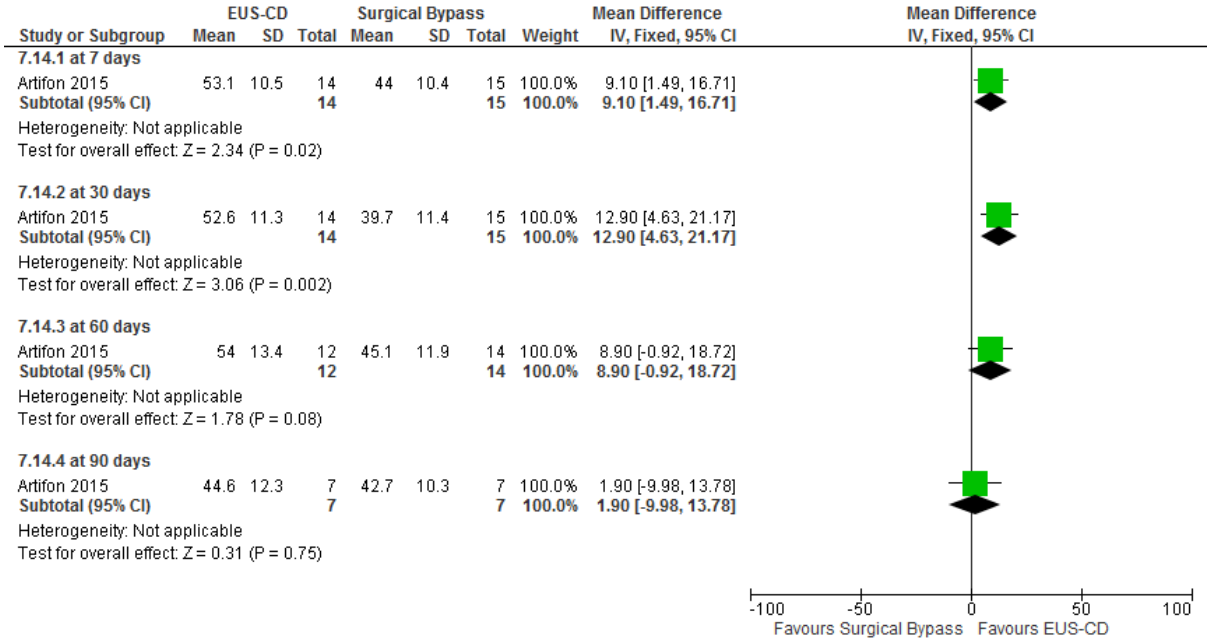


Figure 196: SF-36 Mental Health at 7, 30, 60 and 90 days



H.11 Duodenal obstruction

H.11.1 Prophylactic GJJ and hepaticojejunostomy versus hepaticojejunostomy only

Figure 197: Gastric outlet obstruction at 1 month

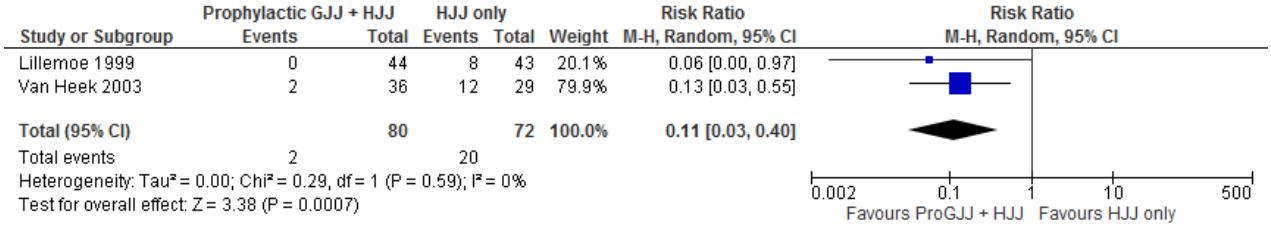


Figure 198: Adverse events (Perioperative morbidity)

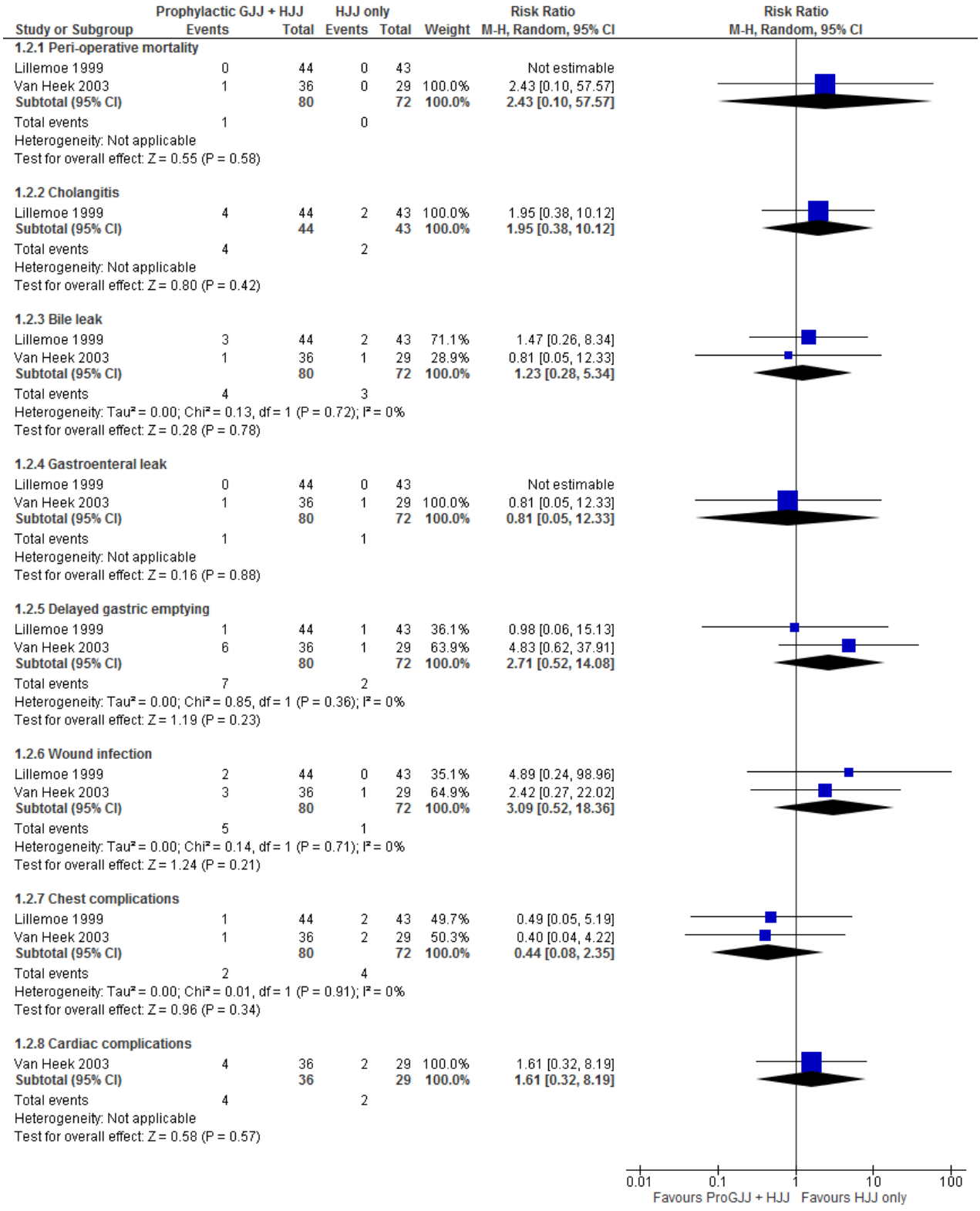
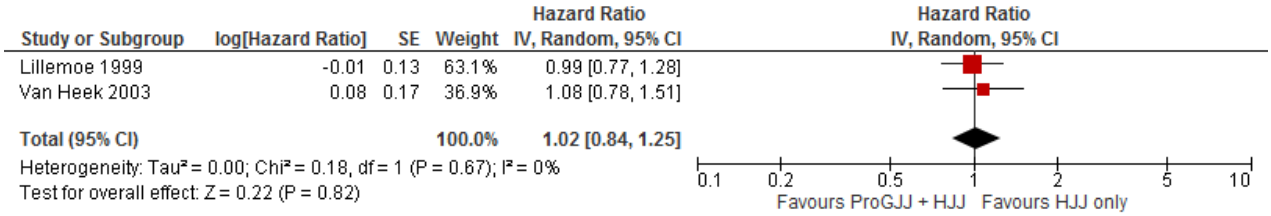
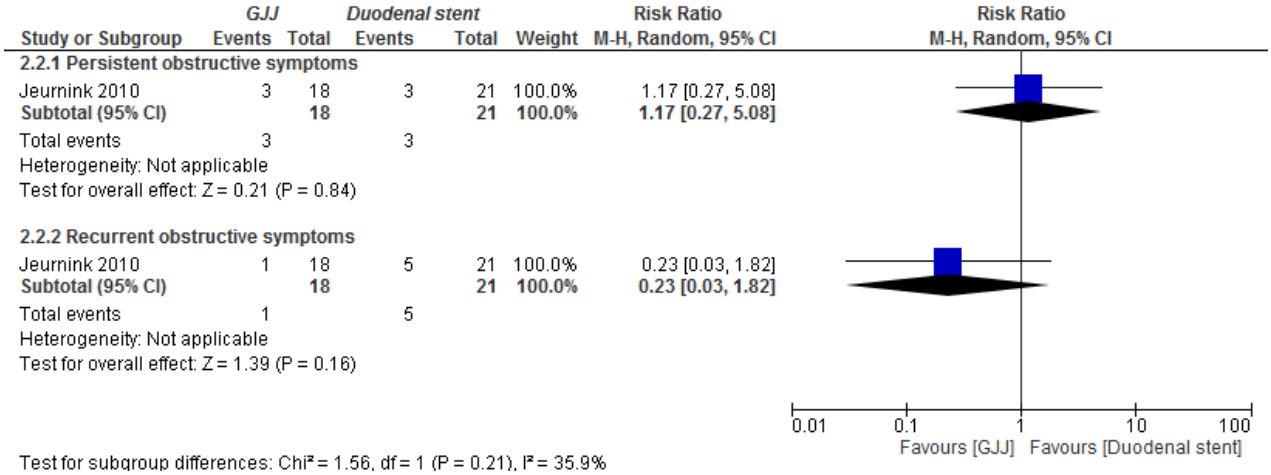


Figure 199: Overall survival



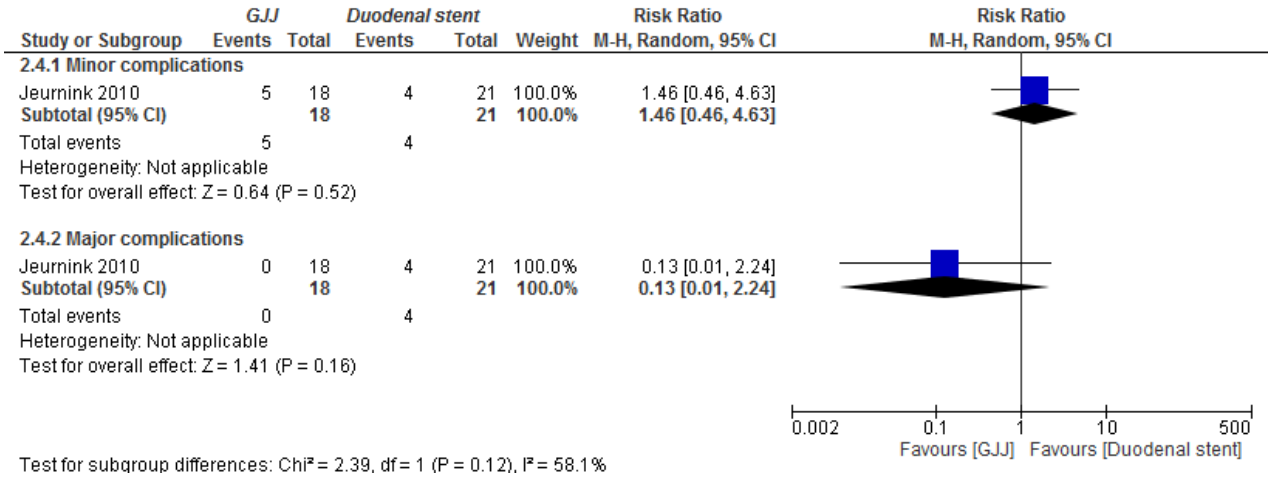
H.11.23 GJJ versus duodenal stent placement

Figure 200: Change in symptoms - Persistent obstructive symptoms



Test for subgroup differences: Chi² = 1.56, df = 1 (P = 0.21), I² = 35.9%

Figure 201: Adverse effects – Minor and Major complications



Test for subgroup differences: Chi² = 2.39, df = 1 (P = 0.12), I² = 58.1%

Figure 202: Overall survival

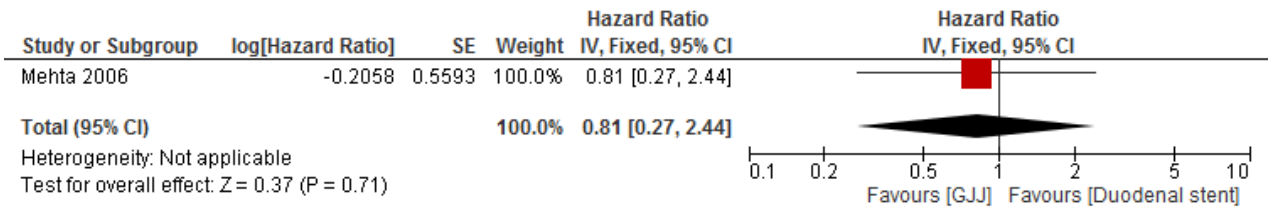


Figure 203: Health-related Quality of Life: SF-36 at 1 month

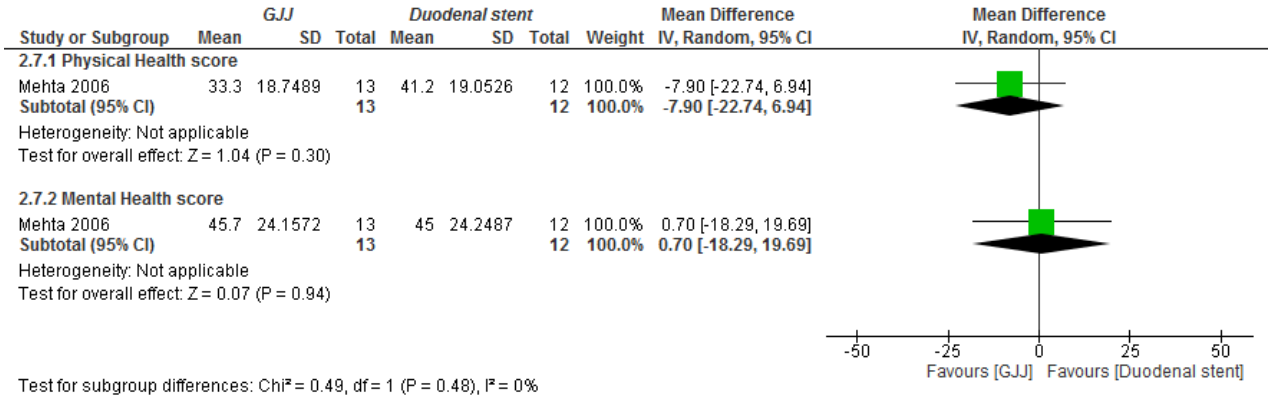
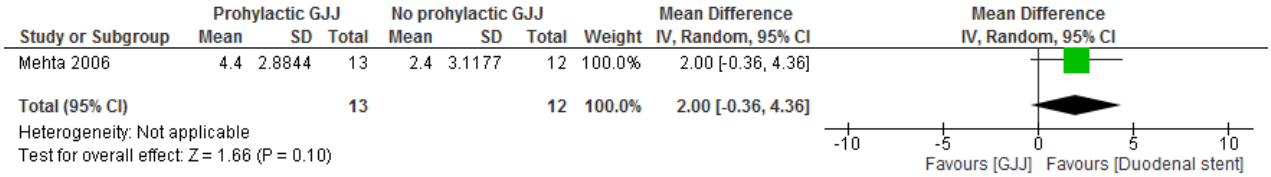


Figure 204: PROMS - Self-report Pain (Visual Analog Scale) at 1 month



H.11.3 Type I GJJ (proximal to the Jejunal limb: Ligament of Treitz) versus Type II GJJ (Pylorus)

Figure 205: Change in symptoms (Clinical symptoms of GOO)

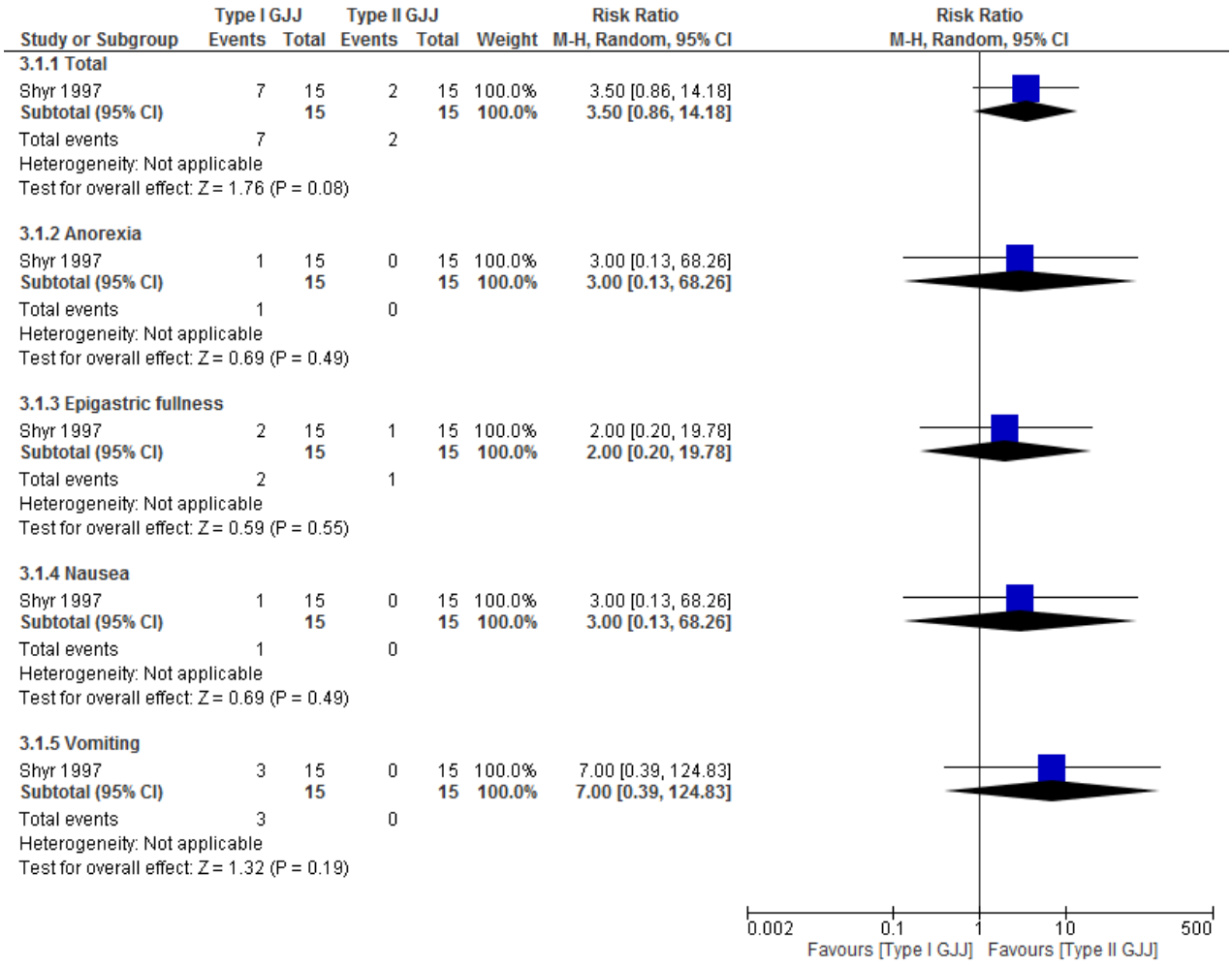


Figure 206: Nutritional status - Gastric emptying time (minutes)

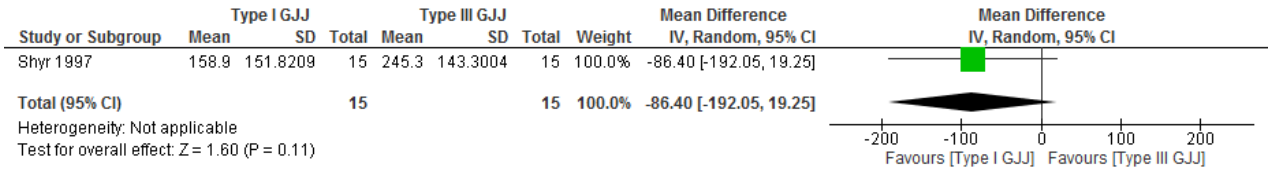
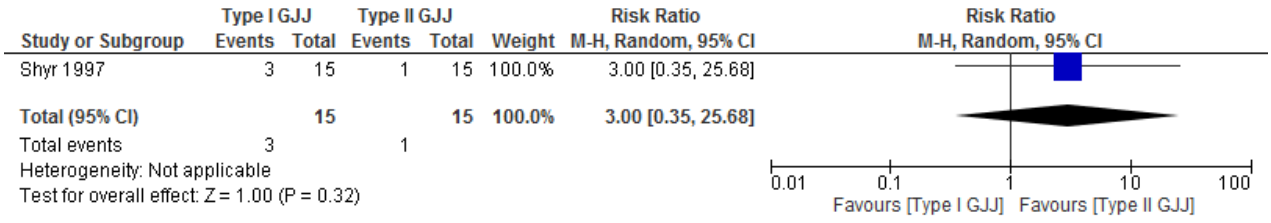
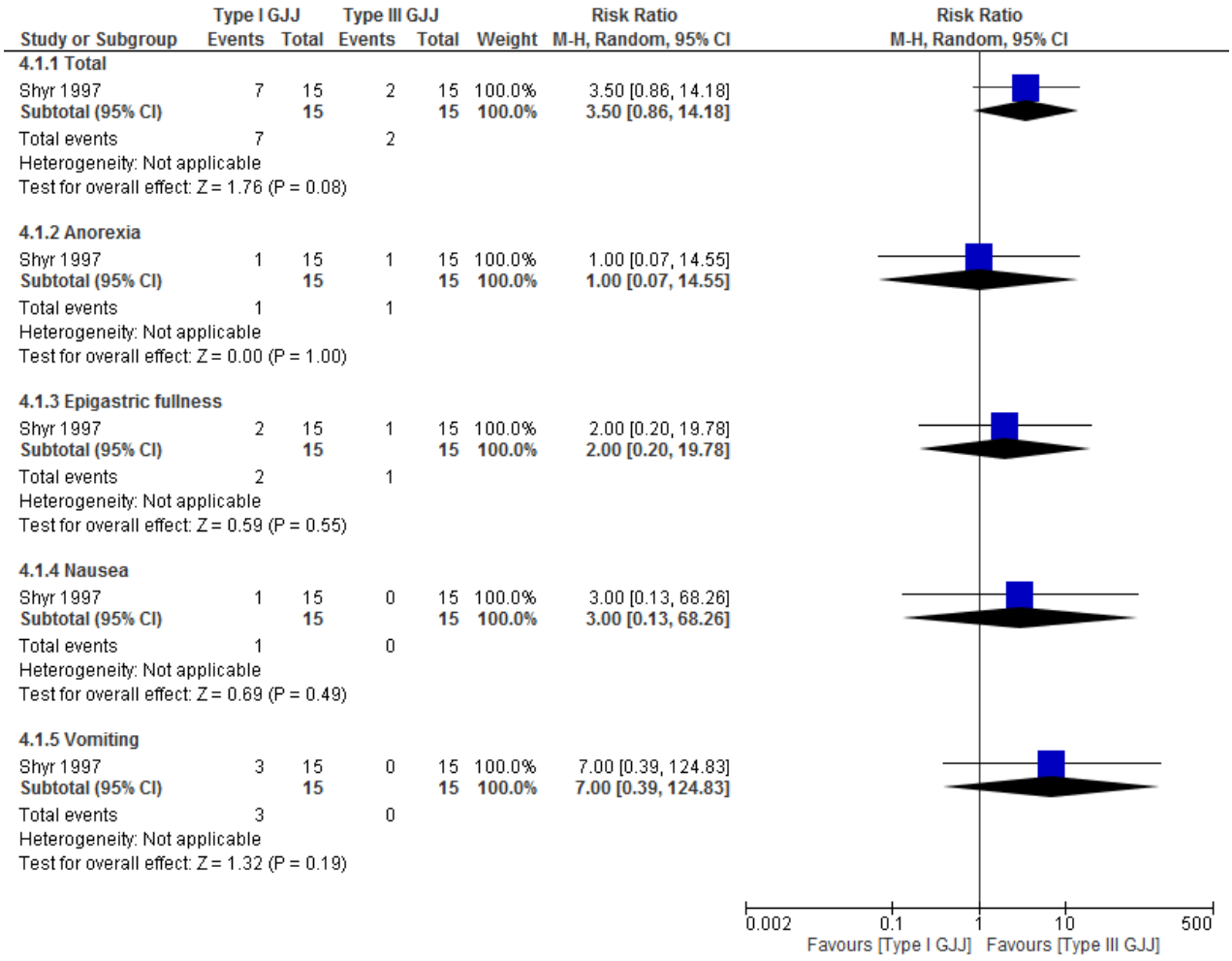


Figure 207: Nutritional status - Patients with delayed gastric emptying

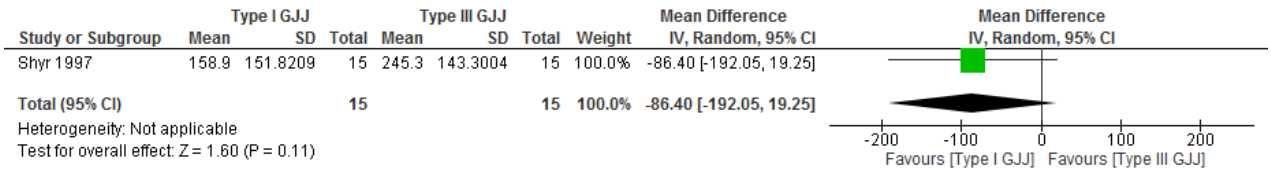


H.11.41 Type I GJJ (proximal to the Jejunal limb: Ligament of Treitz) versus Type III 2 GJJ (proximal to Roux-limb Jejunum)

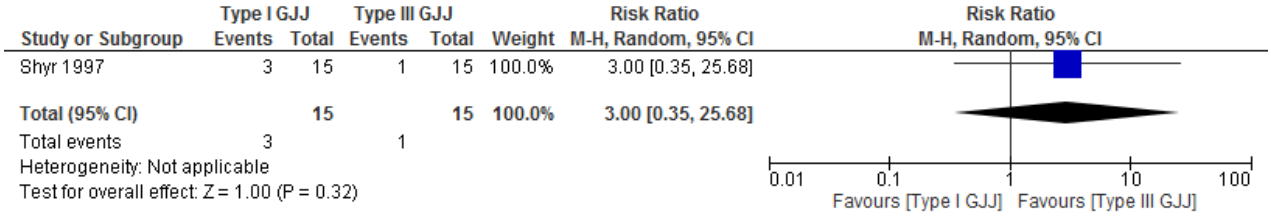
3 Figure 208: Change in symptoms (Clinical symptoms of GOO)



5 Figure 209: Nutritional status - Gastric emptying time (minutes)

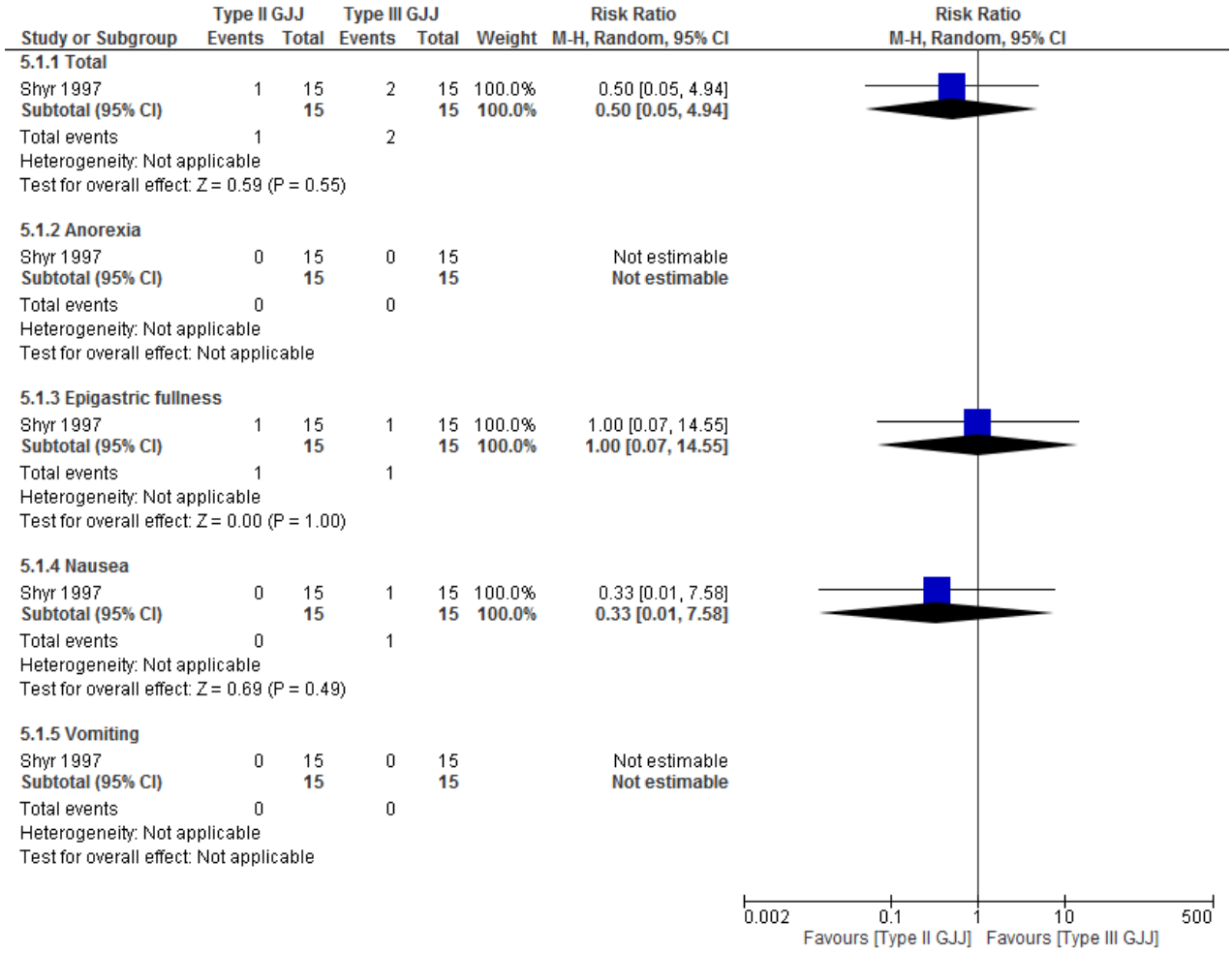


7 Figure 210: Nutritional status - Patients with delayed gastric emptying



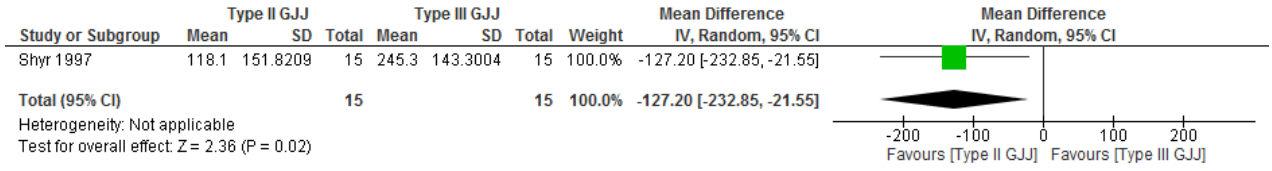
H.11.51 Type II GJJ (Pylorus) versus Type III GJJ (proximal to Roux-limb Jejunum)

2 Figure 211: Change in symptoms (Clinical symptoms of GOO)



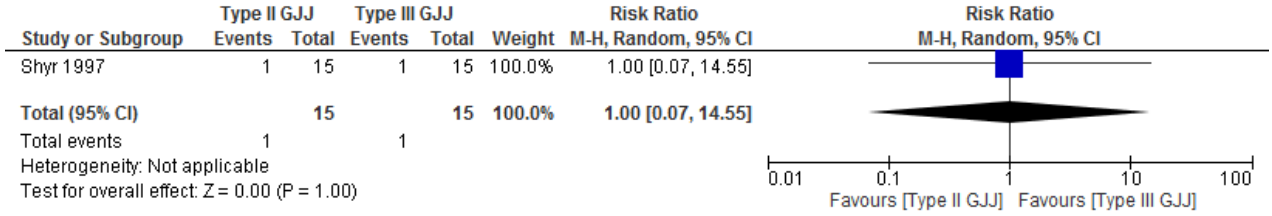
3

4 Figure 212: Nutritional status - Gastric emptying time (minutes)



5

6 Figure 213: Nutritional status - Patients with delayed gastric emptying



7

H.11.61 Duodenal stent-1 versus duodenal stent-2

Figure 214: Relief of obstruction - Duodenal obstruction recurrence

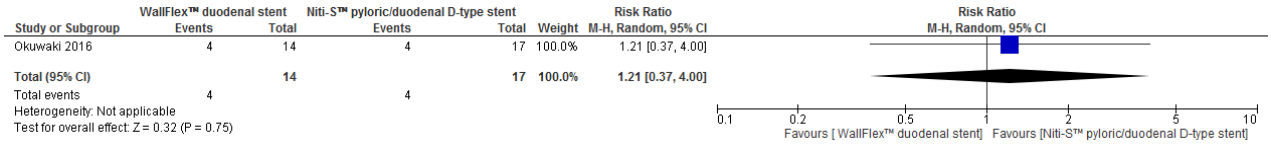


Figure 215: Change in symptoms - Mean change in Nausea and Vomiting Scoring System (NVSS) score

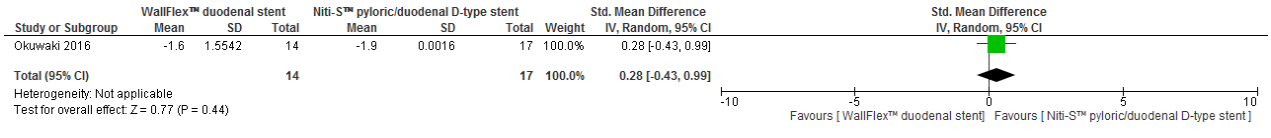


Figure 216: Nutritional status - Mean change in gastric outlet obstruction (GOO) score at 2 weeks recurrence

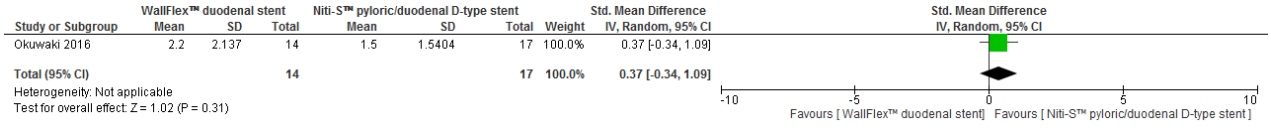


Figure 217: Nutritional status- Mean change in BMI at 4 weeks

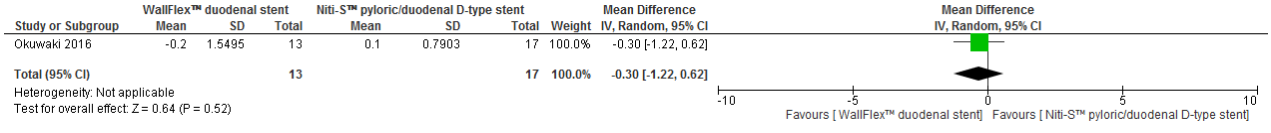


Figure 218: Adverse events (procedure-related)

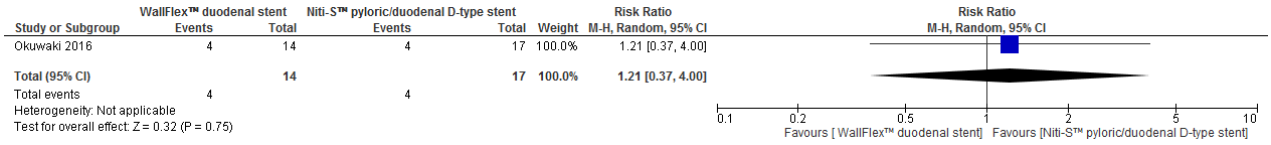


Figure 219: Overall survival

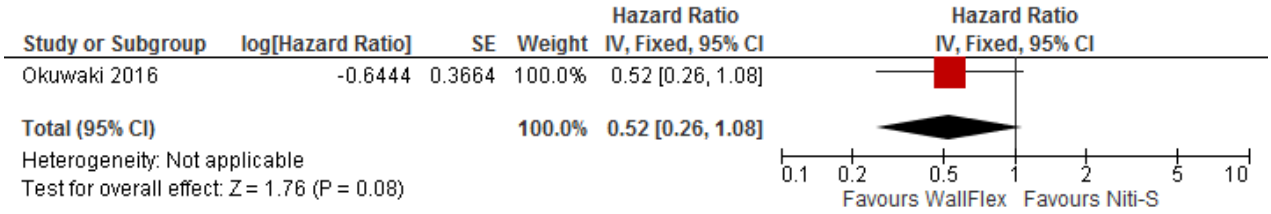


Figure 220: HRQL - Mean change in Karnofsky performance score at 2 weeks

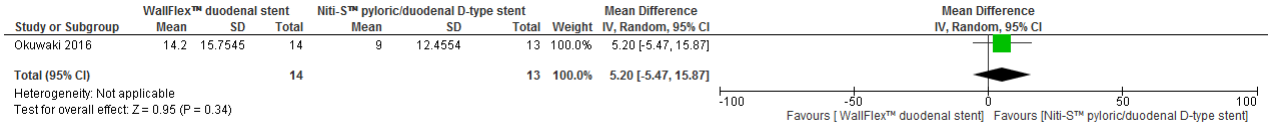
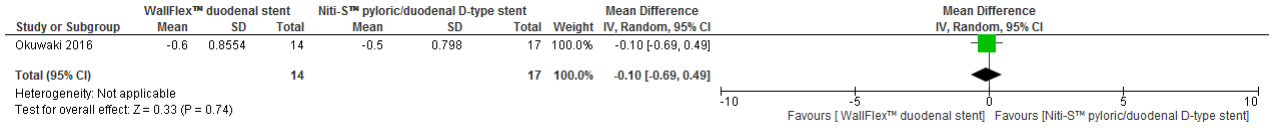


Figure 221: HRQL - Mean change in Performance score at 2 weeks



H.12 Neo-adjuvant treatment

H.12.1 Neoadjuvant chemoradiotherapy followed by surgery versus surgery alone in adults with resectable pancreatic cancer

Figure 222: R0 resection rate

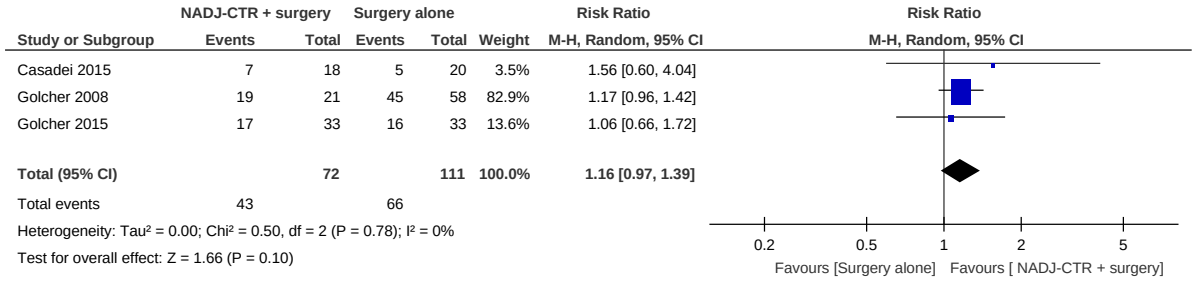


Figure 223: Overall survival

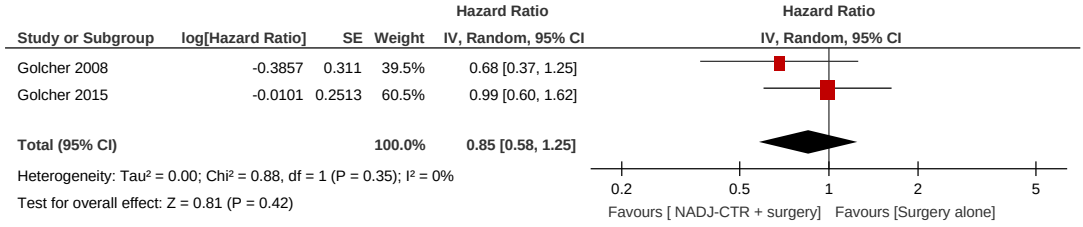


Figure 224: Postoperative complications

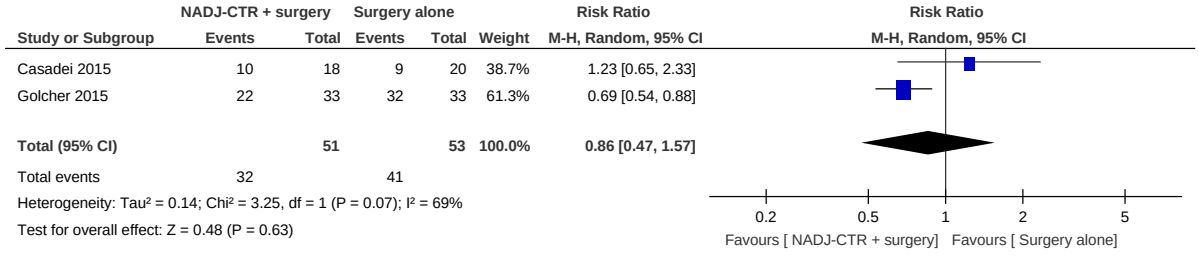


Figure 225: Postoperative complications (Pancreatic fistula)

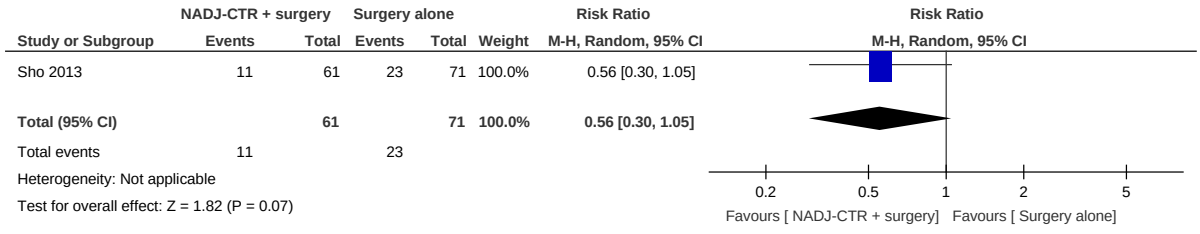
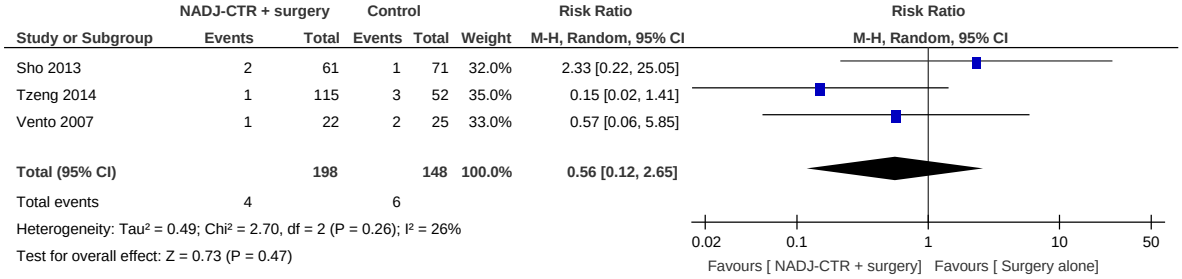


Figure 226: Postoperative complications (Postoperative bleeding)



H.13 Resectable and borderline resectable pancreatic cancer

H.13.1 Minimally invasive (laparoscopic and robotic) pancreaticoduodenectomy versus open pancreaticoduodenectomy

Figure 227: Postoperative Mortality

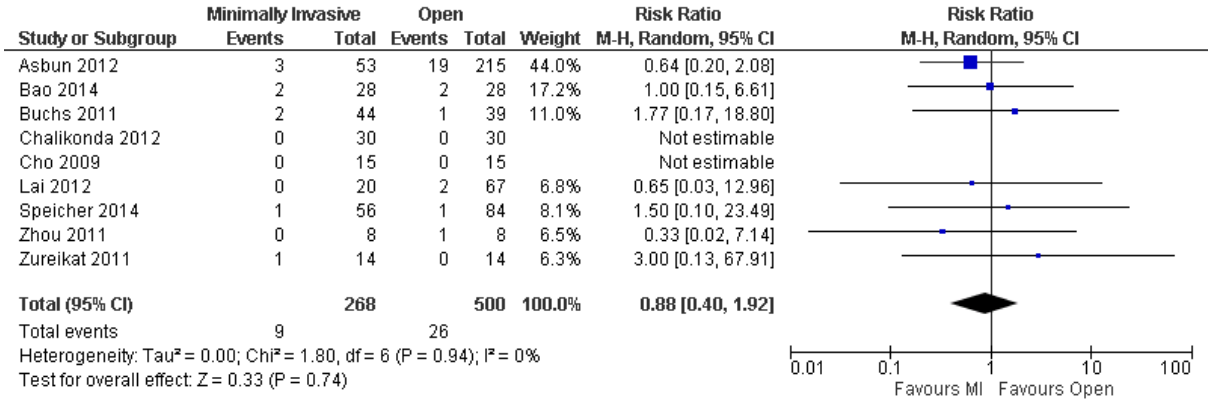


Figure 228: R0 resection rate

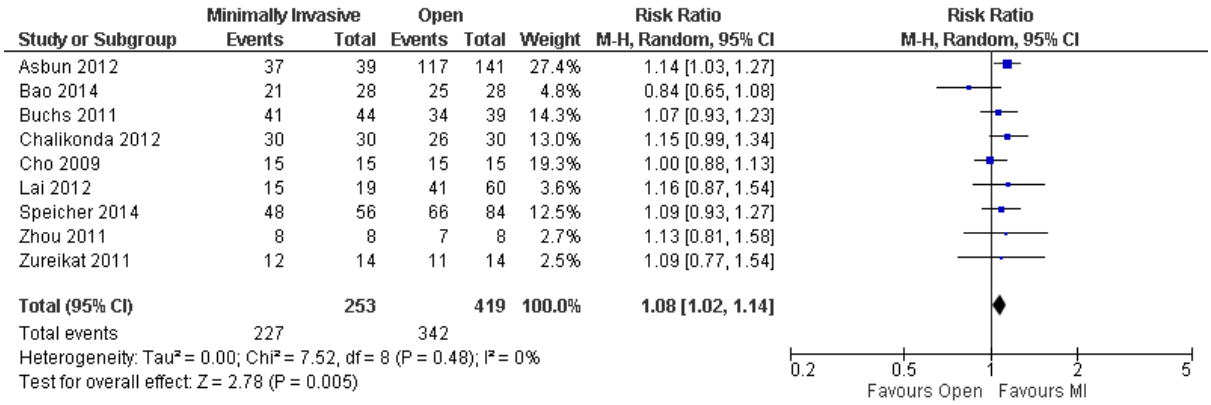


Figure 229: Operation time (mins)

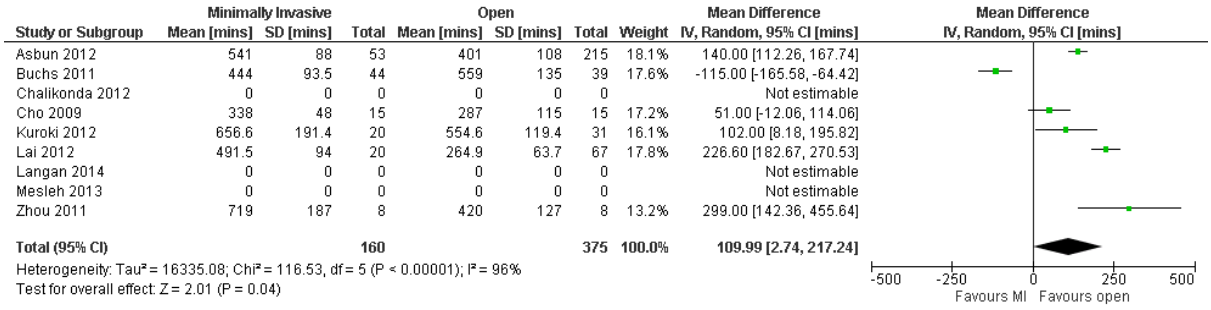


Figure 230: Delayed Gastric Emptying

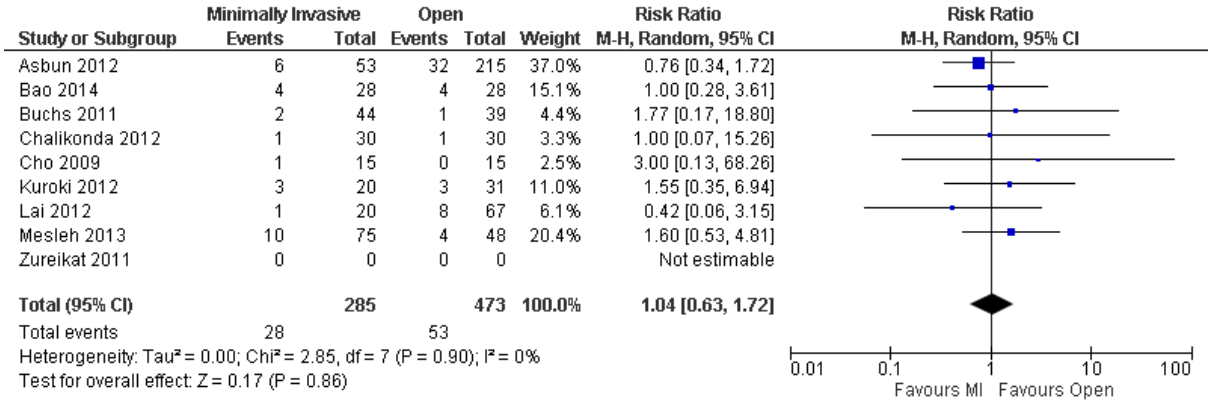


Figure 231: Pancreatic Fistula

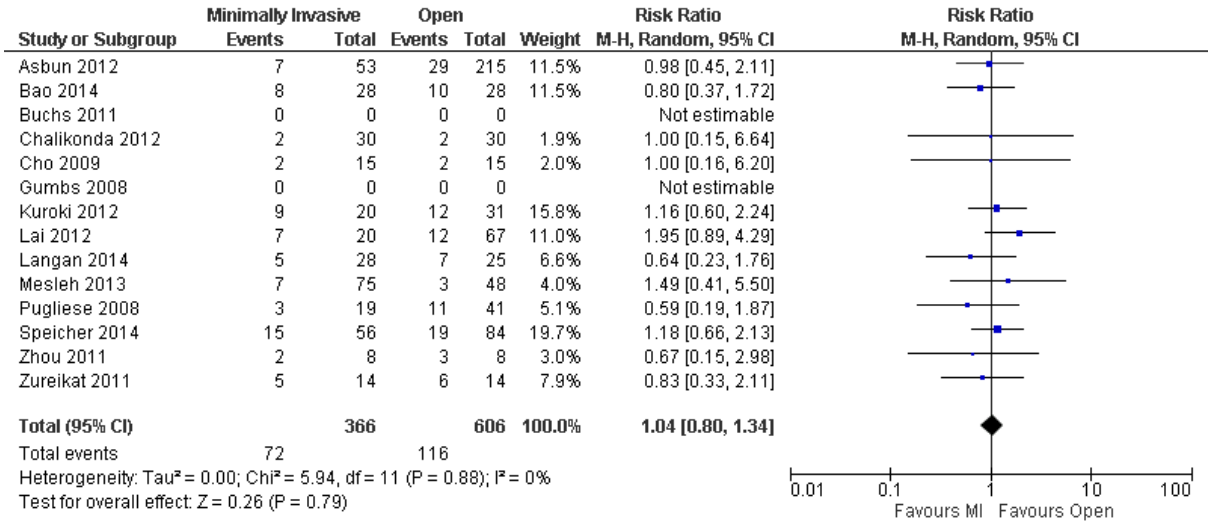


Figure 232: Reoperation

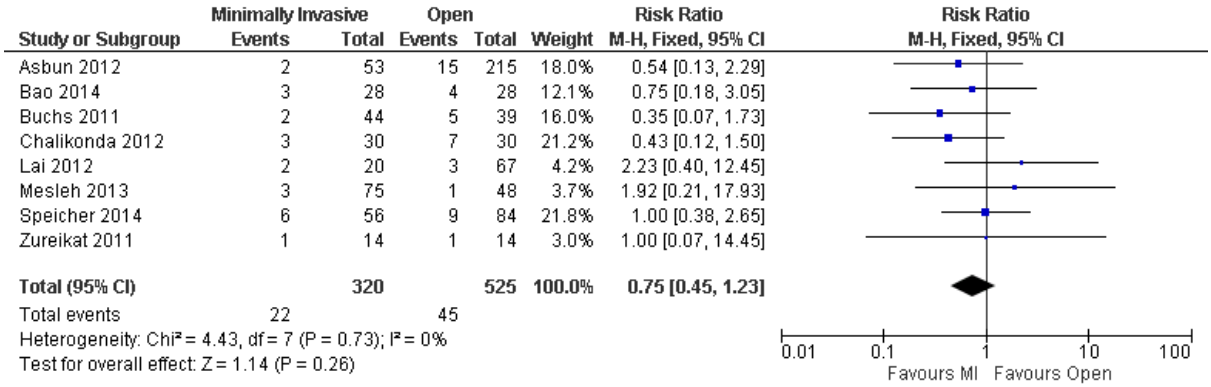


Figure 233: Blood Loss (mls)

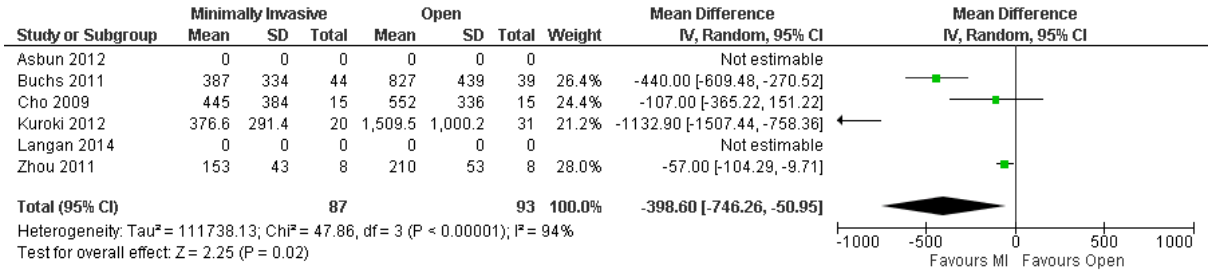
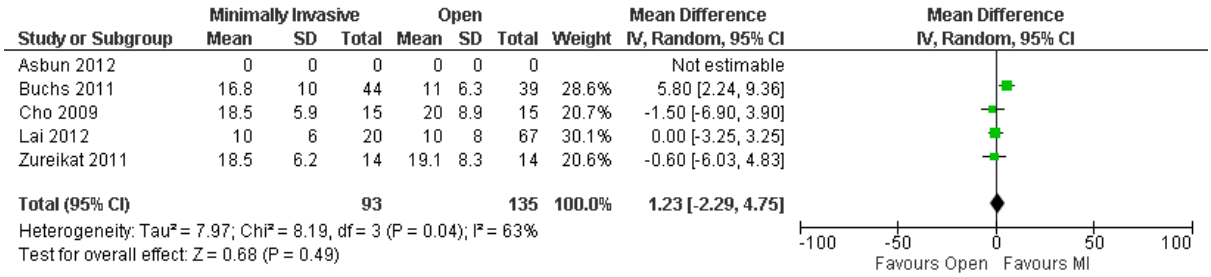


Figure 234: Retrieved Lymph Nodes



H.13.24 Pylorus preserving Whipple versus classic Whipple

Figure 235: Overall Survival (Pancreatic Head Carcinoma)

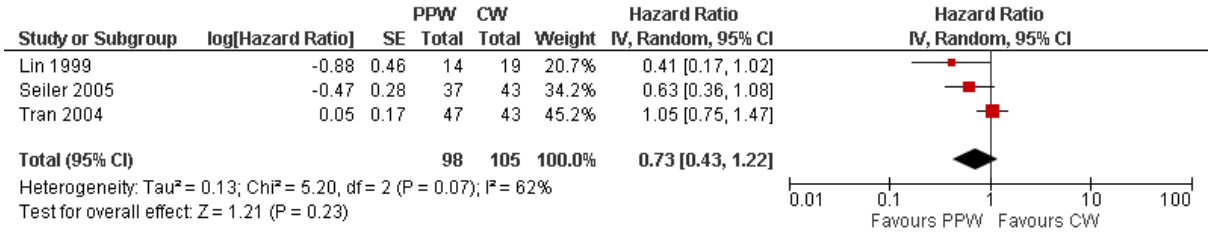


Figure 236: Postoperative Mortality

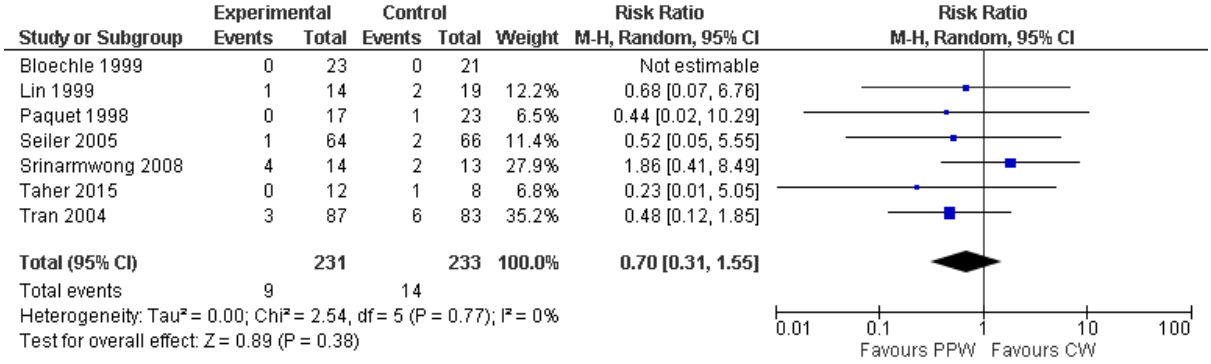


Figure 237: R0 Resection

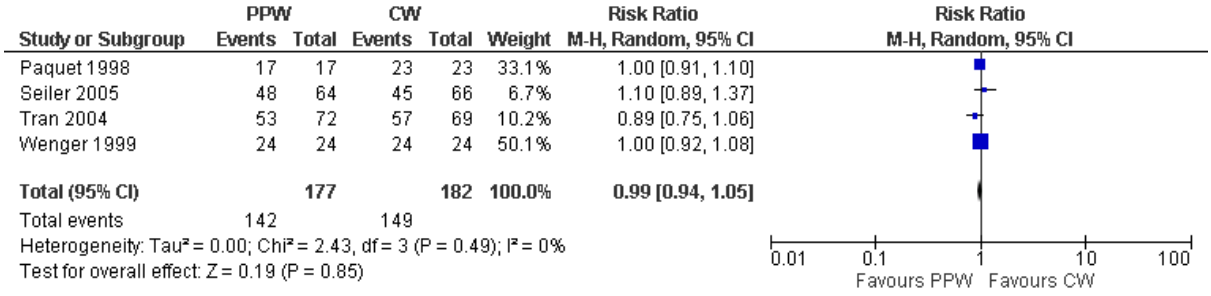


Figure 238: Operating Time (Minutes)

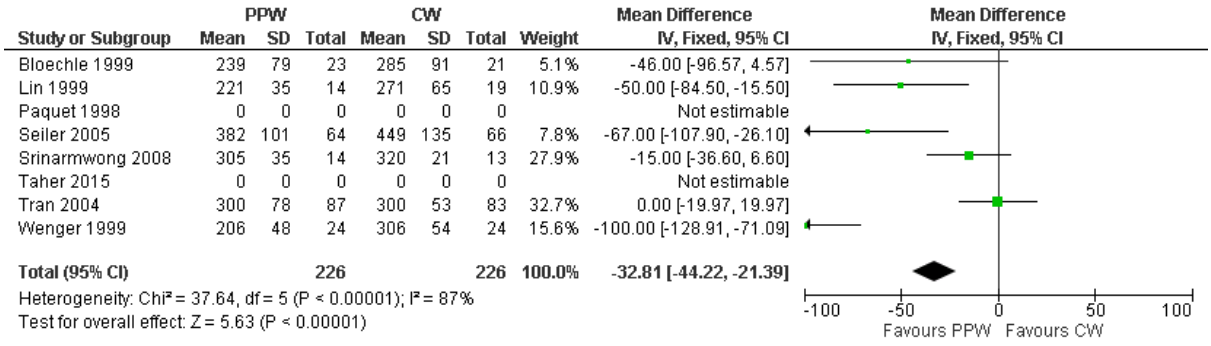


Figure 239: Delayed Gastric Emptying

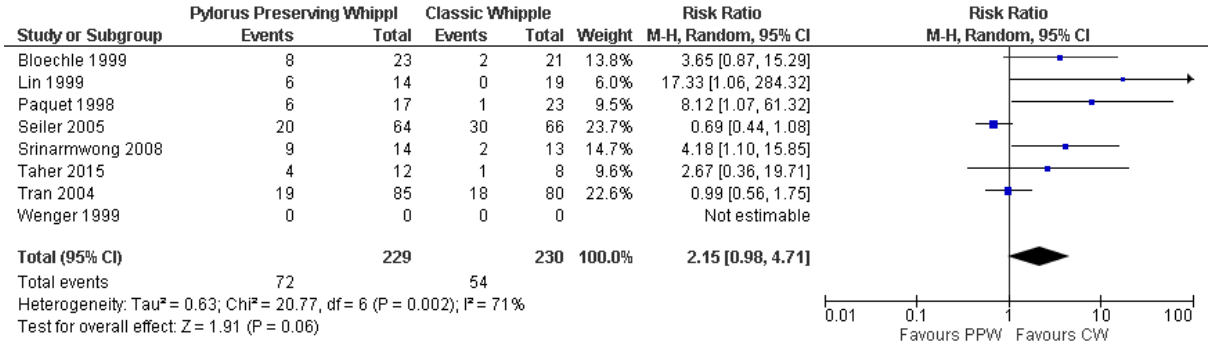


Figure 240: Pancreatic Fistula

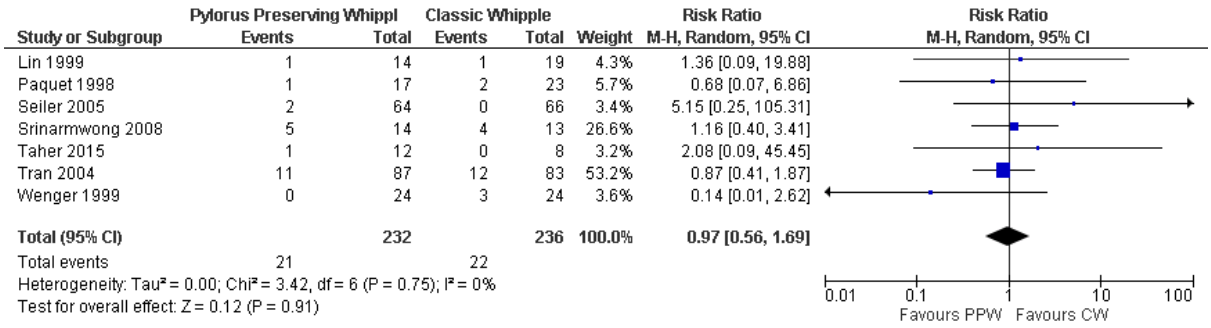


Figure 241: Biliary Leakage

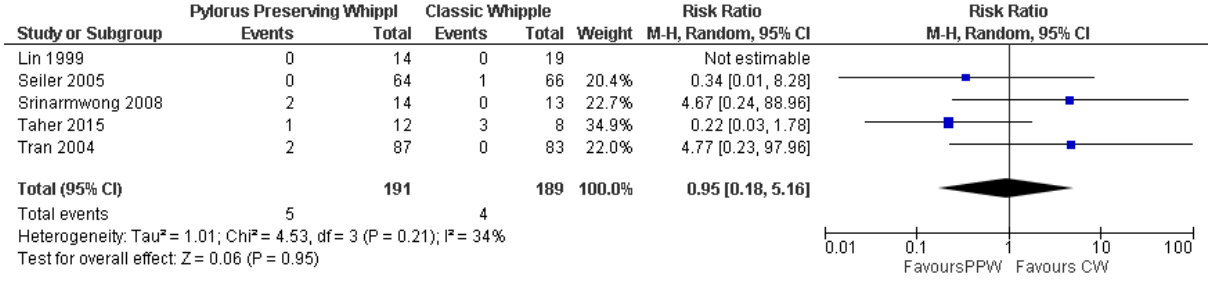


Figure 242: Reoperation

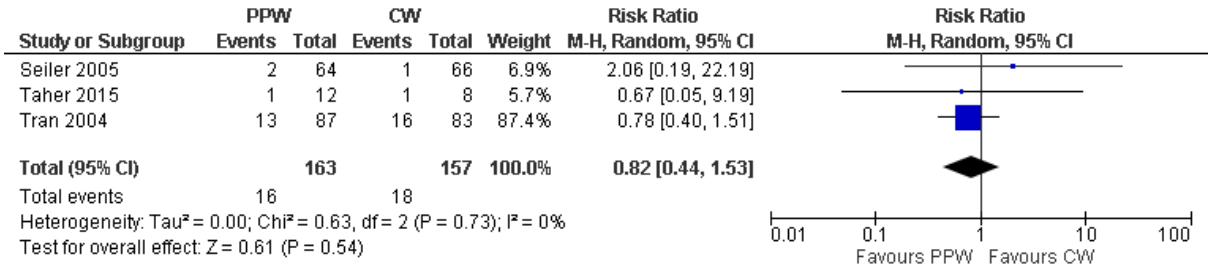


Figure 243: Intraoperative Blood Loss (litres)

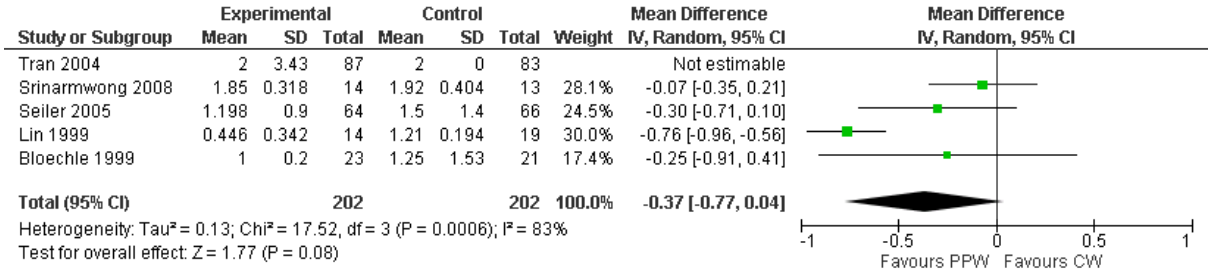


Figure 244: Surgical site Infection

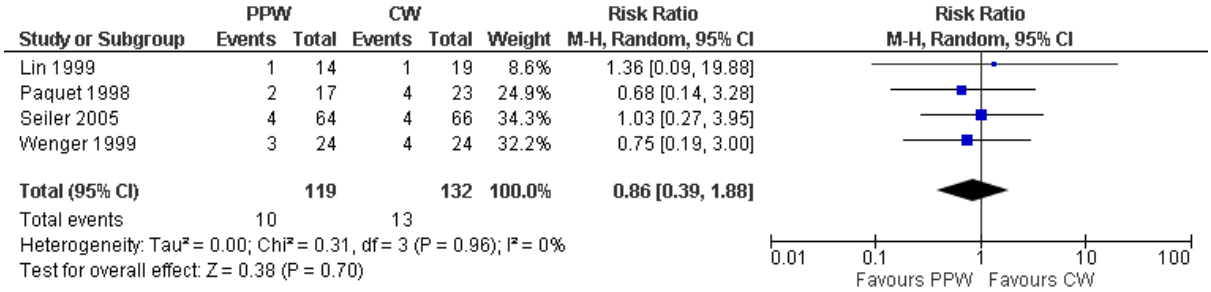
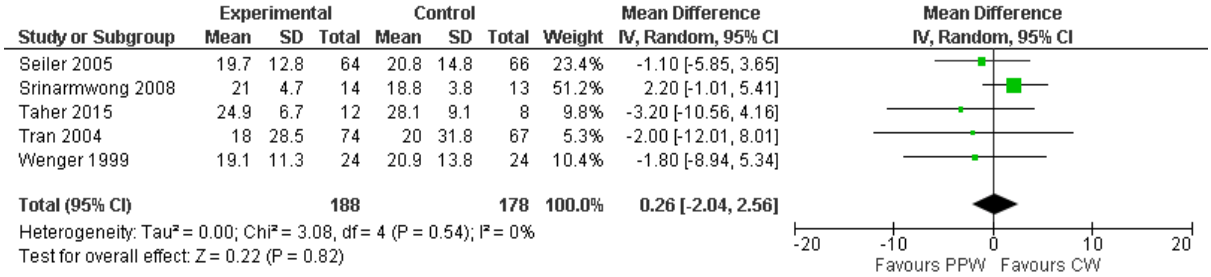


Figure 245: Hospital Stay (days)



H.13.3 Minimally invasive laparoscopic distal pancreatectomy versus open pancreatectomy

Figure 246: Mortality

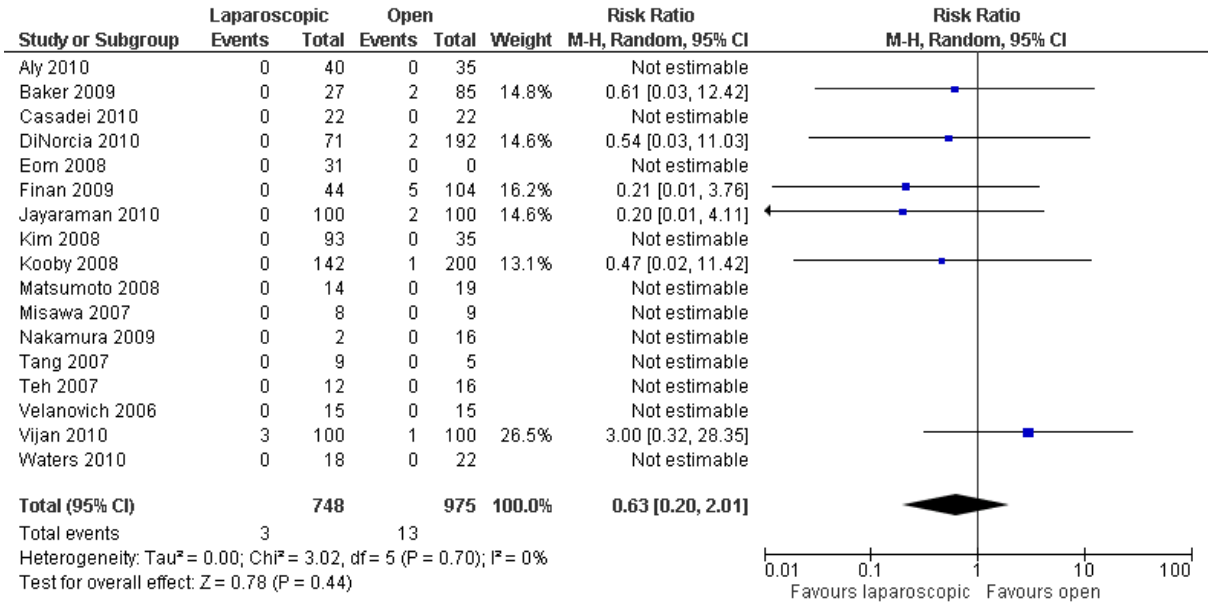


Figure 247: Positive Margins

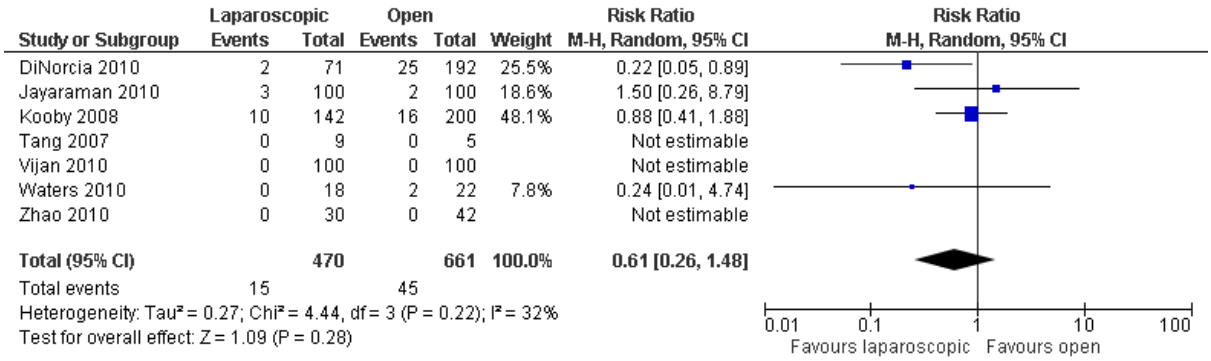


Figure 248: Pancreatic Fistula

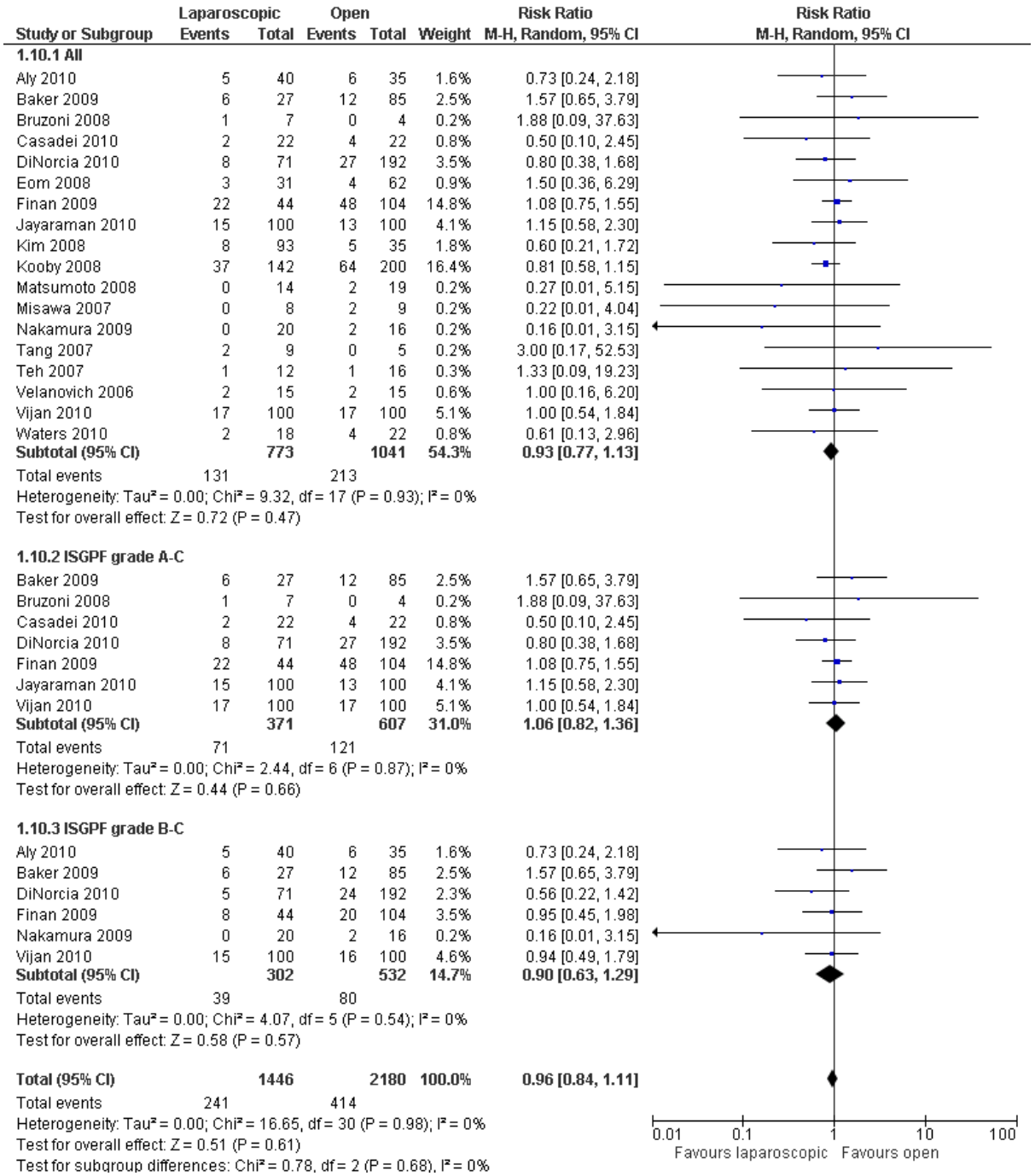


Figure 249: Reoperation

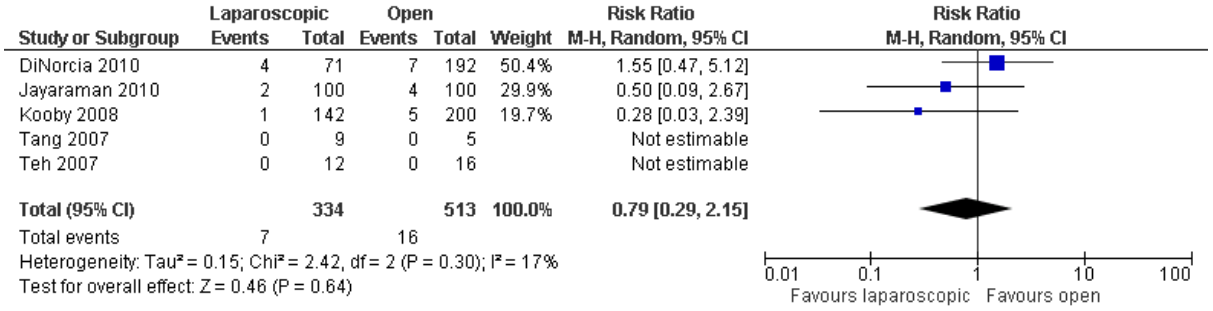


Figure 250: Blood Loss (mls)

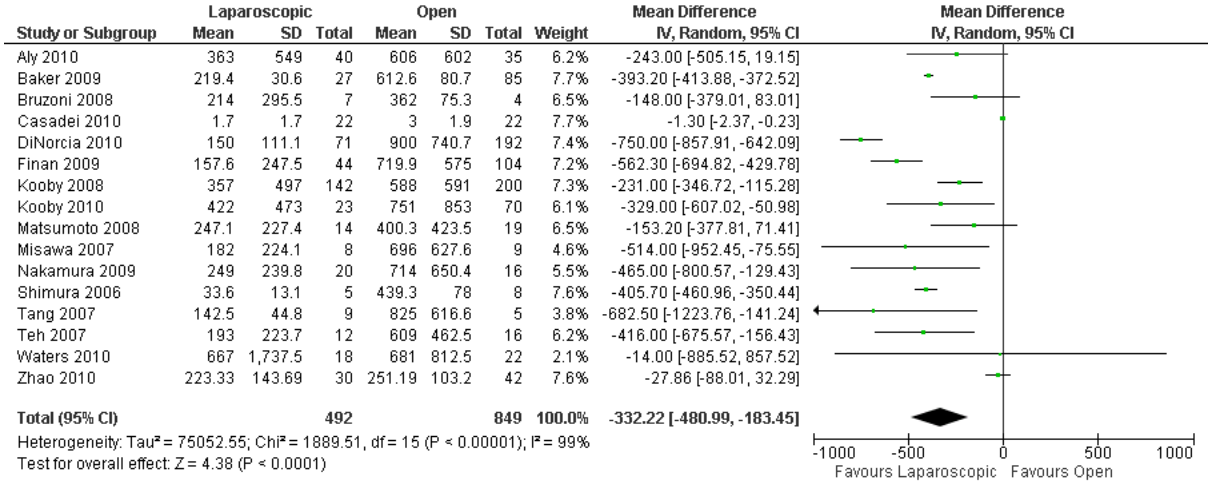


Figure 251: Surgical Site Infection

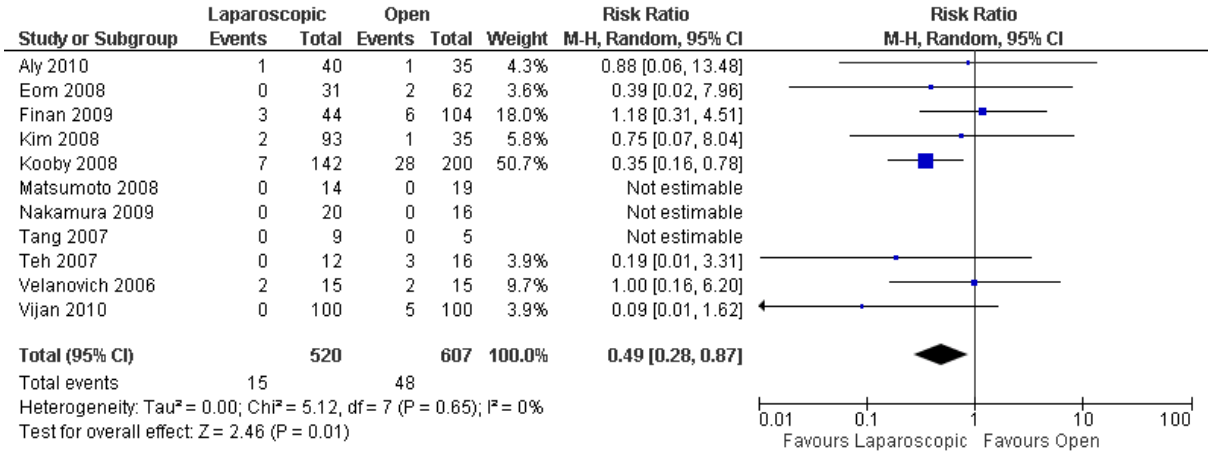


Figure 252: Operative Time (mins)

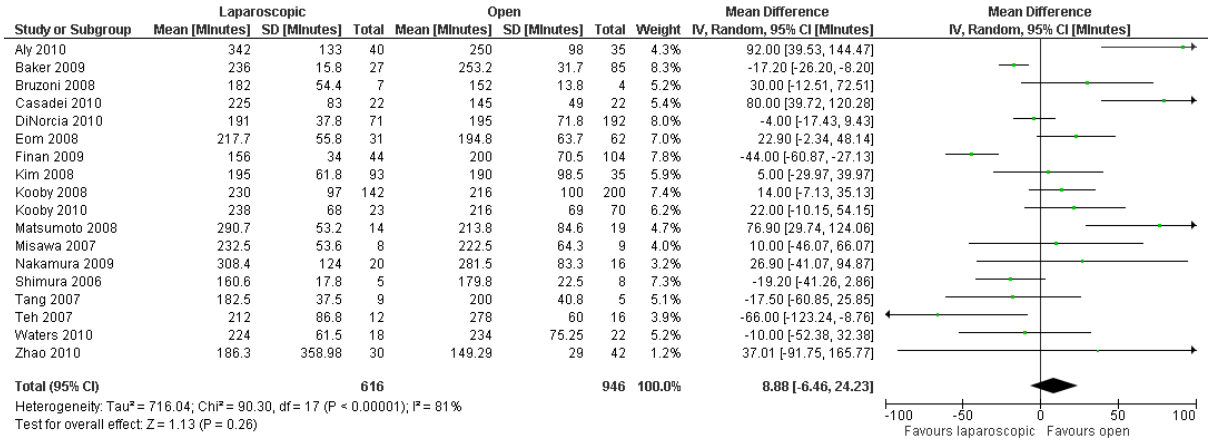


Figure 253: Length of hospital stay

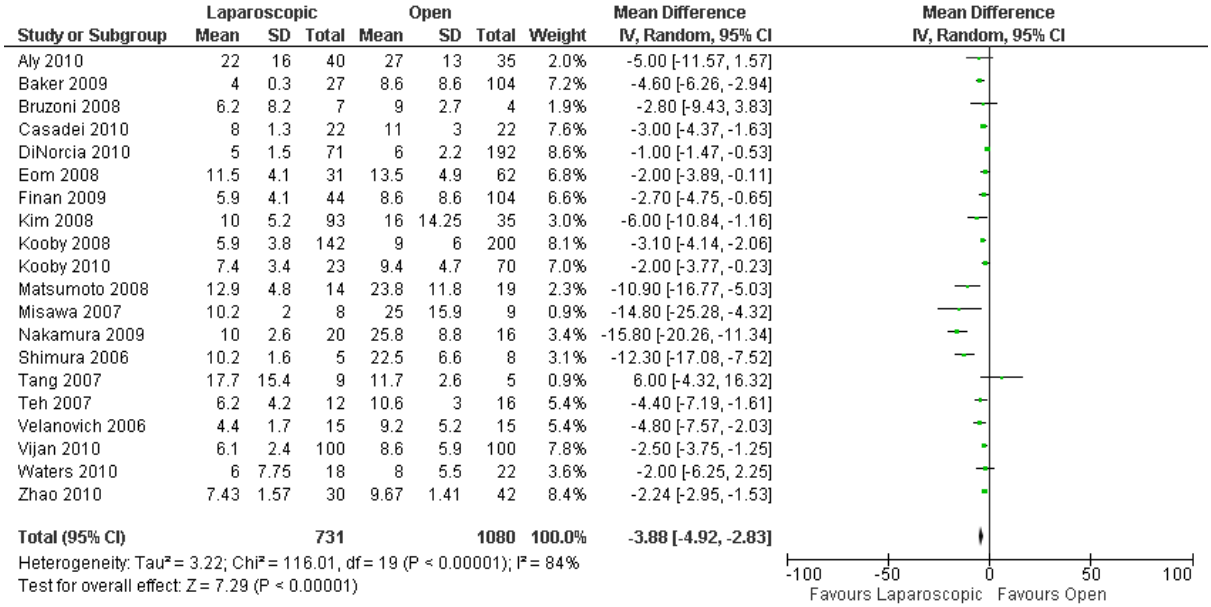
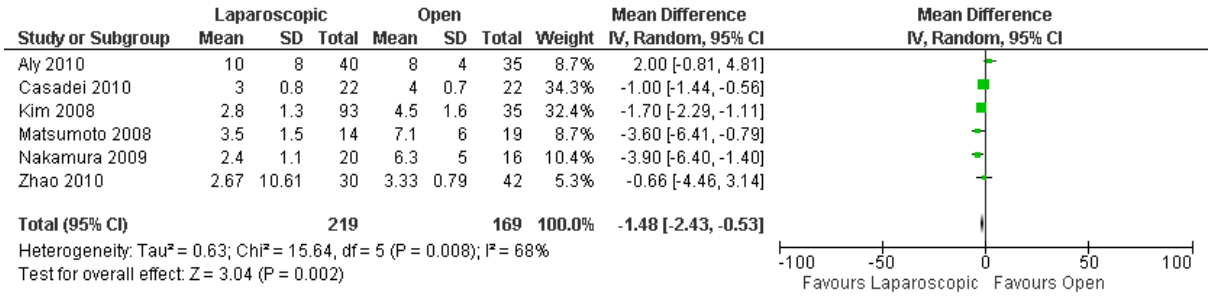


Figure 254: Time to oral intake



H.13.46 Minimally invasive robotic pancreatectomy versus open pancreatectomy

Figure 255: Postoperative Mortality

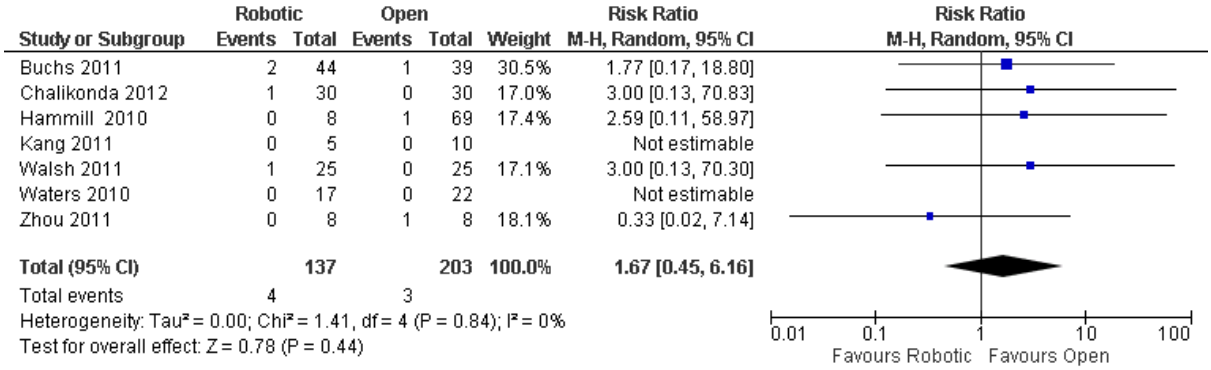


Figure 256: Positive Margin Rate

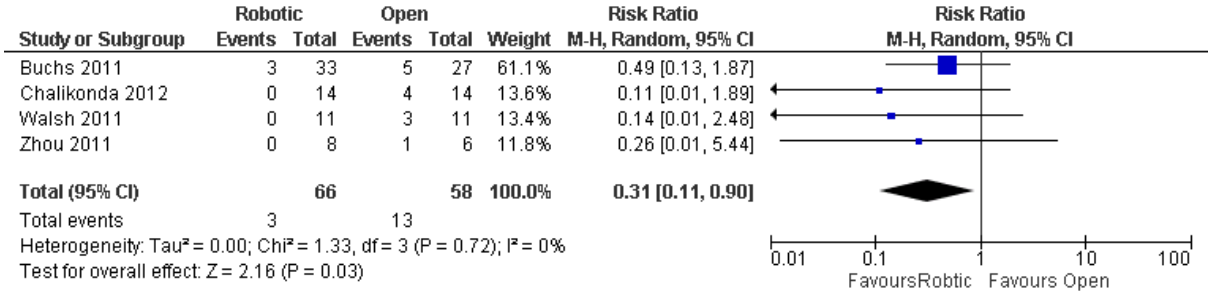


Figure 257: Pancreatic Fistula

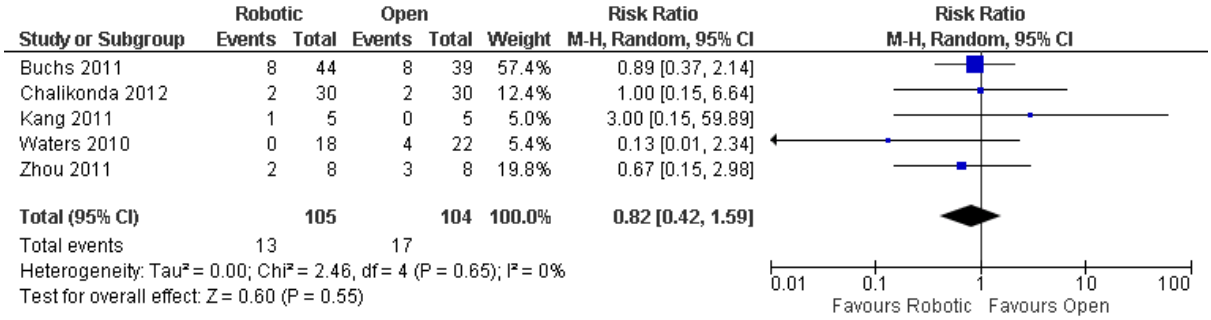


Figure 258: Operative time (mins)

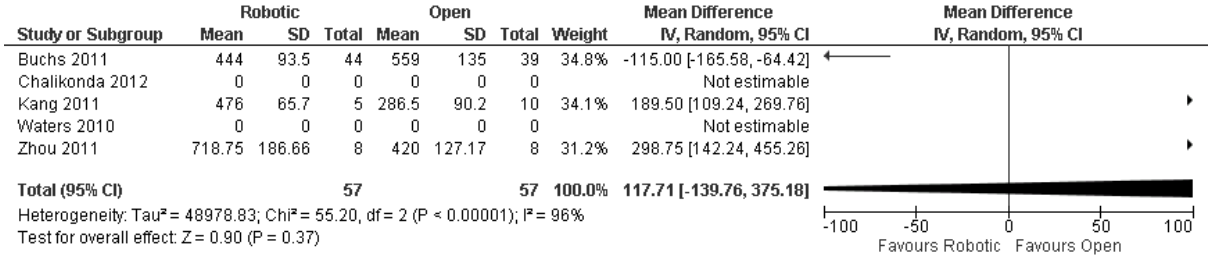
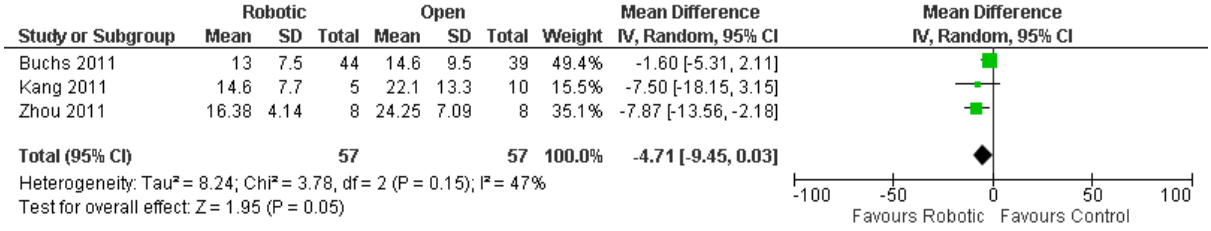


Figure 259: Length of hospital stay (days)



H.13.5 Extended lymphadenectomy versus standard lymphadenectomy

Figure 260: Overall Survival

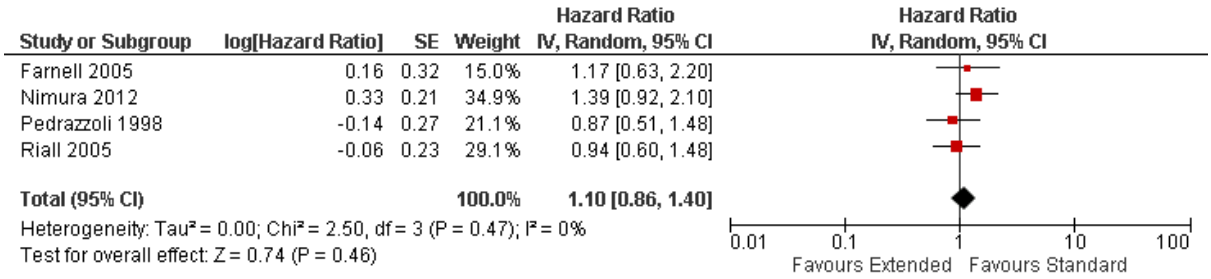


Figure 261: Lymph Node Positive

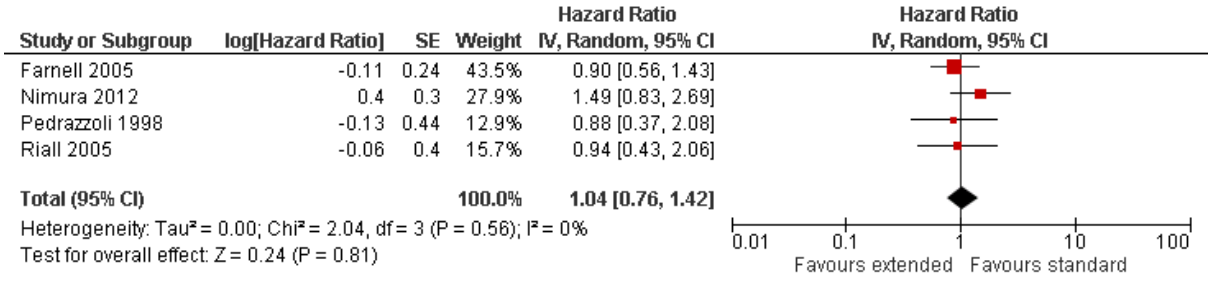


Figure 262: Lymph Node Negative

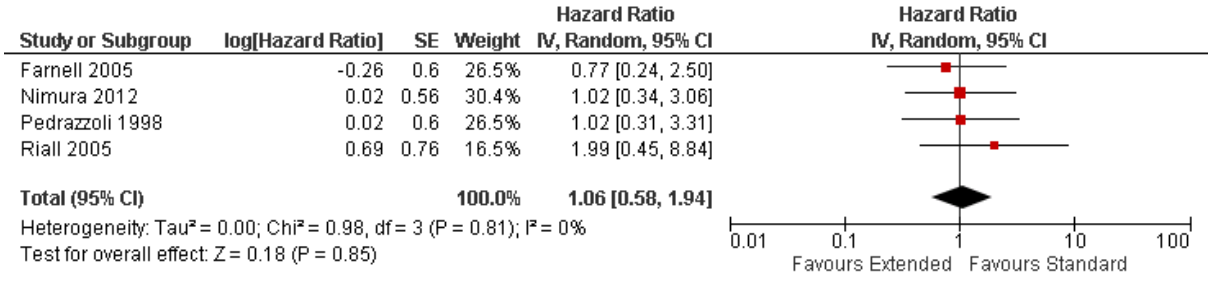


Figure 263 Positive Margins

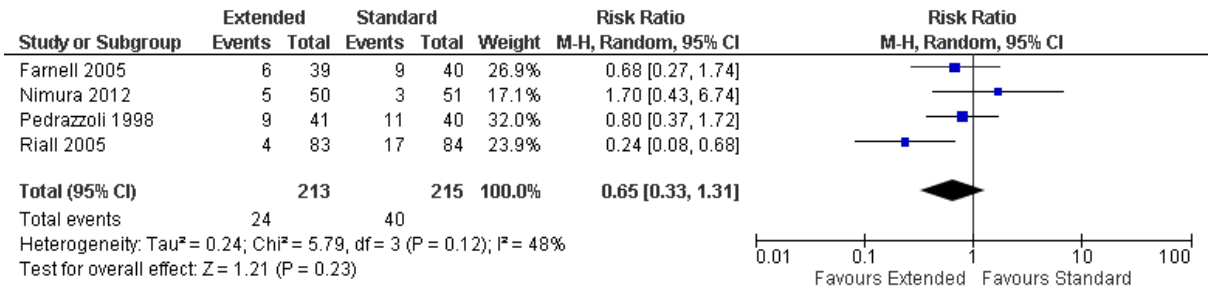
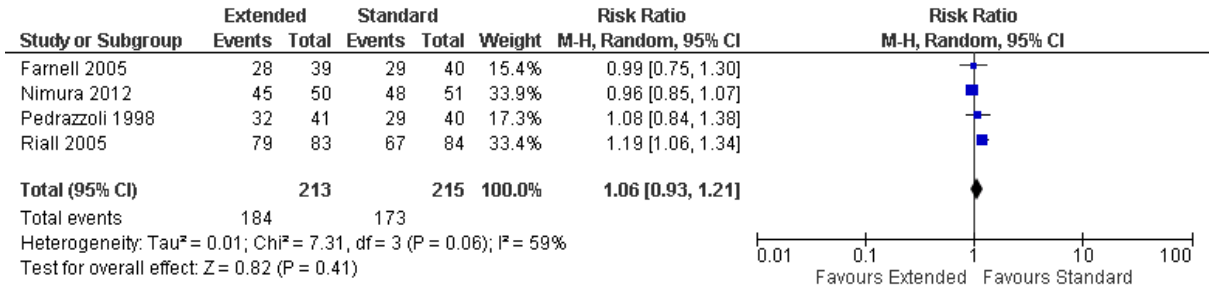


Figure 264: Negative Margins



H.13.64 Arterial resection versus no arterial resection

Figure 265: 1-year Overall Survival

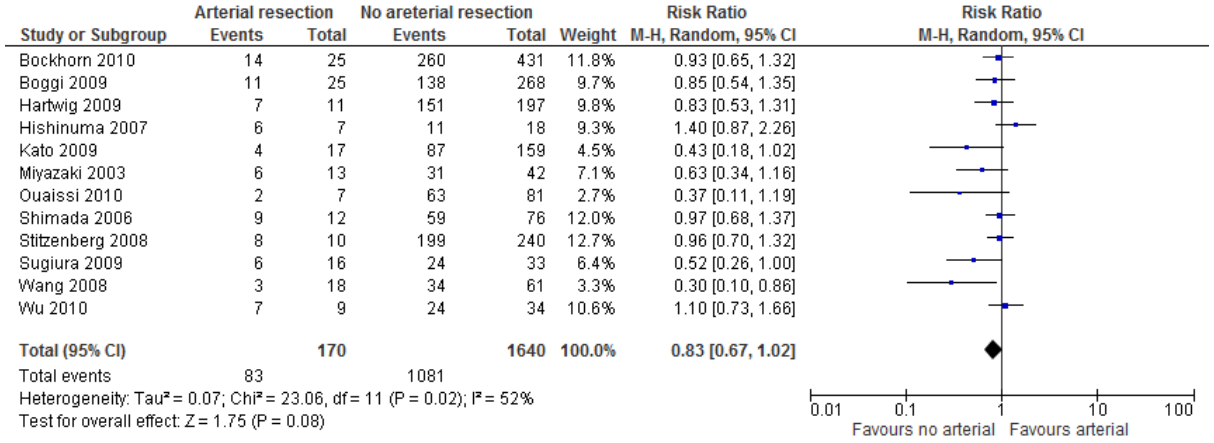


Figure 266: 3-Year Overall Survival

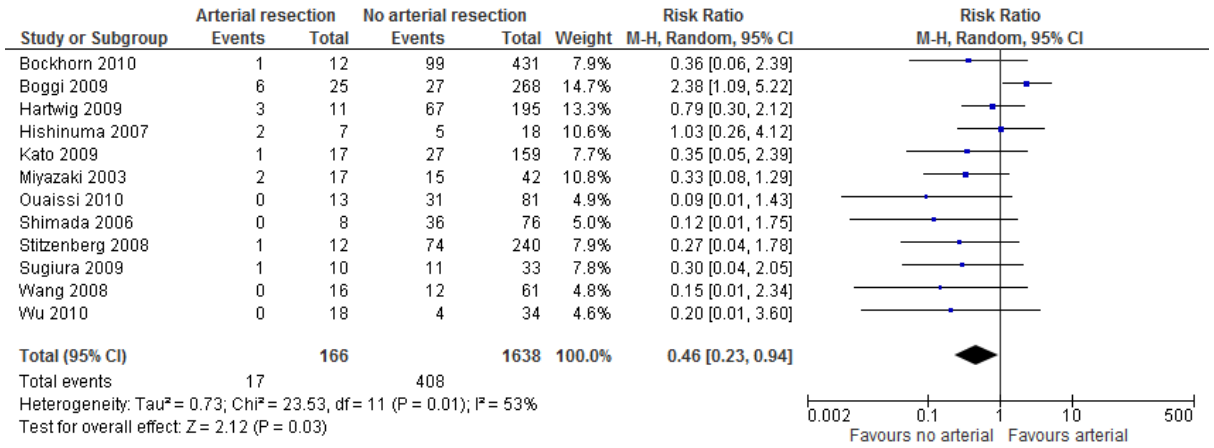


Figure 267: Post operative Mortality

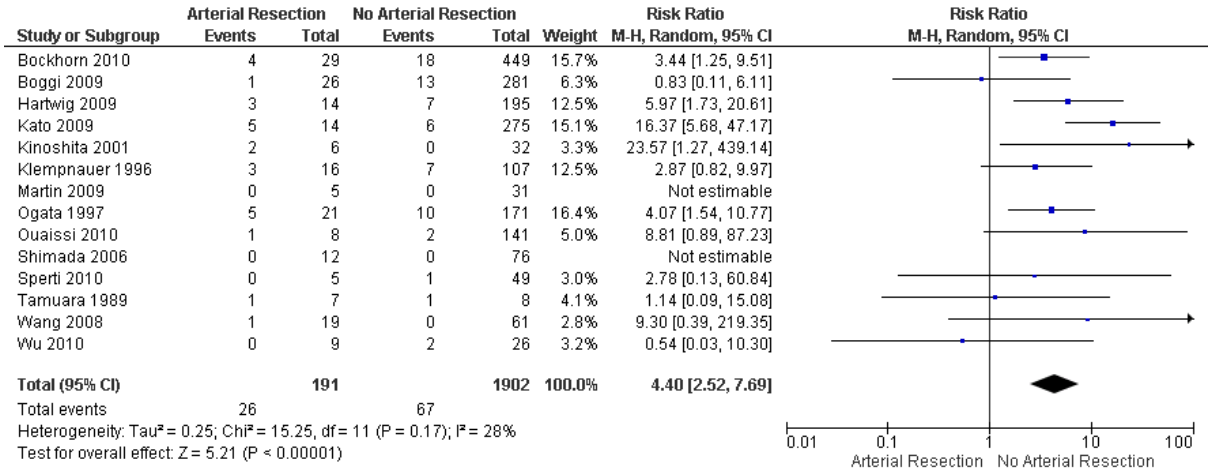


Figure 268: Reoperation Rate

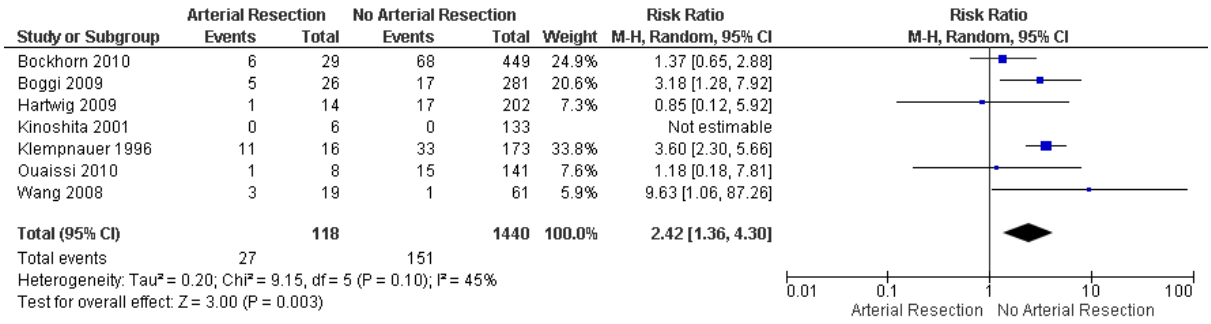


Figure 269: R0 Resection Rate

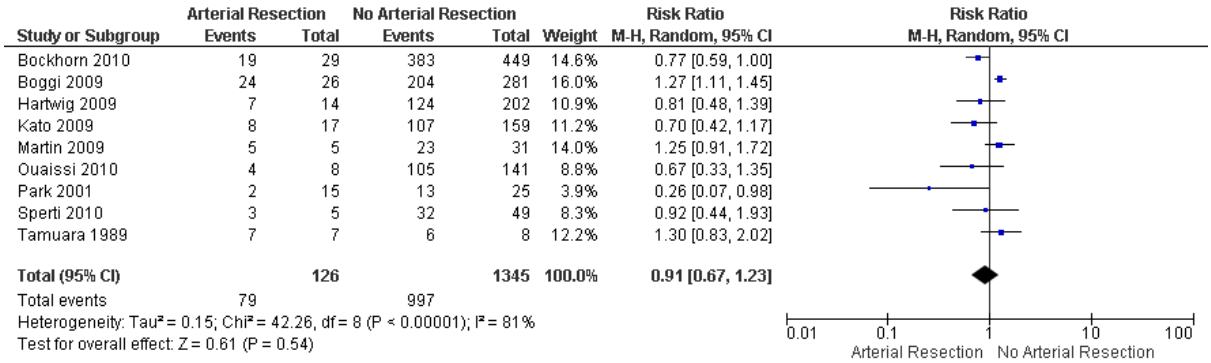


Figure 270: Lymph Node Positive

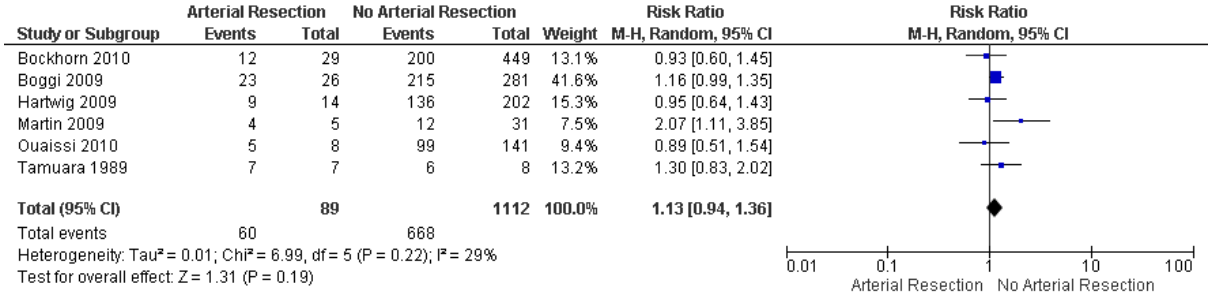
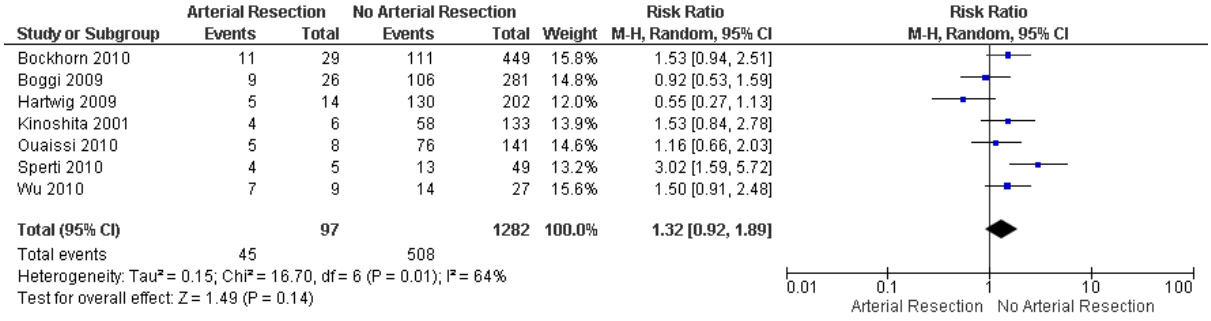


Figure 271: Post-operative Morbidity



H.13.7 Venous resection versus no venous resection

Figure 272: 1-year overall survival

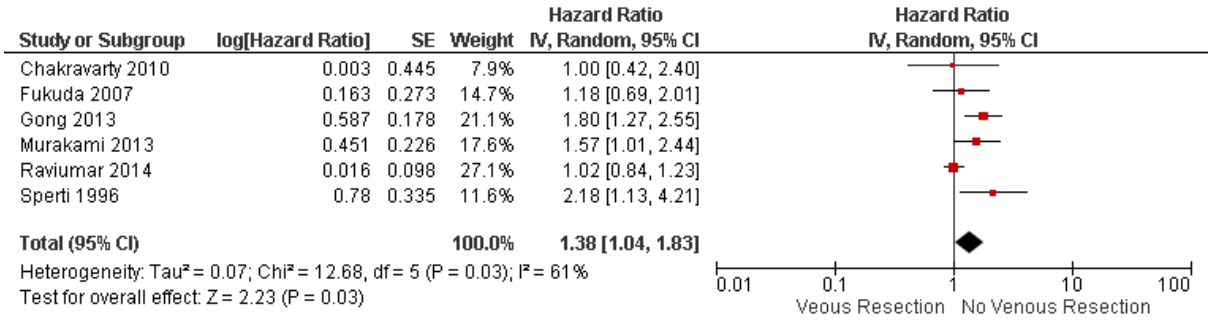


Figure 273: 5-year overall survival

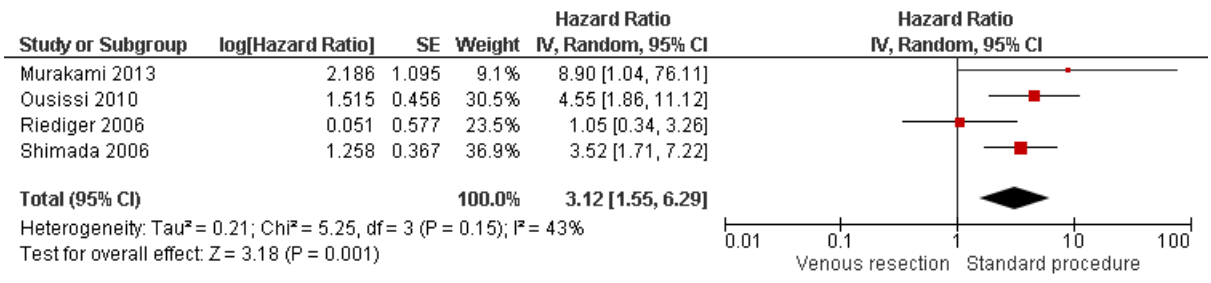


Figure 274: 5-year overall survival (all survival data)

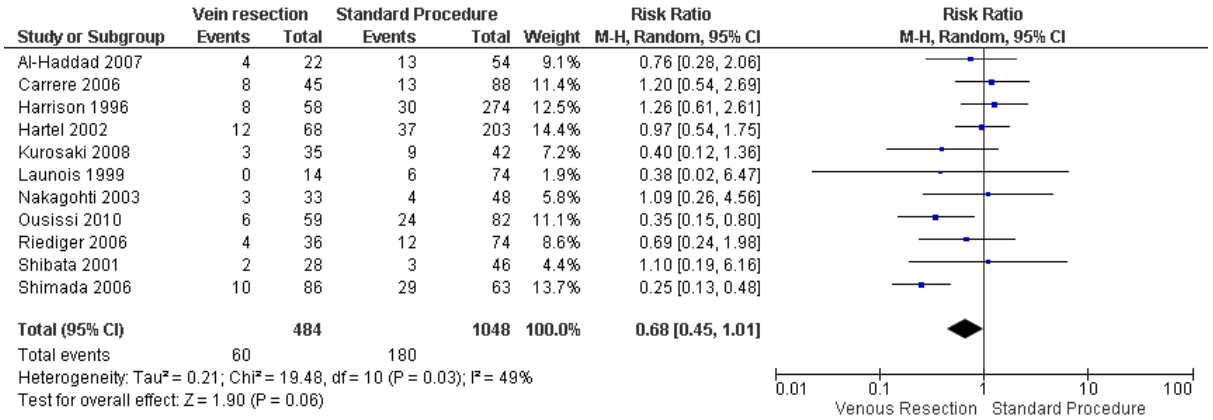


Figure 275: Postoperative Mortality

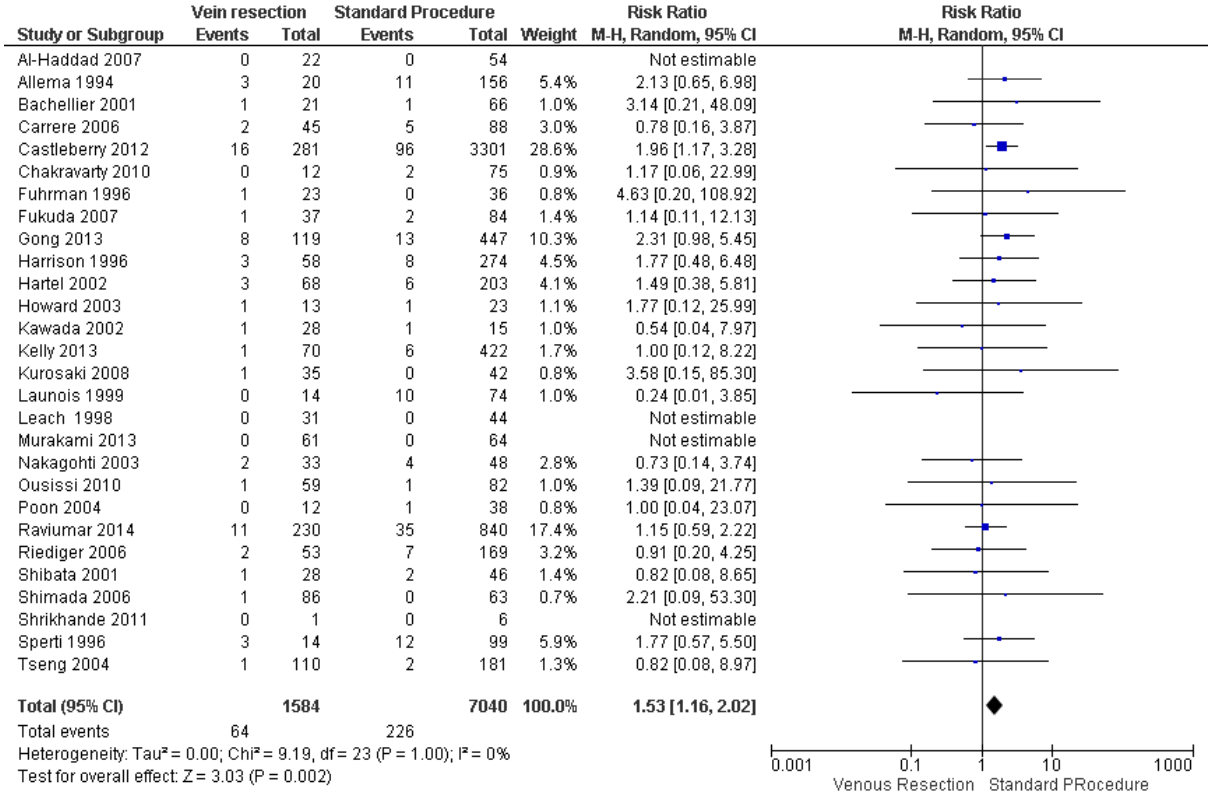


Figure 276: Reoperation Rate

Study or Subgroup	Vein resection Events	Total	Standard Procedure Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Bachellier 2001	2	21	10	66	1.6%	0.63 [0.15, 2.64]
Carrere 2006	10	45	12	88	5.7%	1.63 [0.76, 3.48]
Castleberry 2012	37	281	231	3301	30.9%	1.88 [1.36, 2.60]
Fuhrman 1996	1	23	1	36	0.4%	1.57 [0.10, 23.81]
Gong 2013	38	119	122	447	35.6%	1.17 [0.86, 1.58]
Harrison 1996	7	58	30	254	5.5%	1.02 [0.47, 2.21]
Kurosaki 2008	2	35	2	42	0.9%	1.20 [0.18, 8.09]
Ousissi 2010	8	59	8	82	3.8%	1.39 [0.55, 3.49]
Raviumar 2014	17	230	51	840	11.7%	1.22 [0.72, 2.07]
Riediger 2006	4	53	15	169	2.9%	0.85 [0.29, 2.45]
Shibata 2001	2	86	3	63	1.1%	0.49 [0.08, 2.84]
Total (95% CI)		**1010**		**5388**	**100.0%**	**1.35 [1.13, 1.62]**
Total events	128		485			

Heterogeneity: Tau² = 0.00; Chi² = 8.93, df = 10 (P = 0.54); I² = 0%
Test for overall effect: Z = 3.25 (P = 0.001)

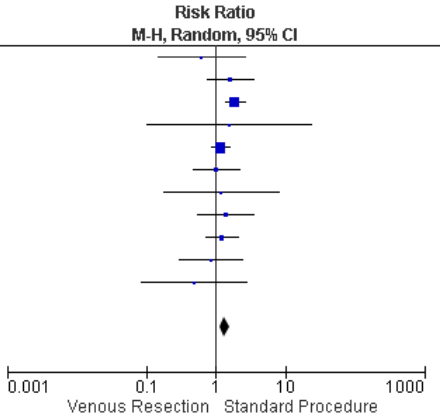


Figure 277: R1-R2 resection Rate

Study or Subgroup	Vein resection Events	Total	Standard Procedure Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Bachellier 2001	8	21	18	66	3.5%	1.40 [0.71, 2.74]
Carrere 2006	8	45	13	88	2.5%	1.20 [0.54, 2.69]
Chakravarty 2010	0	12	27	75	0.2%	0.11 [0.01, 1.64]
Fuhrman 1996	4	23	5	36	1.1%	1.25 [0.37, 4.18]
Fukuda 2007	14	37	23	84	5.2%	1.38 [0.81, 2.37]
Harrison 1996	17	58	66	274	7.2%	1.22 [0.77, 1.91]
Hartel 2002	23	68	39	203	7.6%	1.76 [1.14, 2.72]
Kelly 2013	22	70	105	422	9.5%	1.26 [0.86, 1.85]
Kurosaki 2008	5	35	6	42	1.3%	1.00 [0.33, 3.00]
Leach 1998	4	31	7	44	1.3%	0.81 [0.26, 2.53]
Murakami 2013	30	61	18	64	6.7%	1.75 [1.10, 2.79]
Nakagohti 2003	8	33	10	48	2.4%	1.16 [0.51, 2.63]
Ousissi 2010	25	59	11	82	4.0%	3.16 [1.69, 5.90]
Poon 2004	1	12	4	38	0.4%	0.79 [0.10, 6.42]
Raviumar 2014	145	230	433	840	39.5%	1.22 [1.09, 1.38]
Shibata 2001	8	28	8	46	2.2%	1.64 [0.70, 3.88]
Shrikhande 2011	0	1	2	6	0.2%	0.70 [0.05, 9.41]
Tseng 2004	24	110	22	181	5.4%	1.80 [1.06, 3.04]
Total (95% CI)		**934**		**2639**	**100.0%**	**1.37 [1.20, 1.56]**
Total events	346		817			

Heterogeneity: Tau² = 0.01; Chi² = 18.81, df = 17 (P = 0.34); I² = 10%
Test for overall effect: Z = 4.78 (P < 0.00001)

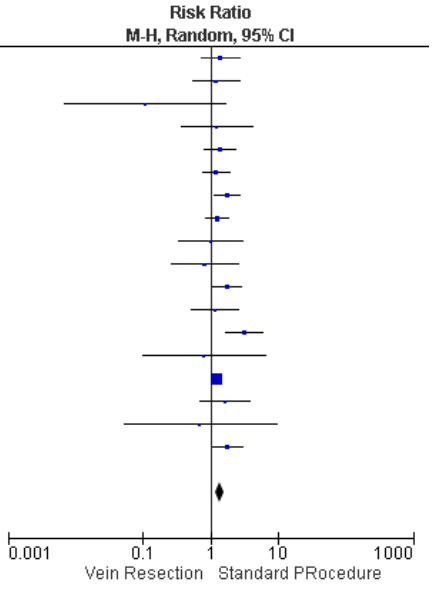
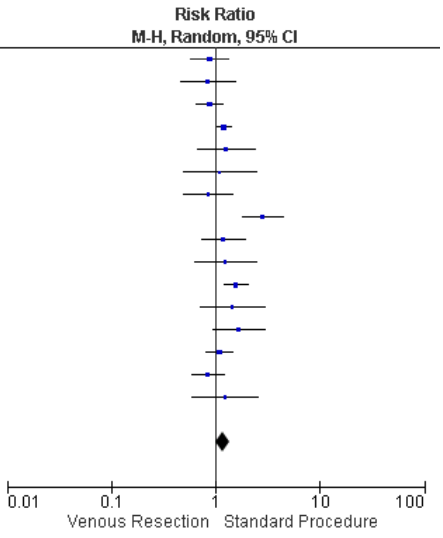


Figure 278: Overall post-operative morbidity

Study or Subgroup	Vein resection Events	Total	Standard Procedure Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Allema 1994	11	20	98	156	7.0%	0.88 [0.58, 1.33]
Bachellier 2001	8	21	30	66	4.5%	0.84 [0.46, 1.54]
Carrere 2006	25	45	56	88	9.0%	0.87 [0.64, 1.18]
Castleberry 2012	112	281	1099	3301	12.1%	1.20 [1.03, 1.39]
Chakravarty 2010	6	12	30	75	4.2%	1.25 [0.67, 2.35]
Fuhrman 1996	7	23	10	36	2.9%	1.10 [0.49, 2.47]
Fukuda 2007	12	37	32	84	5.2%	0.85 [0.50, 1.46]
Gong 2013	28	119	37	447	6.4%	2.84 [1.82, 4.45]
Hartel 2002	18	68	45	203	6.1%	1.19 [0.74, 1.92]
Howard 2003	7	13	10	23	3.8%	1.24 [0.62, 2.46]
Kelly 2013	36	70	139	422	9.8%	1.56 [1.20, 2.04]
Kurosaki 2008	12	35	10	42	3.6%	1.44 [0.71, 2.93]
Murakami 2013	22	61	14	64	4.8%	1.65 [0.93, 2.92]
Ousissi 2010	35	59	45	82	9.3%	1.08 [0.81, 1.44]
Riediger 2006	22	53	84	169	8.0%	0.84 [0.59, 1.19]
Shibata 2001	9	28	12	46	3.5%	1.23 [0.60, 2.55]
Total (95% CI)		**945**		**5304**	**100.0%**	**1.18 [1.01, 1.38]**
Total events	370		1751			

Heterogeneity: Tau² = 0.05; Chi² = 33.34, df = 15 (P = 0.004); I² = 55%
Test for overall effect: Z = 2.04 (P = 0.04)



H.14 Adjuvant treatment

H.14.1 Adjuvant chemotherapy versus no adjuvant therapy in resected pancreatic cancer patients

Figure 279: Overall survival

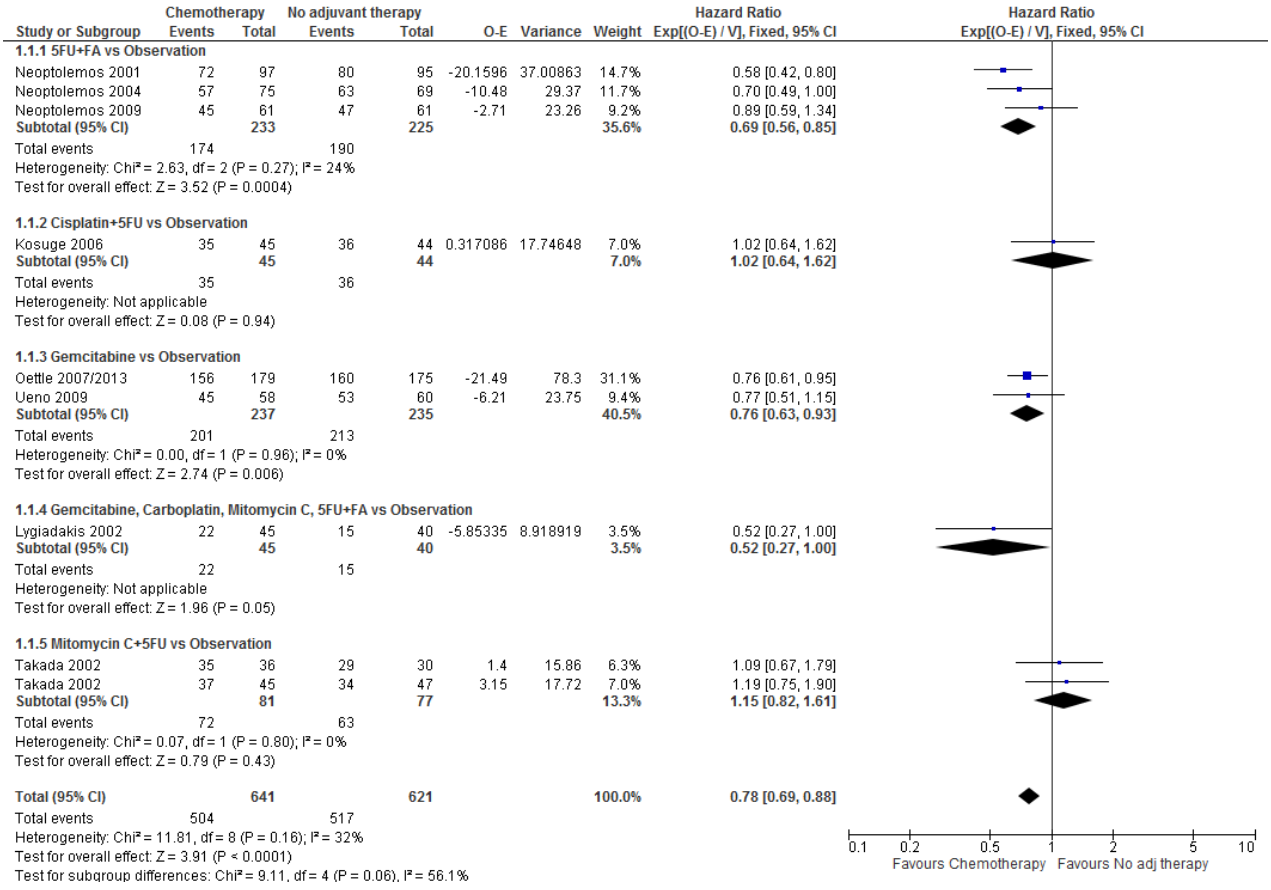


Figure 280: Disease-free survival

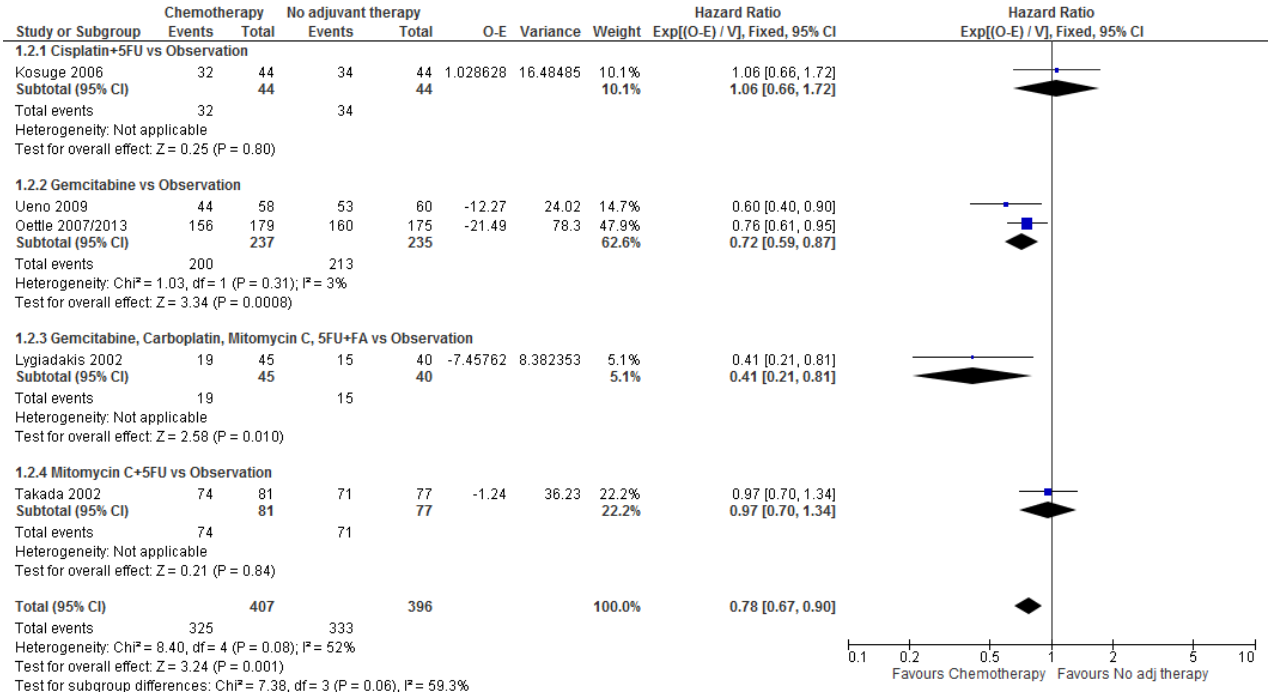


Figure 281: # patients with serious adverse events

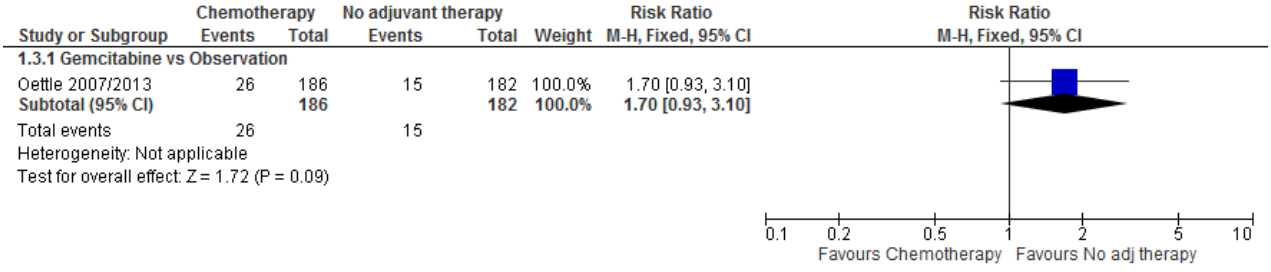


Figure 282: # patients with any Grade 3 or 4 haematological toxicity

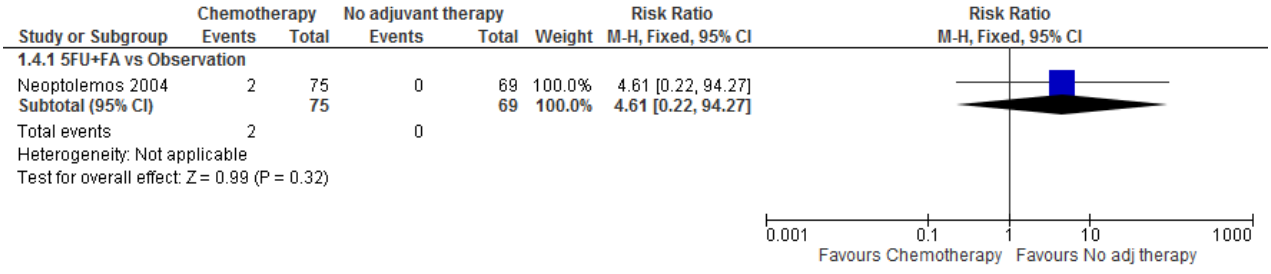


Figure 283: # patients with Grade 3 or 4 non-haematological toxicity

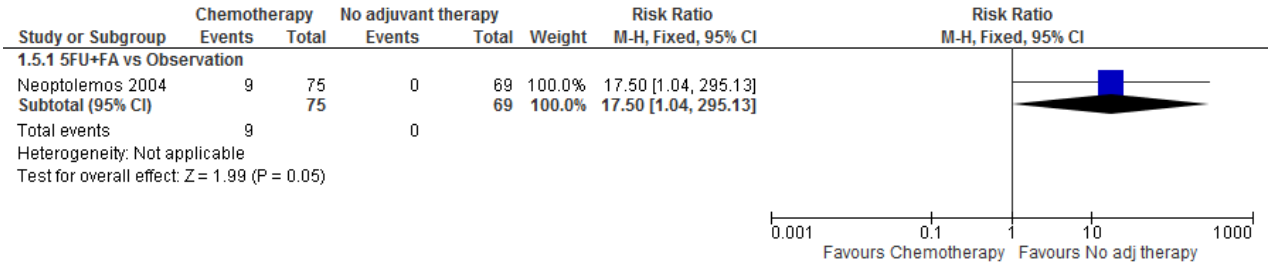


Figure 284: # patients with Grade 3 or 4 abscess

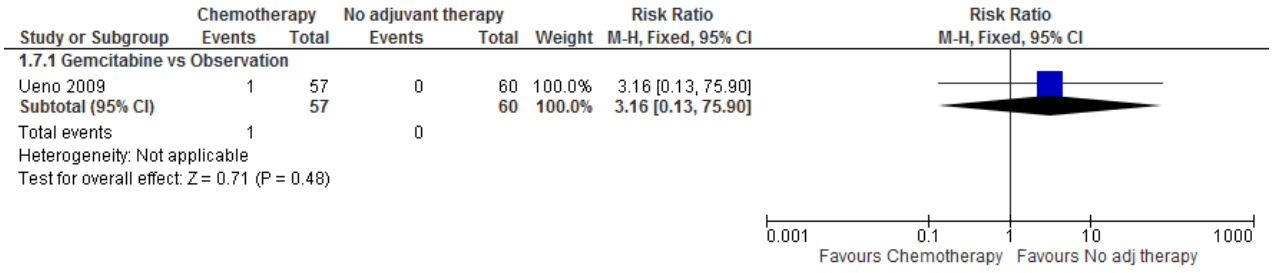


Figure 285: # patients with Grade 3 or 4 alanine aminotransferase

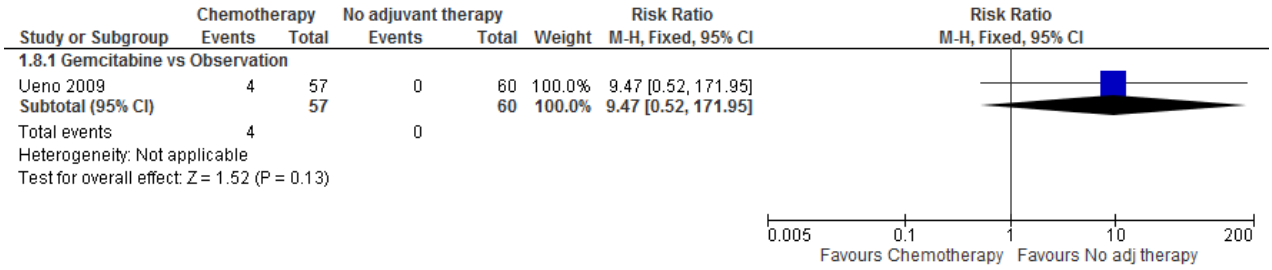


Figure 286: # patients with Grade 3 or 4 anaemia

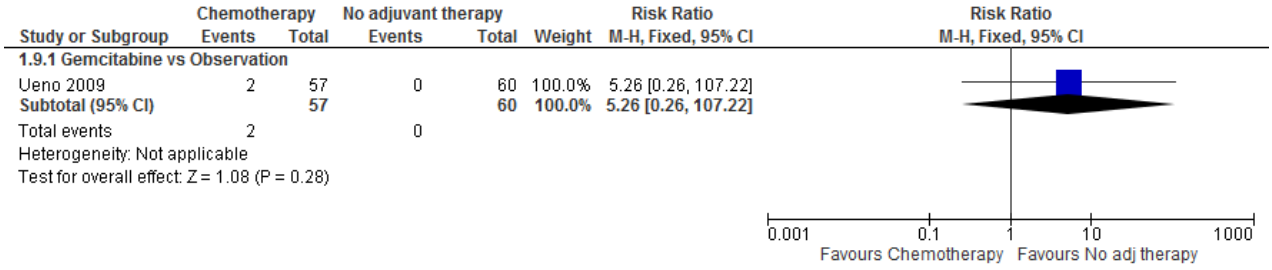


Figure 287: # patients with Grade 3 or 4 anorexia

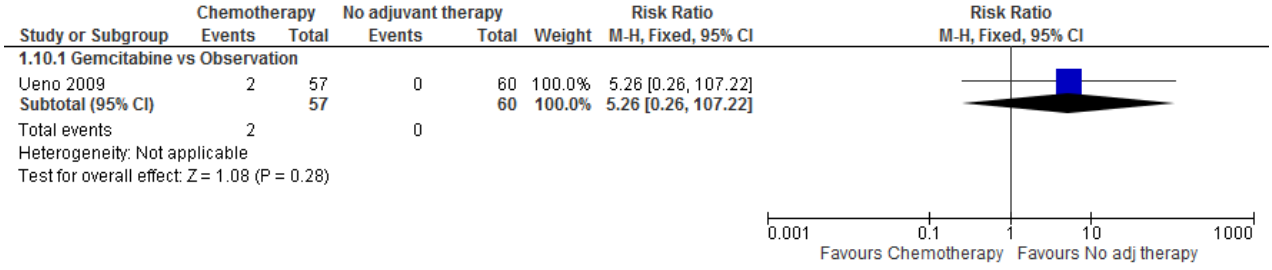


Figure 288: # patients with Grade 3 or 4 diarrhoea

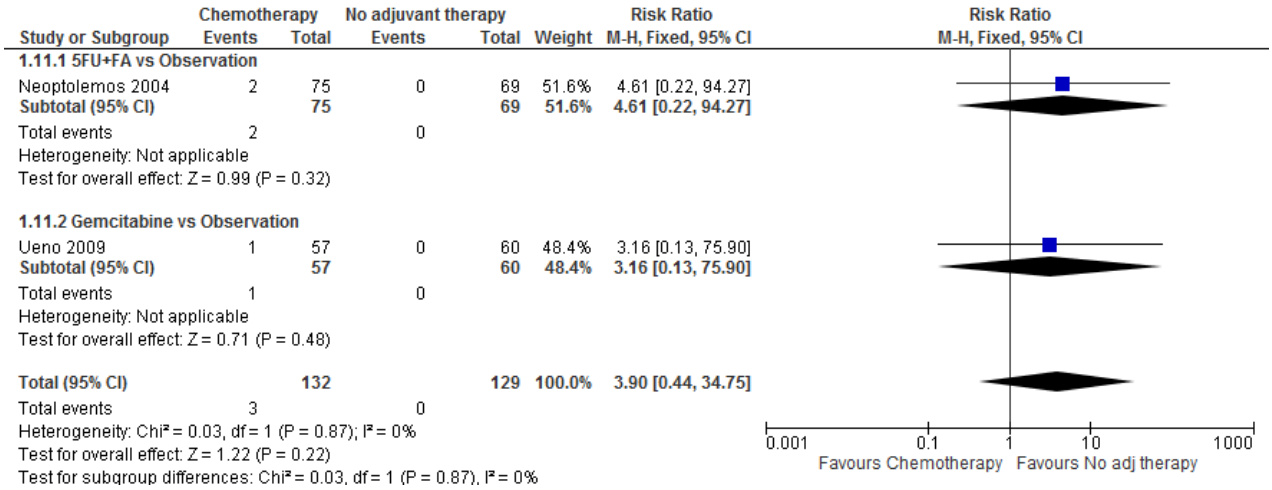


Figure 289: # patients with Grade 3 or 4 aspartate aminotransferase

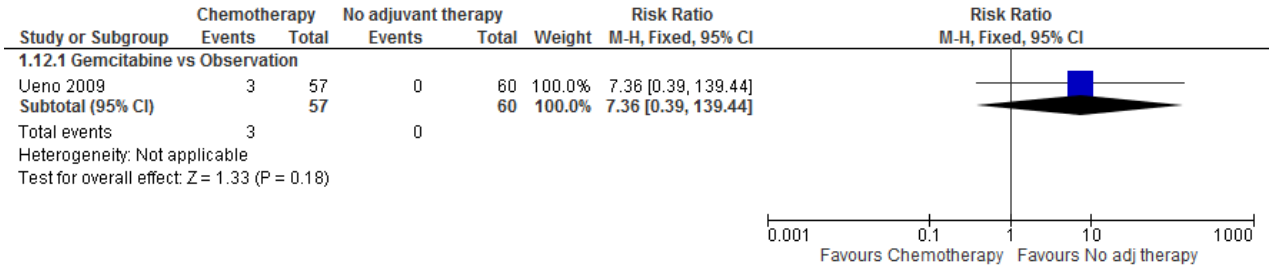


Figure 290: # patients with Grade 3 or 4 fatigue

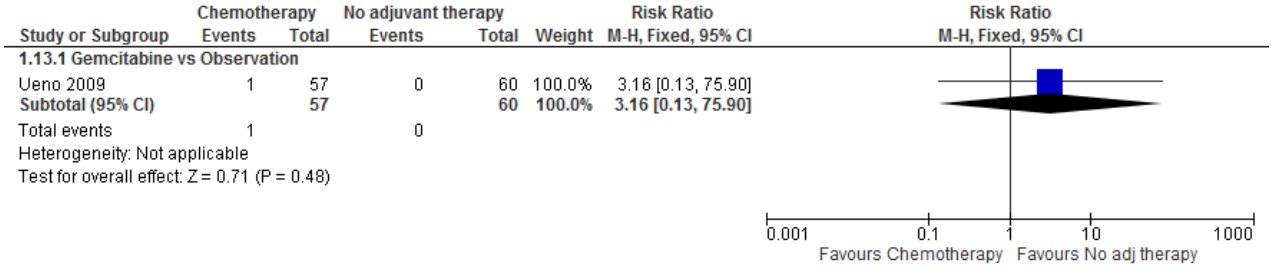


Figure 291: # patients with Grade 3 or 4 fever

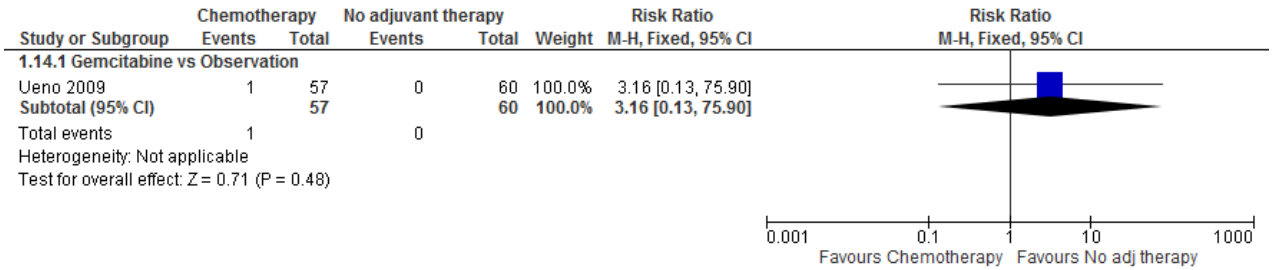


Figure 292: # patients with Grade 3 or 4 granulocytopenia

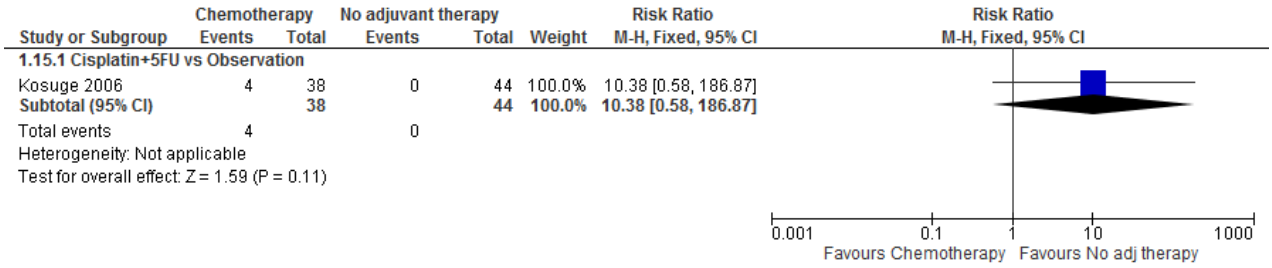


Figure 293: # patients with Grade 3 or 4 hepatic

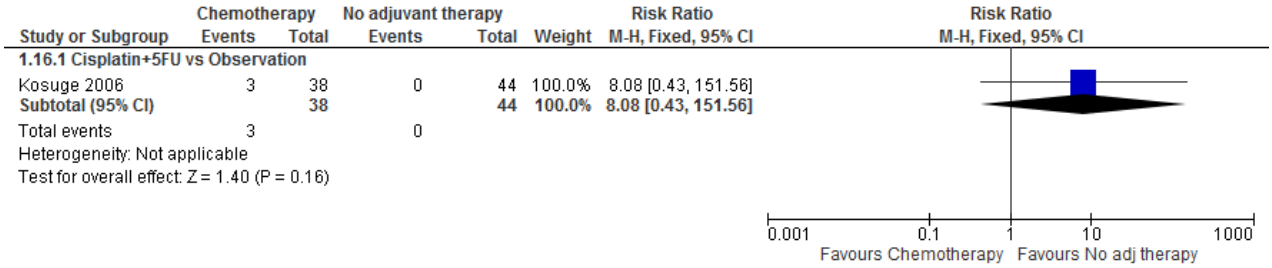


Figure 294: # patients with Grade 3 or 4 leukopenia

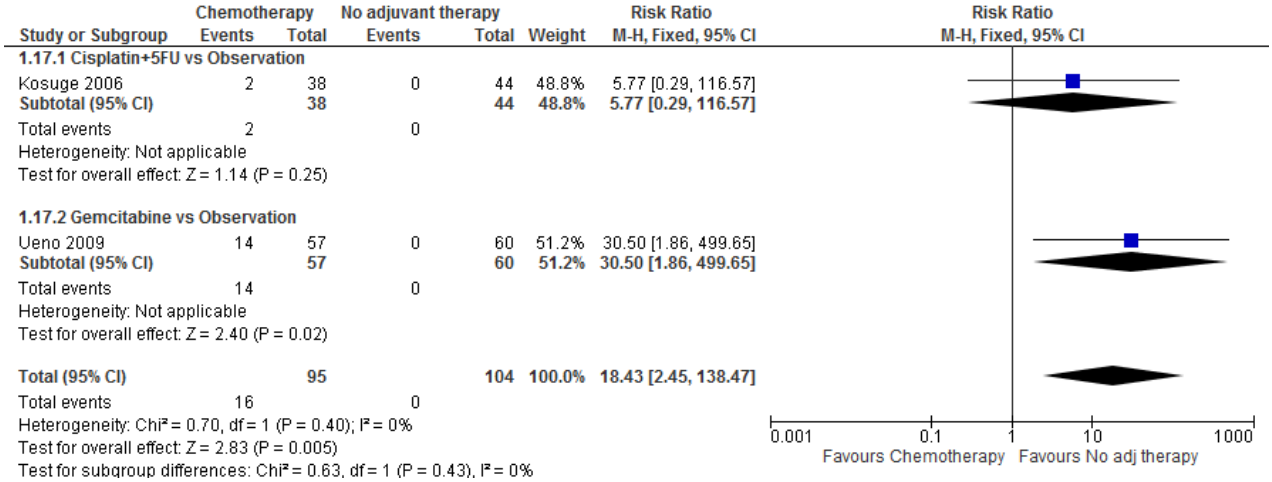


Figure 295: # patients with Grade 3 or 4 mucositis

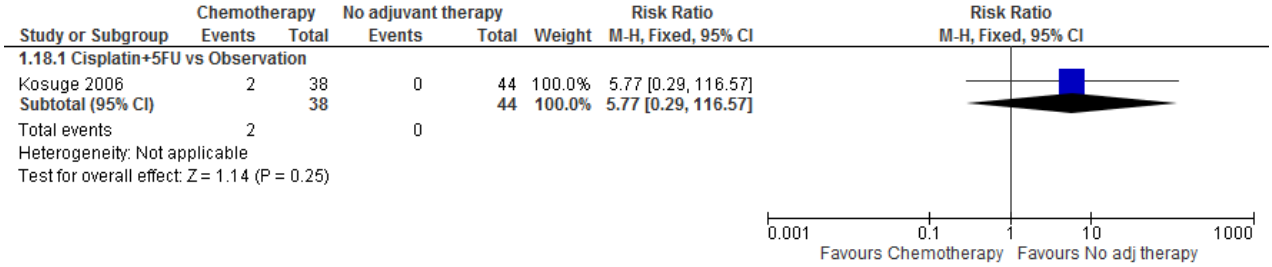


Figure 296: # patients with Grade 3 or 4 nausea/vomiting

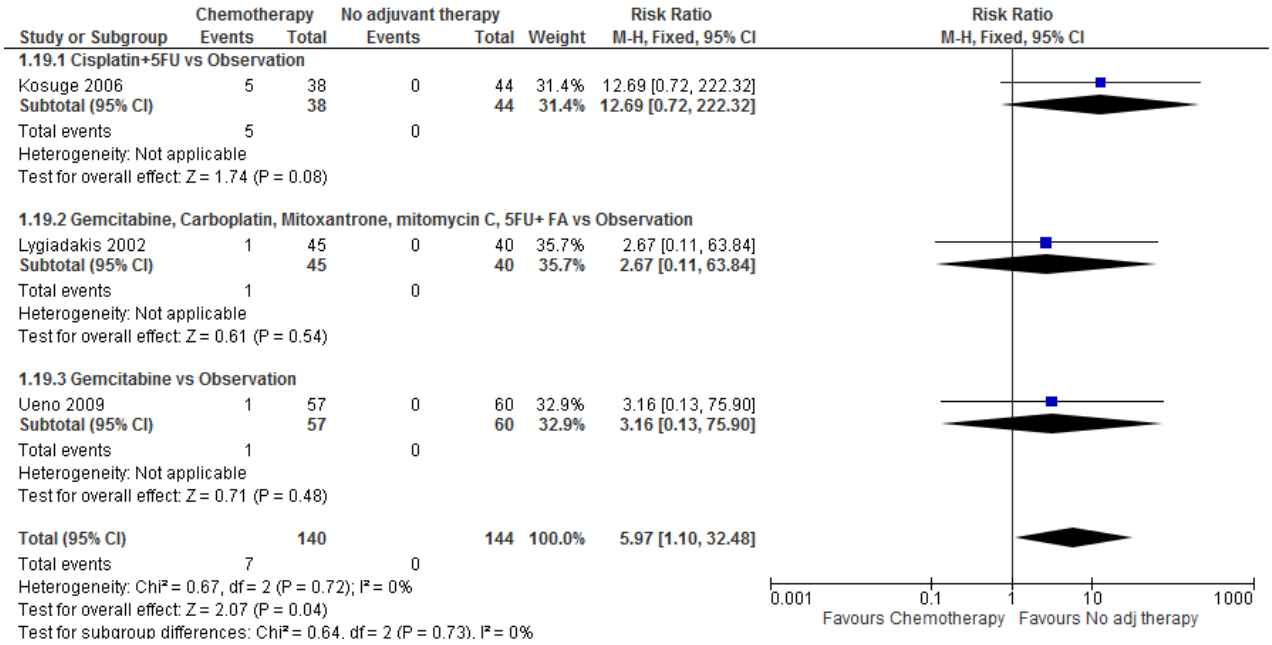


Figure 297: # patients with Grade 3 or 4 neutropenia

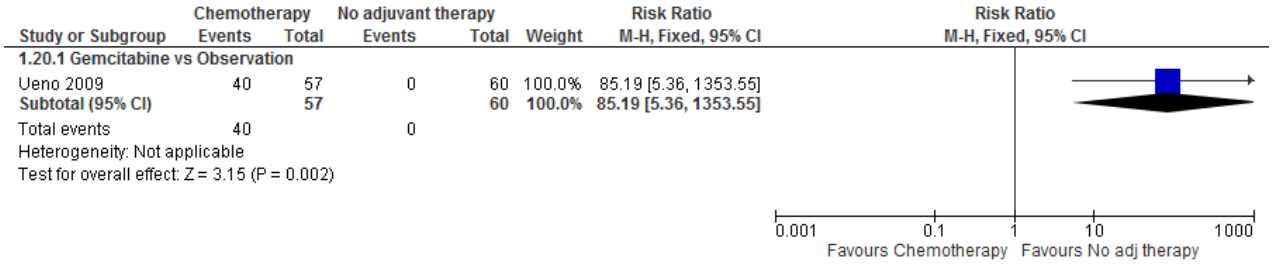


Figure 298: # patients with Grade 3 or 4 stomatitis

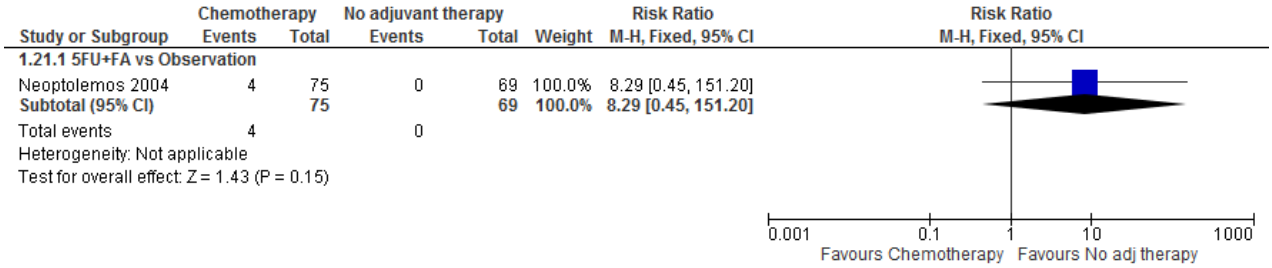


Figure 299: # patients with Grade 3 or 4 thrombocytopenia

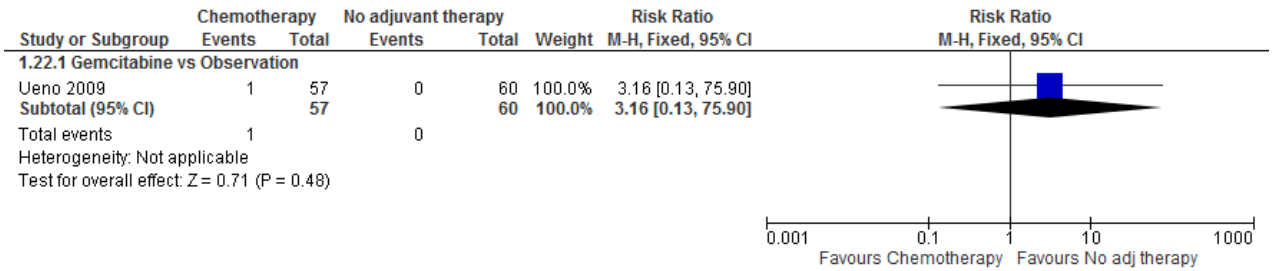


Figure 300: ESPAC-1 QoL overall score – change scores

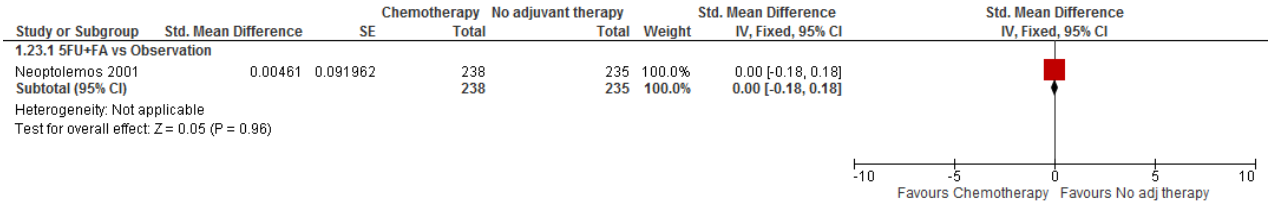


Figure 301: # patients with improving ESPAC-1 QoL role functioning subscale scores

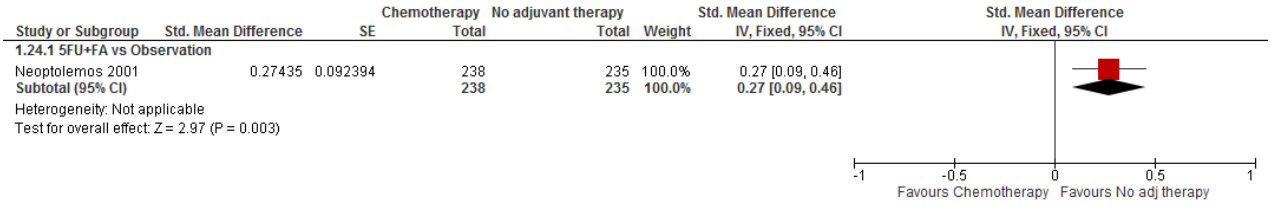
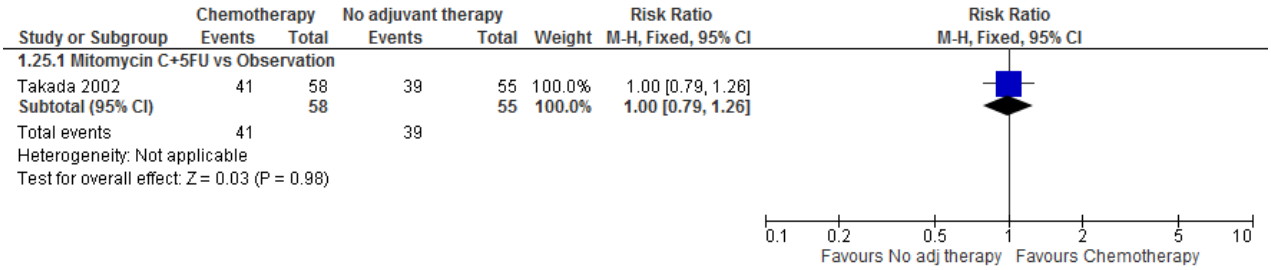


Figure 302: # patients improving by 1 or more ECOG performance score grade



H.14.2 Adjuvant chemotherapy-1 (gemcitabine) versus adjuvant chemotherapy-2 (other) in resected pancreatic cancer patients

Figure 303: Overall survival (random effects analysis)

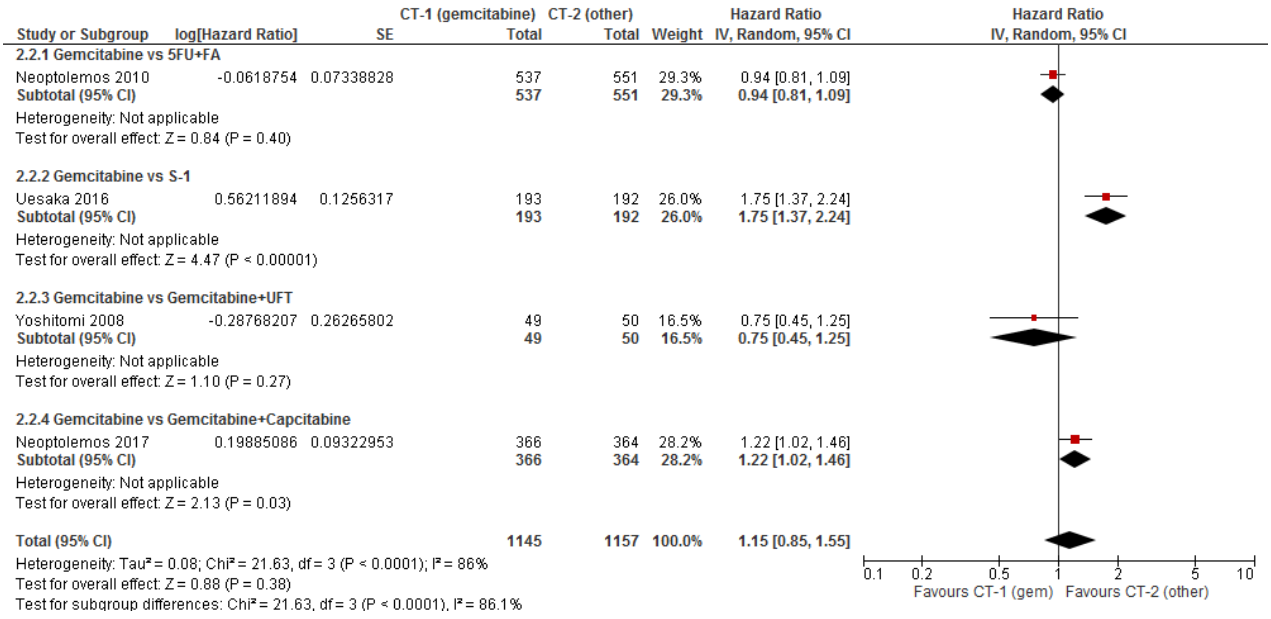


Figure 304: Overall Survival (fixed effects analysis)

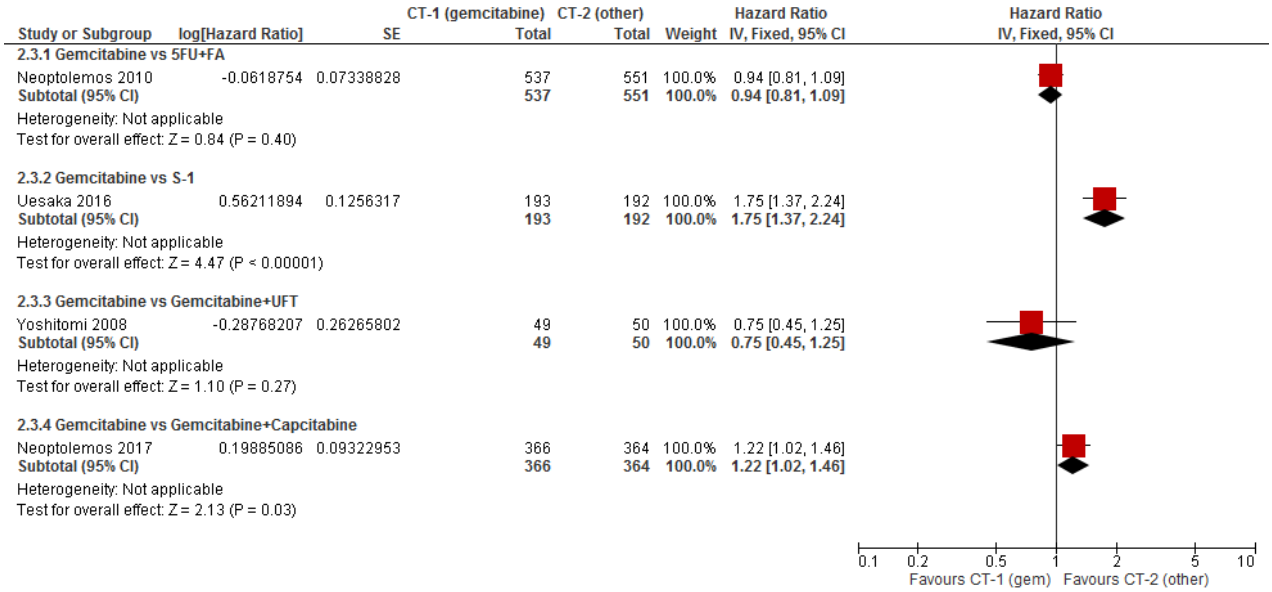


Figure 305: Relapse-free Survival

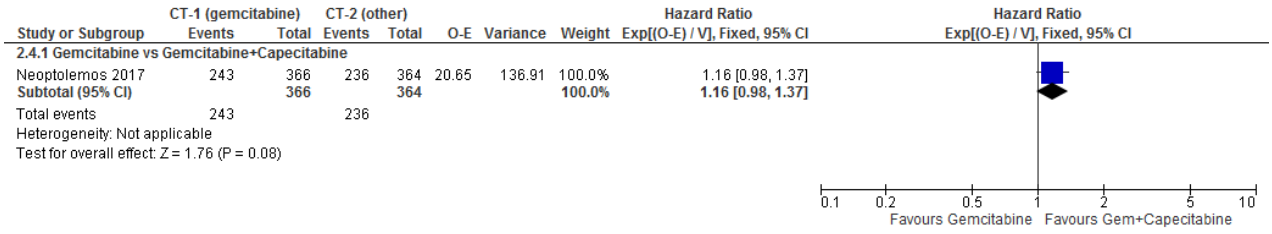


Figure 306: Disease-free survival

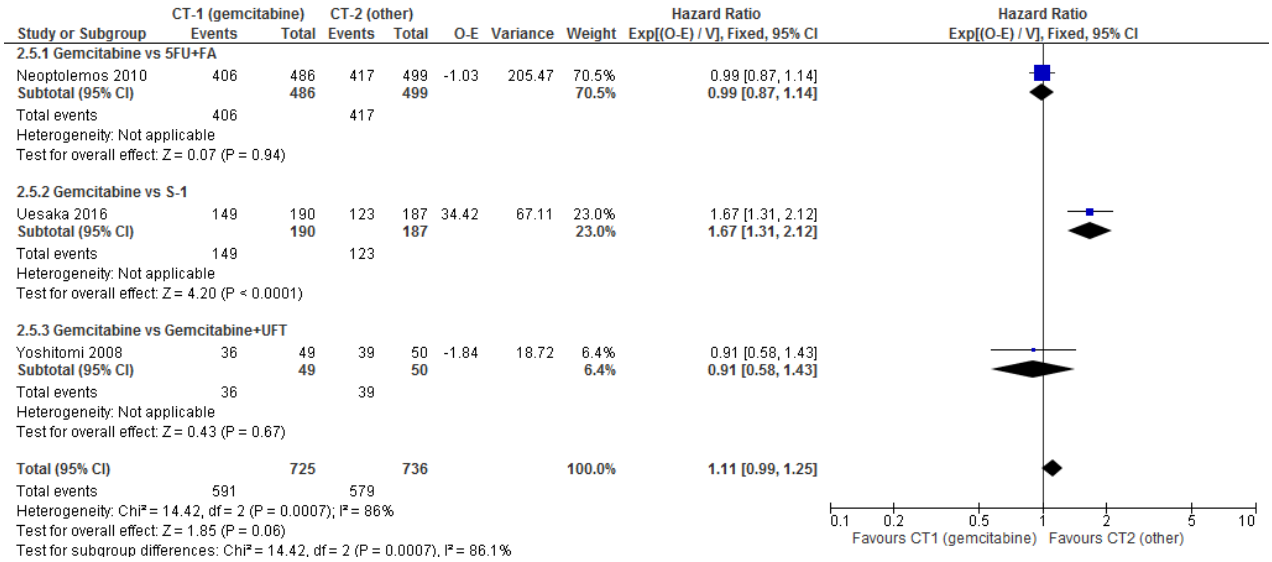


Figure 307: # patients with serious treatment-related adverse events (random effects analysis)

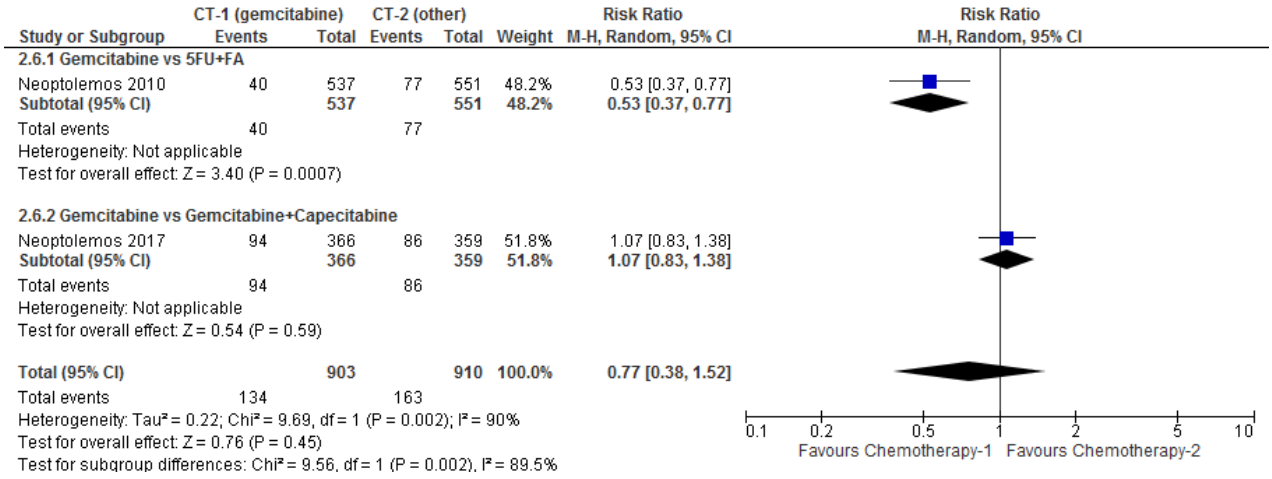


Figure 308: # patients with serious treatment-related adverse events (fixed effects analysis)

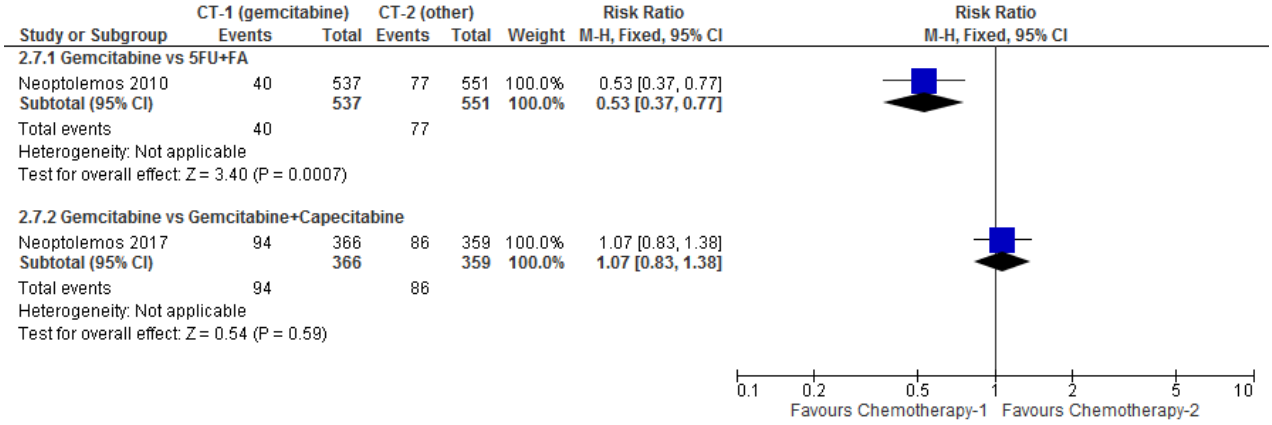


Figure 309: # patients with Grade 3 or 4 alanine aminotransferase/aspartate aminotransferase (random effects analysis)

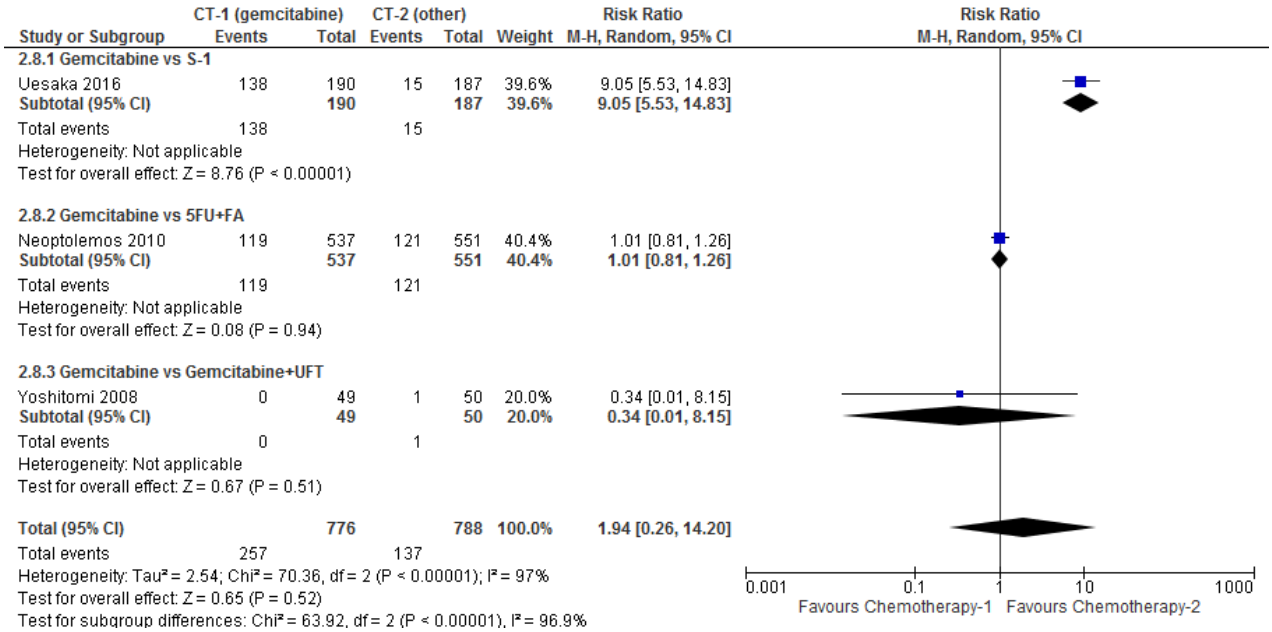
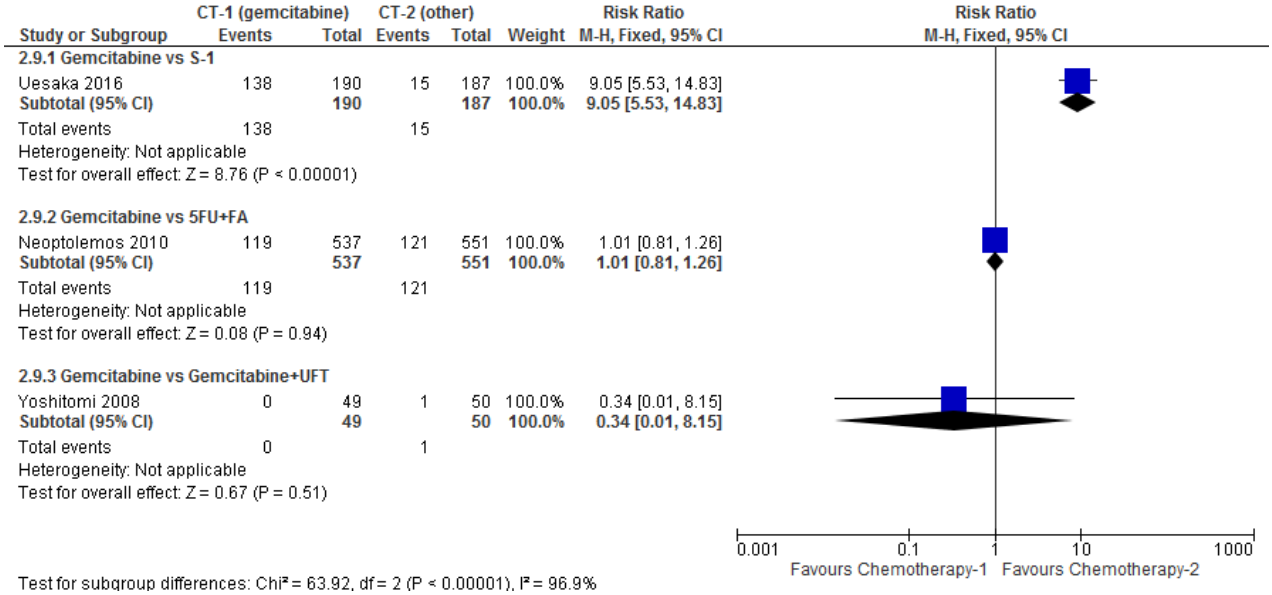
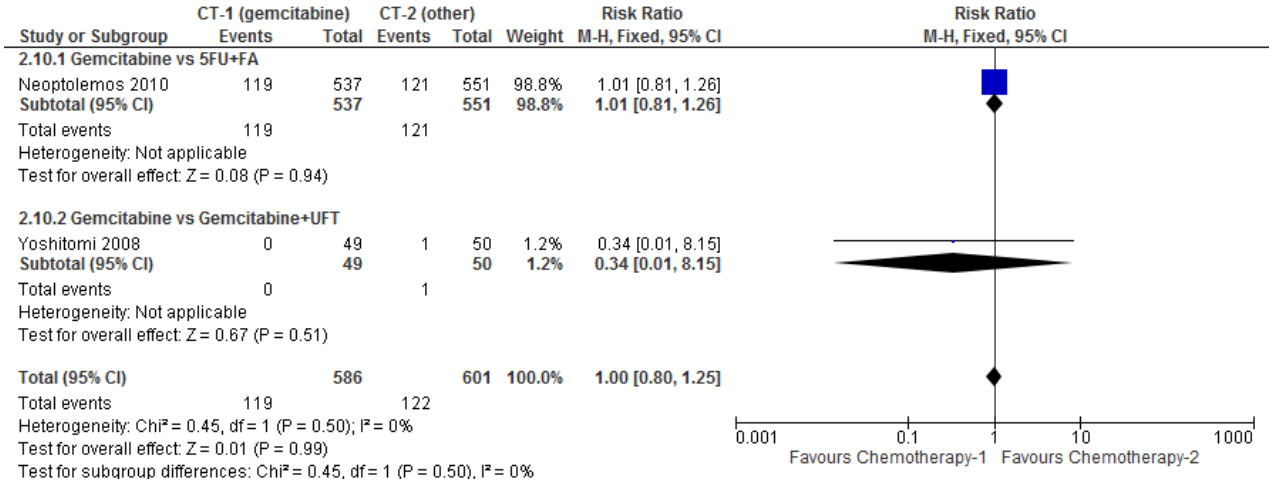


Figure 310: # patients with Grade 3 or 4 alanine aminotransferase/aspartate aminotransferase (fixed effects analysis)



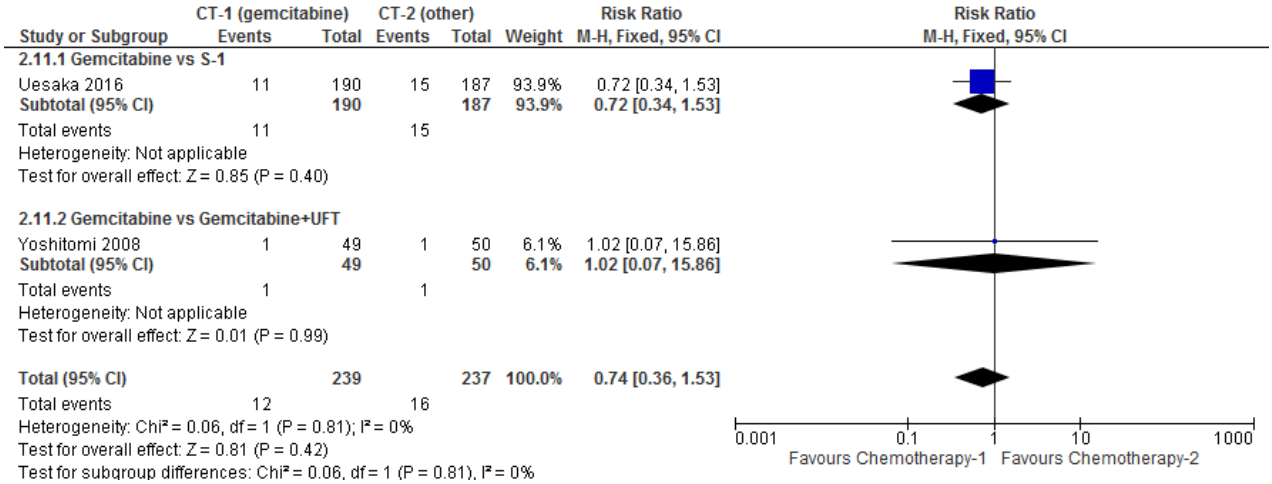
Test for subgroup differences: Chi² = 63.92, df = 2 (P < 0.00001), I² = 96.9%

Figure 311: # patients with Grade 3 or 4 alanine aminotransferase/aspartate aminotransferase (fixed effects – sensitivity analysis)



Test for subgroup differences: Chi² = 0.45, df = 1 (P = 0.50), I² = 0%

Figure 312: # patients with Grade 3 or 4 anorexia



Test for subgroup differences: Chi² = 0.06, df = 1 (P = 0.81), I² = 0%

Figure 313: # patients with Grade 3 or 4 bilirubin

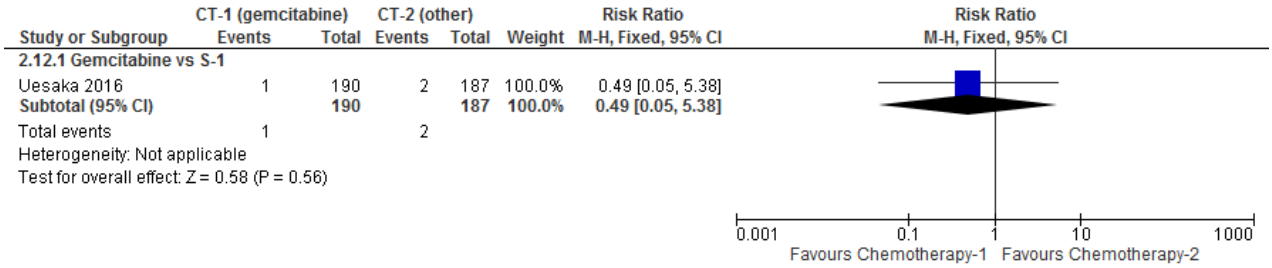


Figure 314: # patients with Grade 3 or 4 creatinine

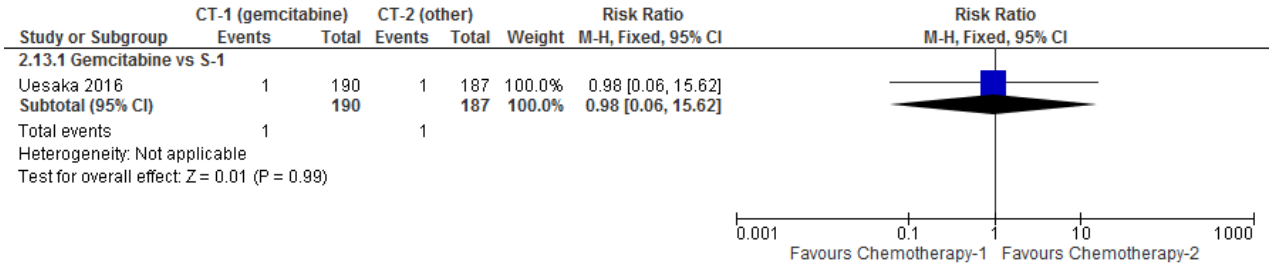


Figure 315: # patients with Grade 3 or 4 diarrhoea

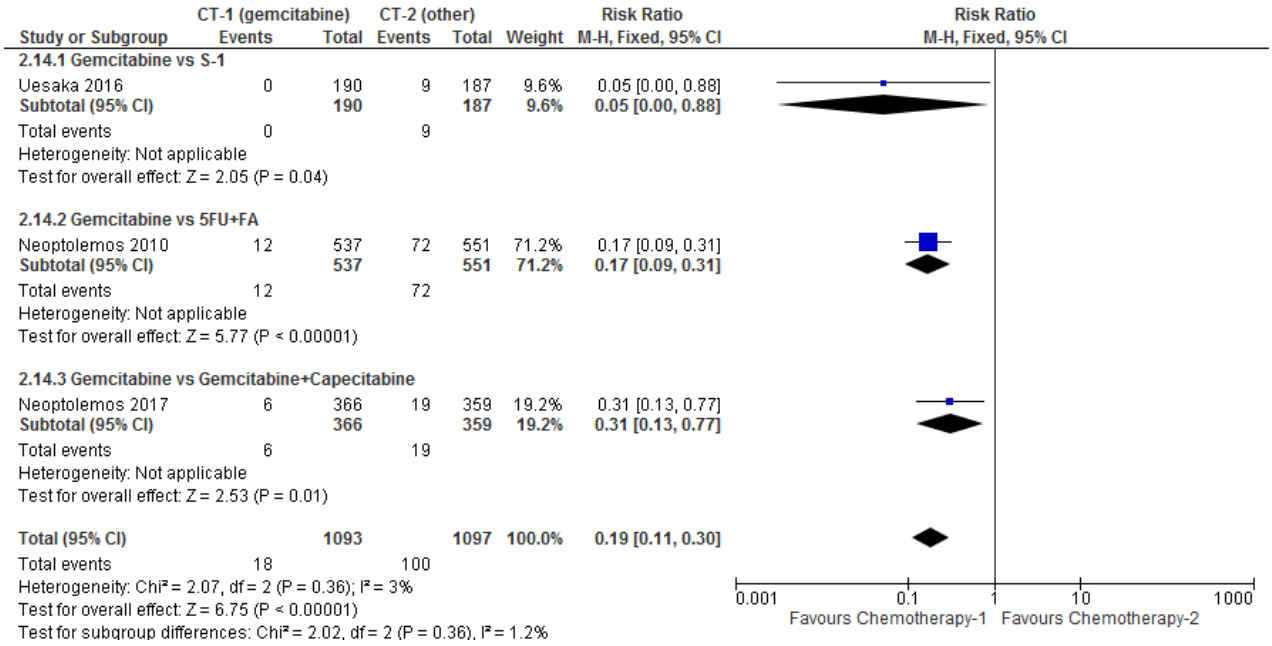


Figure 316: # patients with Grade 3 or 4 fatigue/tiredness

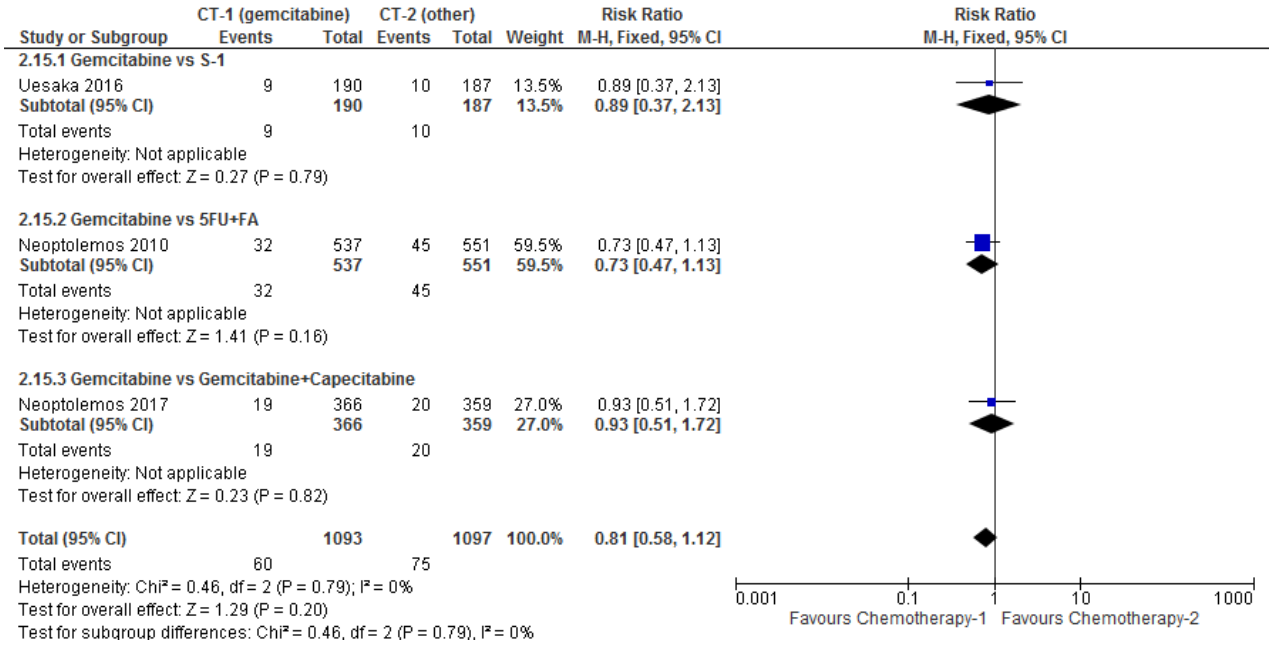


Figure 317: # patients with Grade 3 or 4 febrile neutropenia

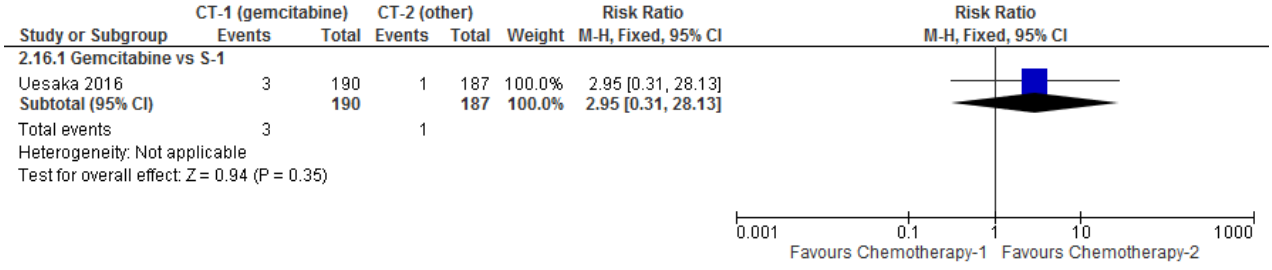


Figure 318: # patients with Grade 3 or 4 fever

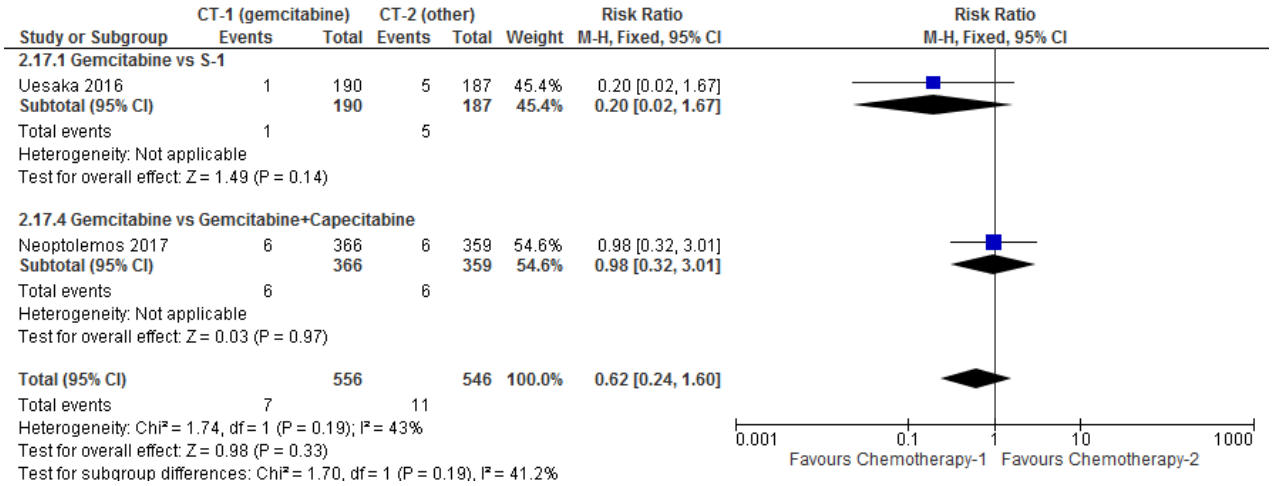


Figure 319: # patients with Grade 3 or 4 glucose intolerance

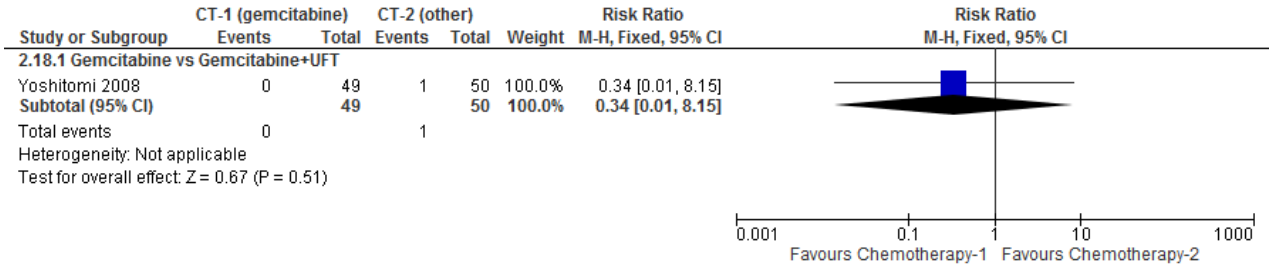


Figure 320: # patients with Grade 3 or 4 haemoglobin

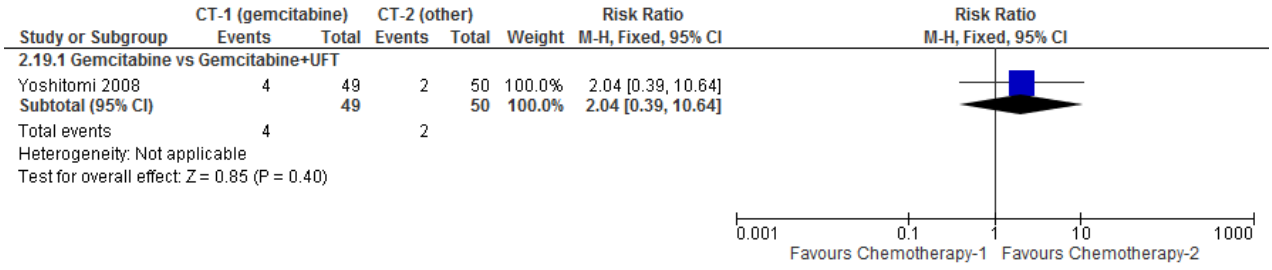


Figure 321: # patients with Grade 3 or 4 hand foot syndrome

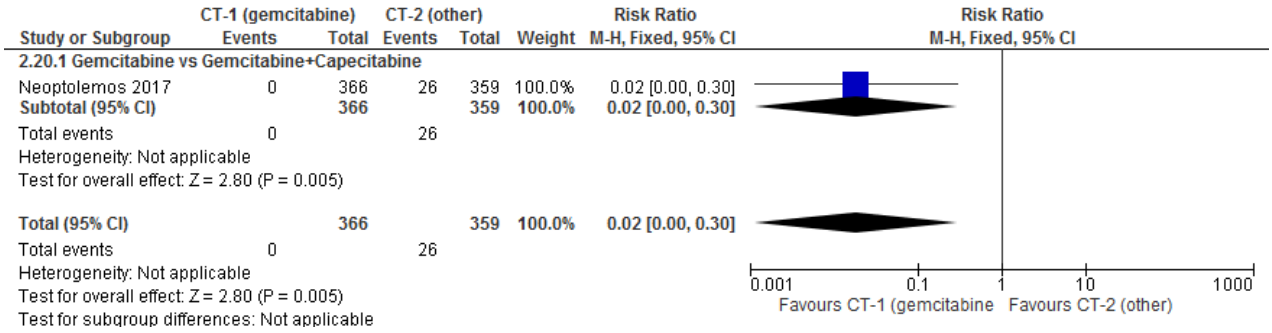


Figure 322: # patients with Grade 3 or 4 infection

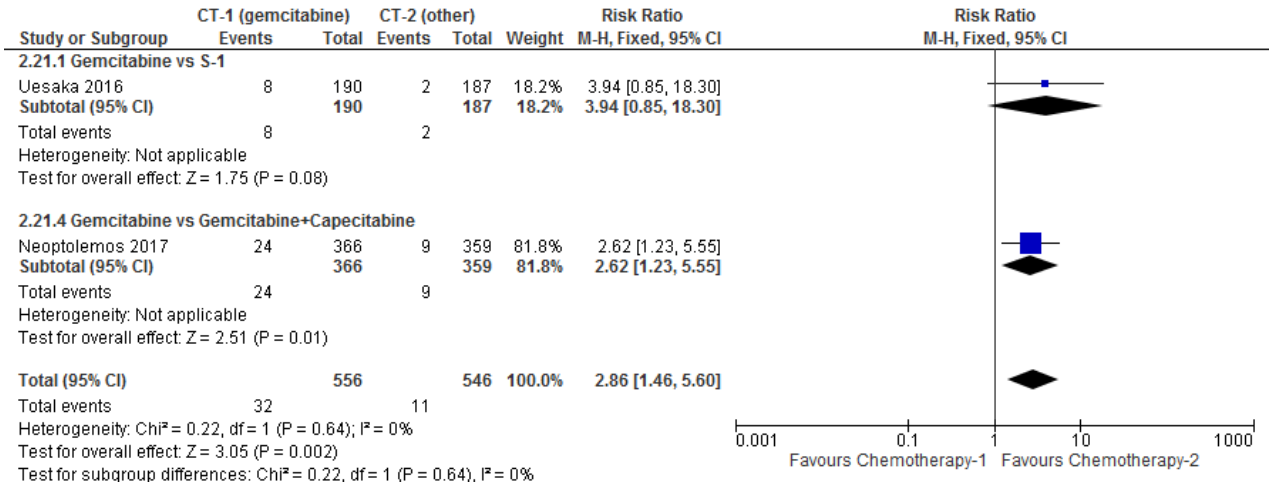


Figure 323: # patients with Grade 3 or 4 leukocytes

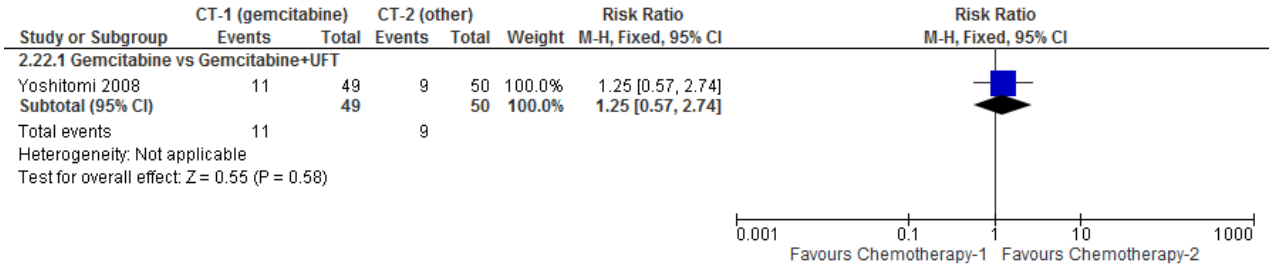


Figure 324: # patients with Grade 3 or 4 nausea

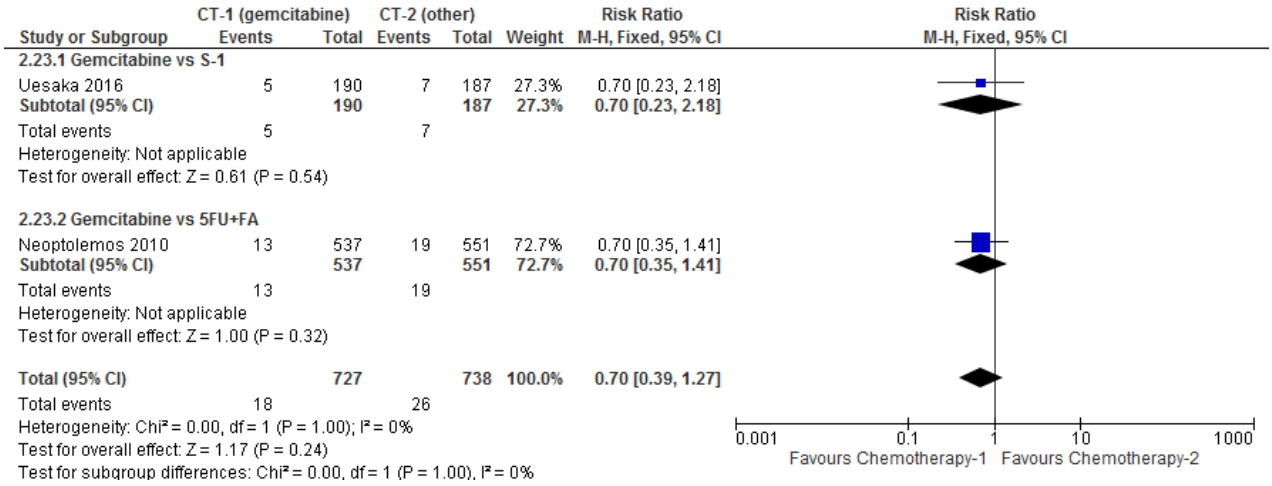


Figure 325: # patients with Grade 3 or 4 neutropenia

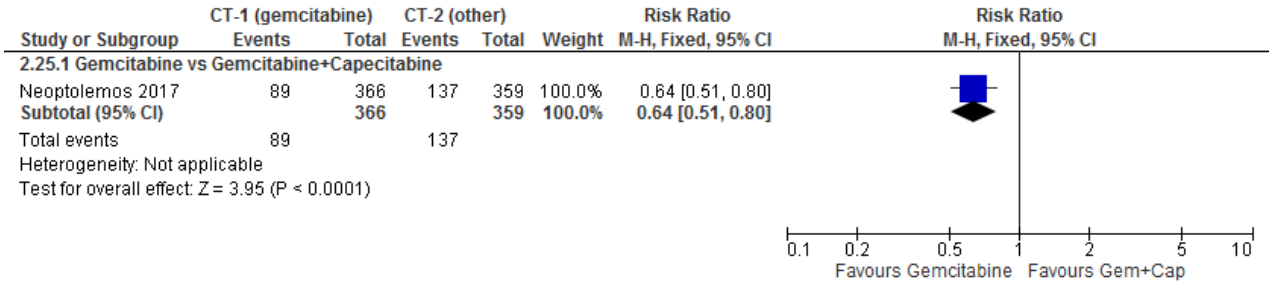


Figure 326: # patients with Grade 3 or 4 neutrophils (random effects)

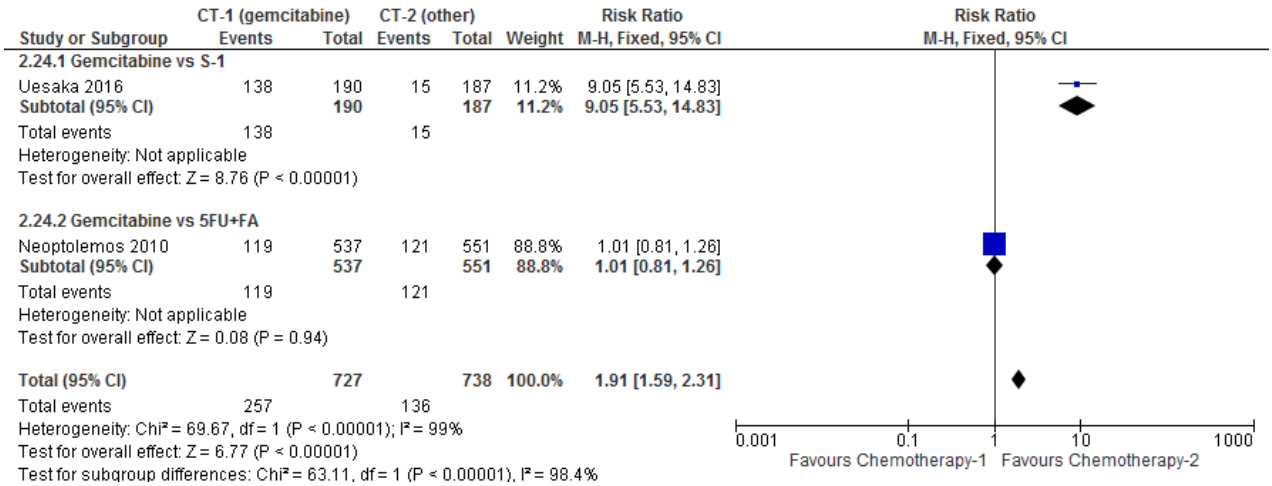
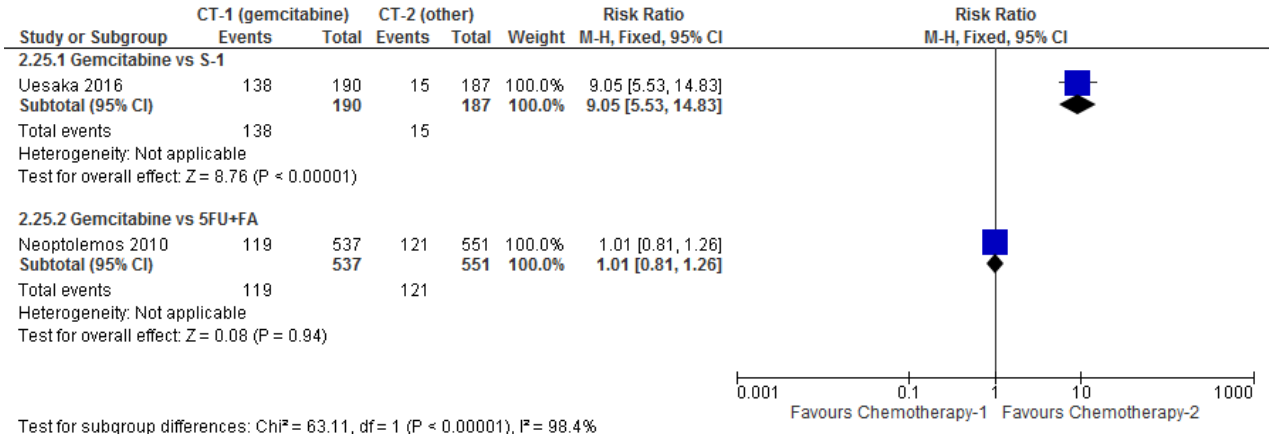
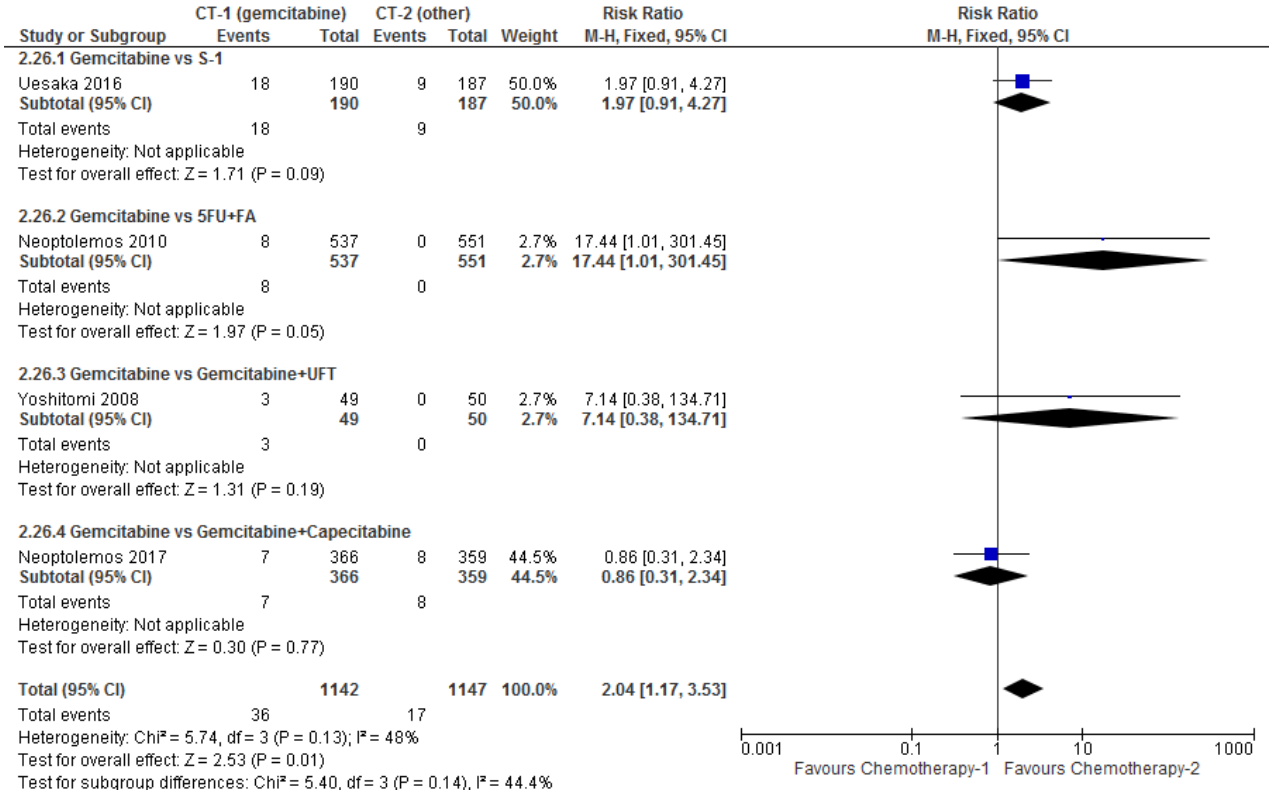


Figure 327: # patients with Grade 3 or 4 neutrophils (fixed effects)



Test for subgroup differences: Chi² = 63.11, df = 1 (P < 0.00001), I² = 98.4%

Figure 328: # patients with Grade 3 or 4 platelets



Test for subgroup differences: Chi² = 5.40, df = 3 (P = 0.14), I² = 44.4%

Figure 329: # patients with Grade 3 or 4 stomatitis

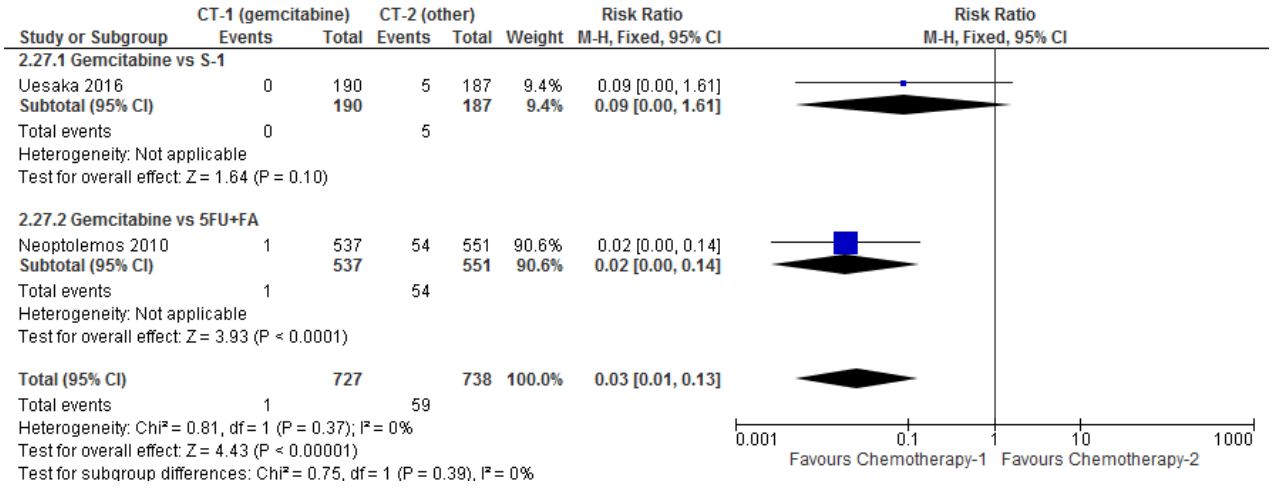


Figure 330: # patients with Grade 3 or 4 vomiting

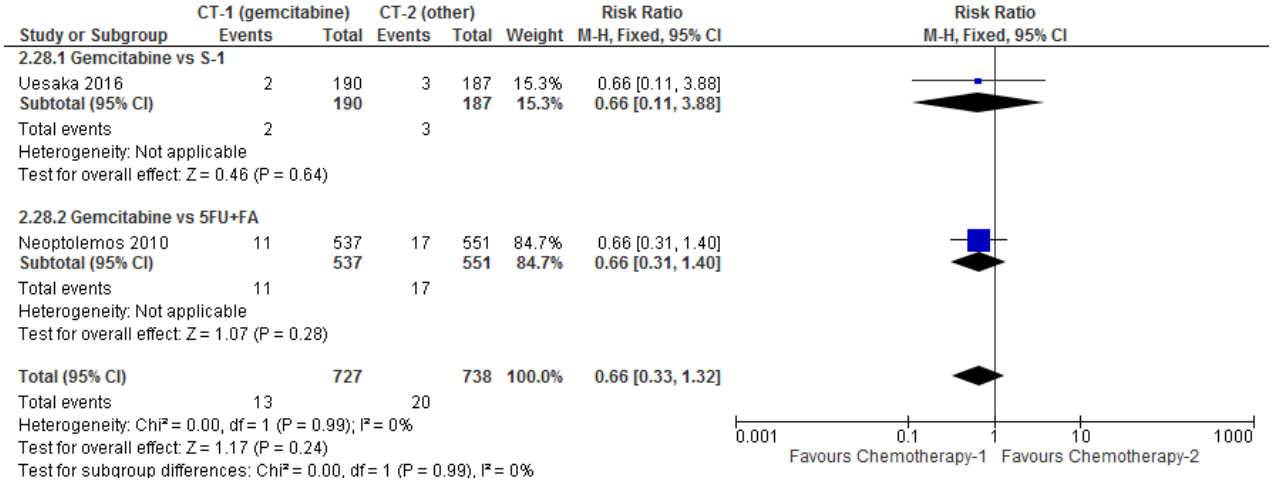


Figure 331: # patients with Grade 3 or 4 white blood cell count (random effects analysis)

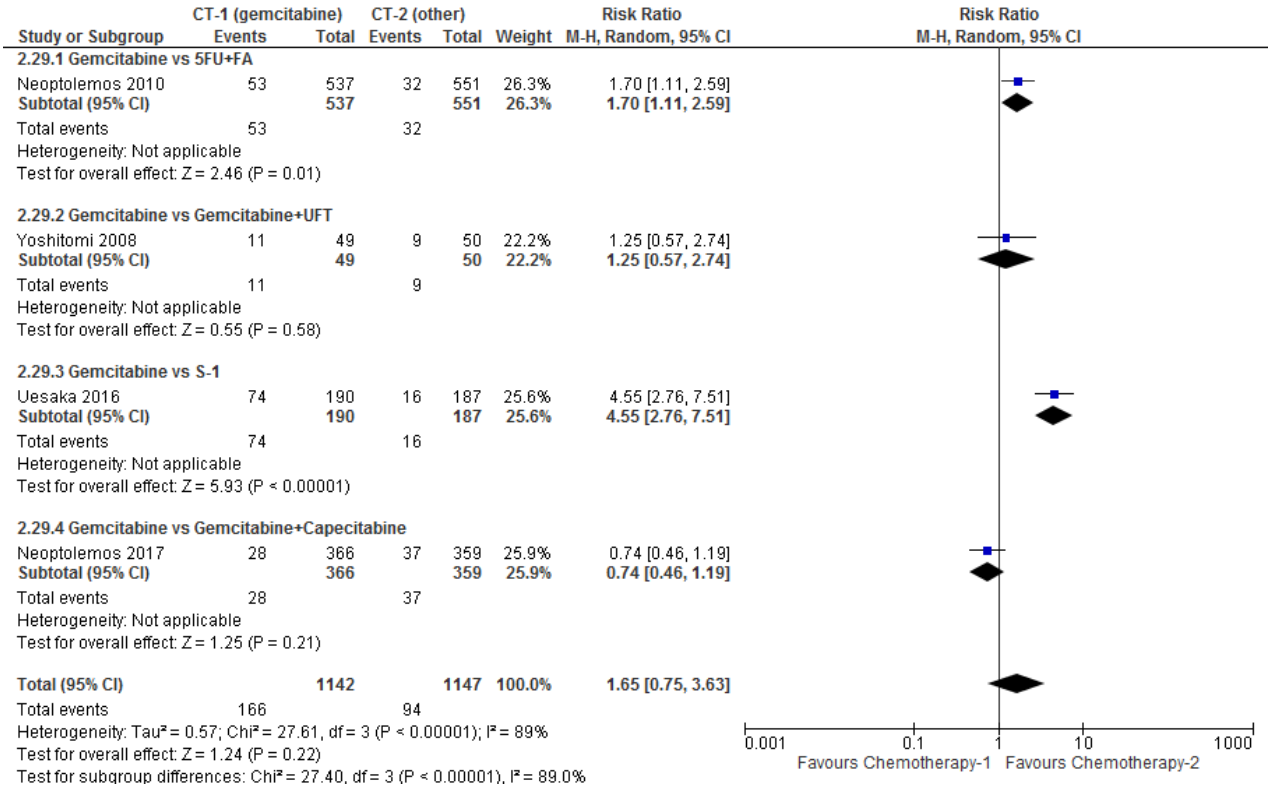


Figure 332: # patients with Grade 3 or 4 white blood cell count (fixed effects analysis)

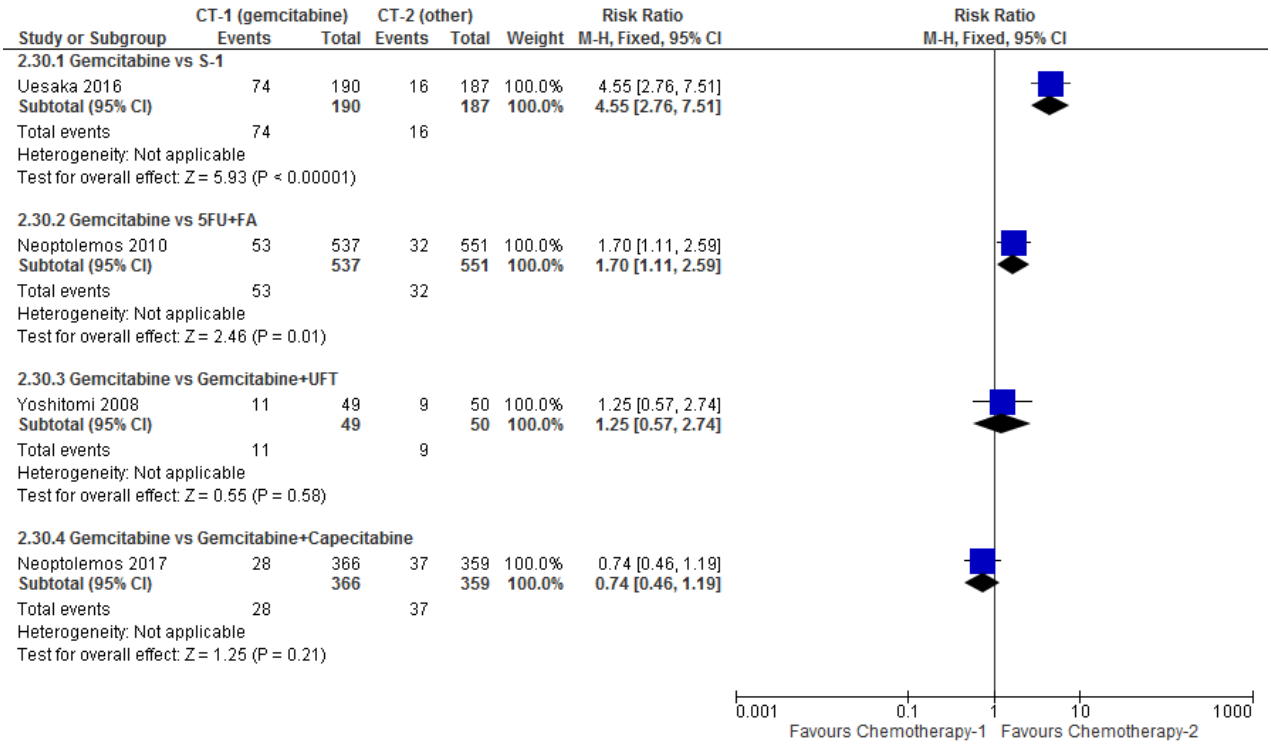


Figure 333: EQ-5D Quality of Life

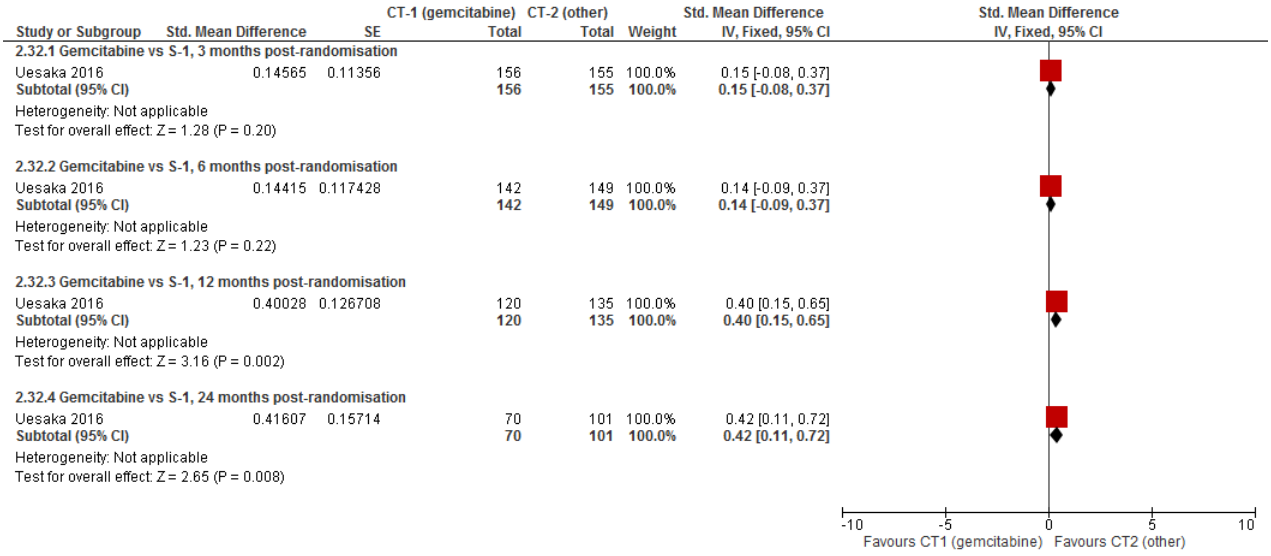
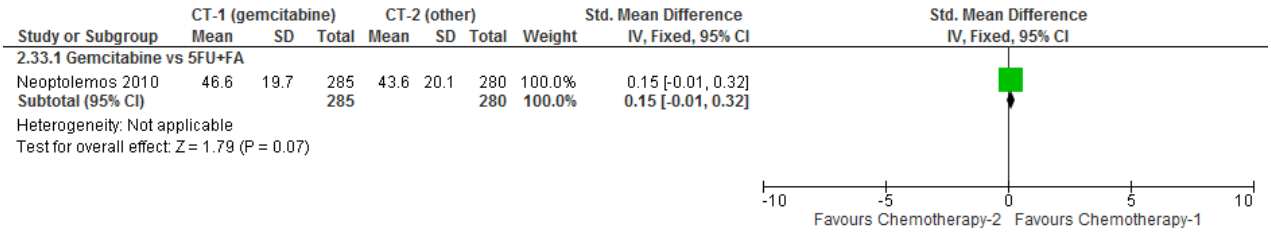


Figure 334: Global quality of life



H.14.3 Adjuvant chemotherapy versus adjuvant chemoradiotherapy in resected pancreatic cancer patients

Figure 335: Overall survival

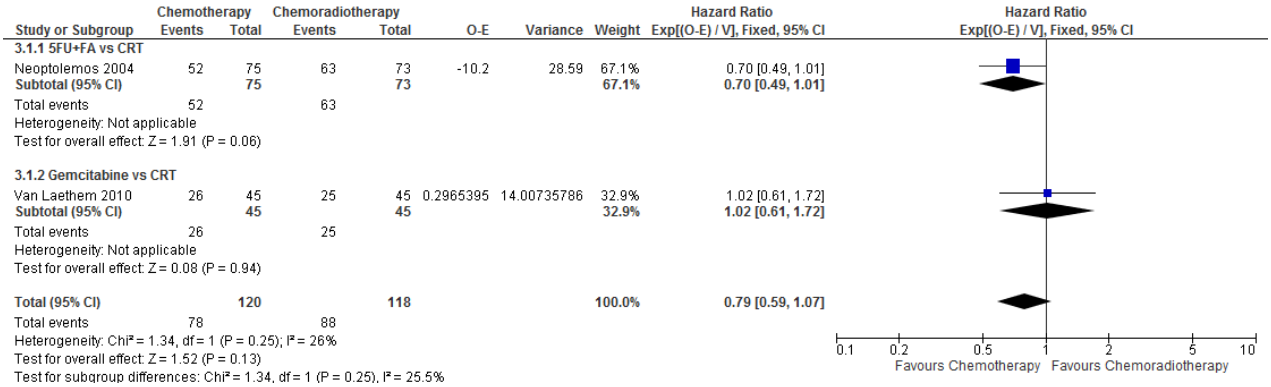


Figure 336: Disease-free survival

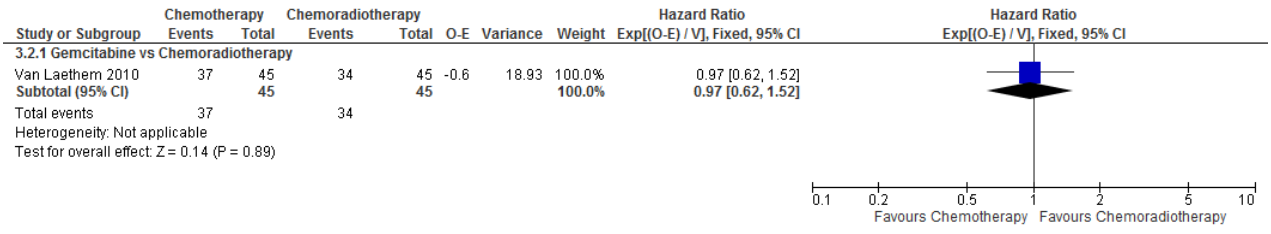


Figure 337: # patients with any Grade 3 or 4 haematological toxicity

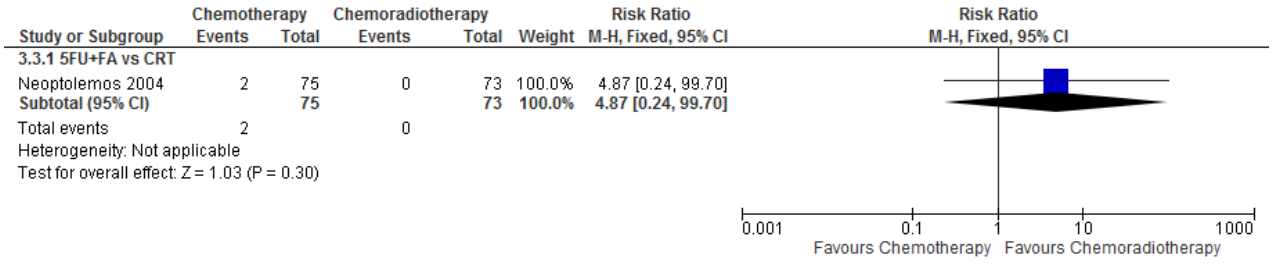


Figure 338: # patients with any Grade 3 or 4 non-haematological toxicity

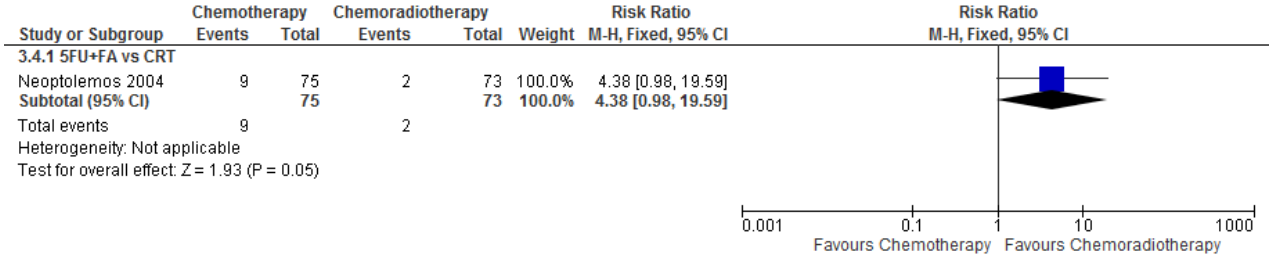


Figure 339: # patients with Grade 3 or 4 anorexia

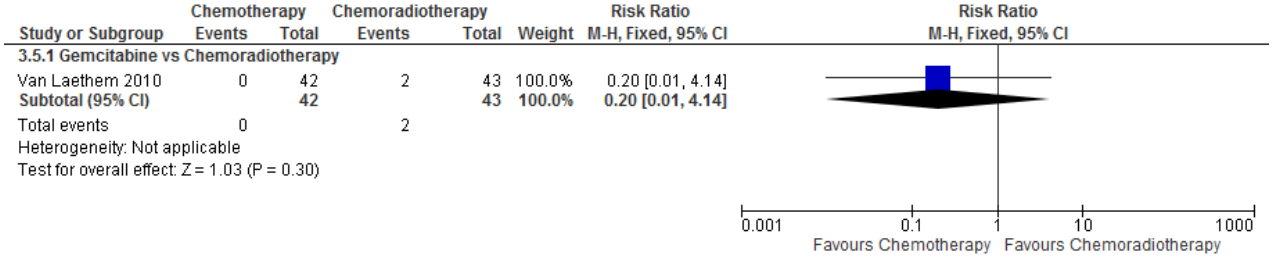


Figure 340: # patients with Grade 3 or 4 diarrhoea

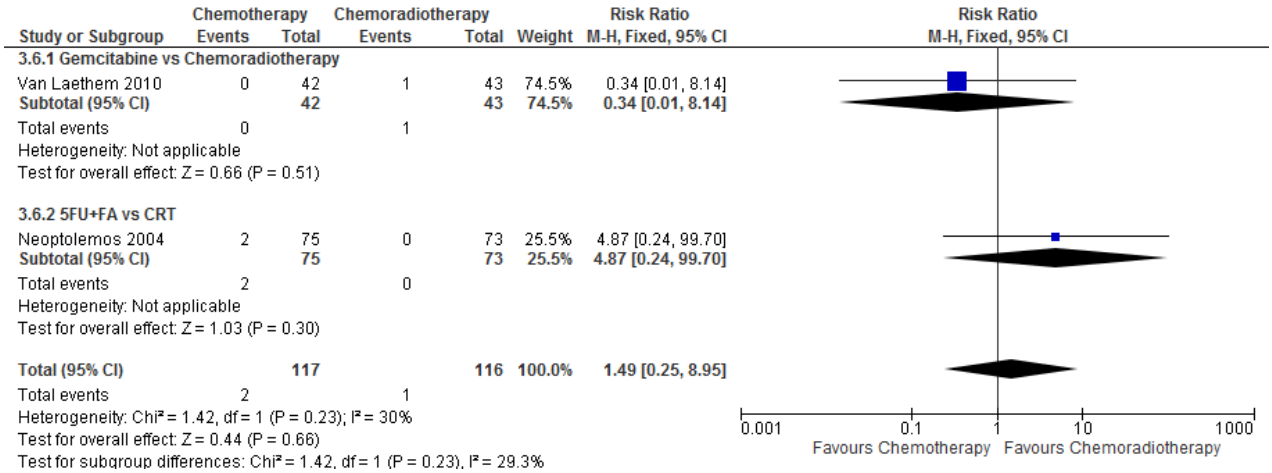


Figure 341: # patients with Grade 3 or 4 fatigue

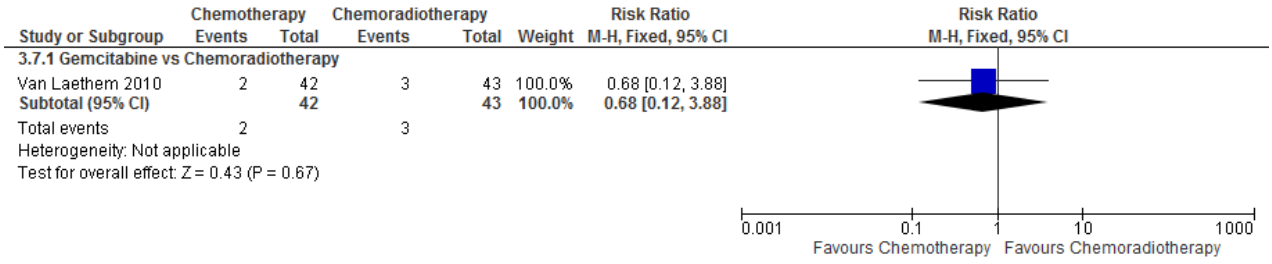


Figure 342: # patients with Grade 3 or 4 fever

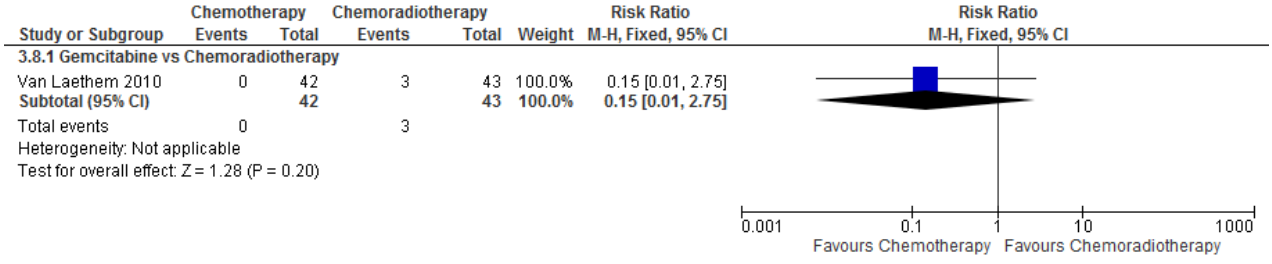


Figure 343: # patients with Grade 3 or 4 gastritis

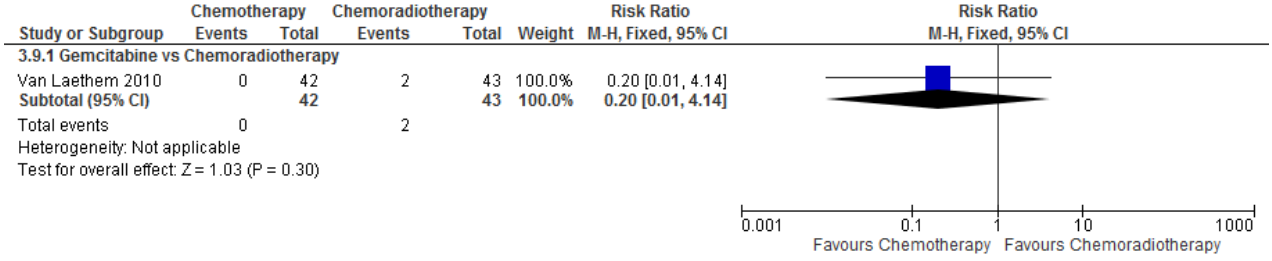


Figure 344: # patients with Grade 3 or 4 haemoglobin

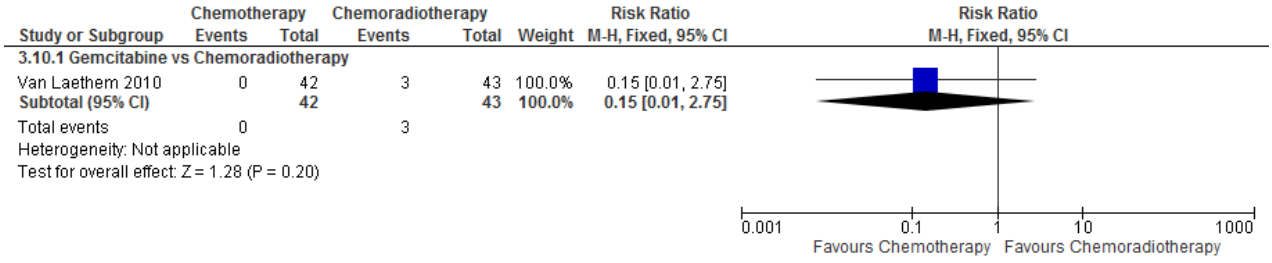


Figure 345: # patients with Grade 3 or 4 haemorrhage

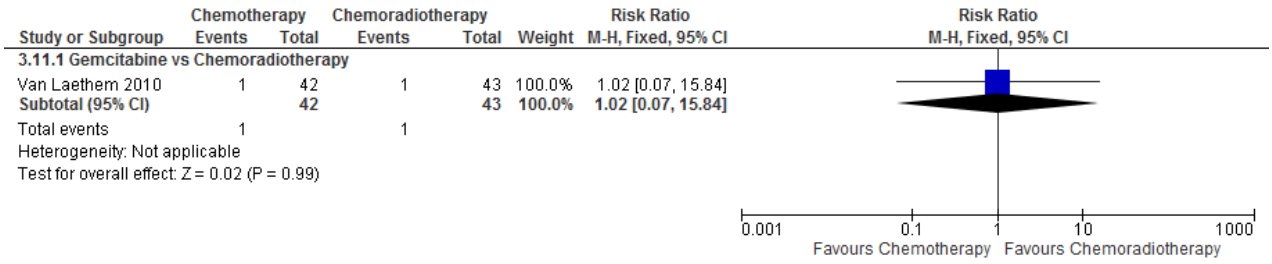


Figure 346: # patients with Grade 3 or 4 nausea

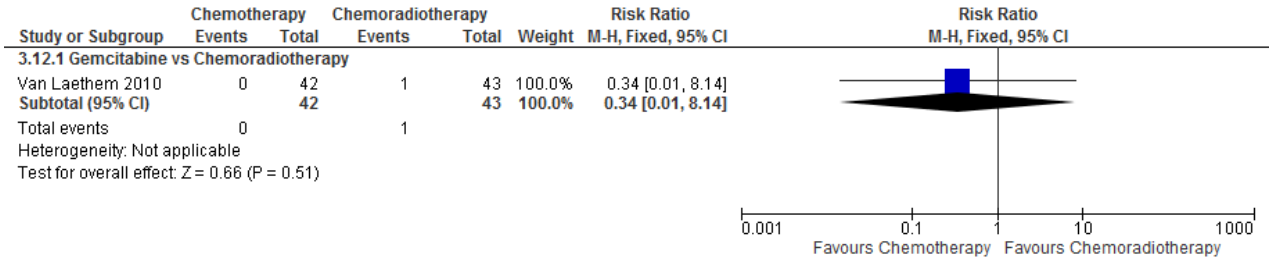


Figure 347: # patients with Grade 3 or 4 neutrophils

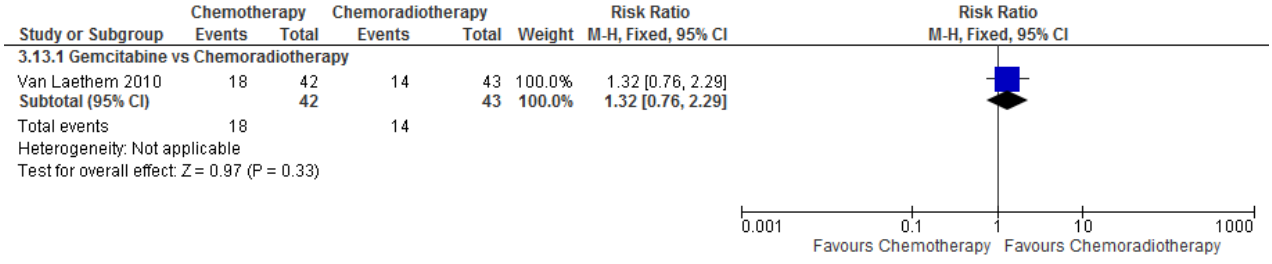


Figure 348: # patients with Grade 3 or 4 other gastrointestinal toxicity

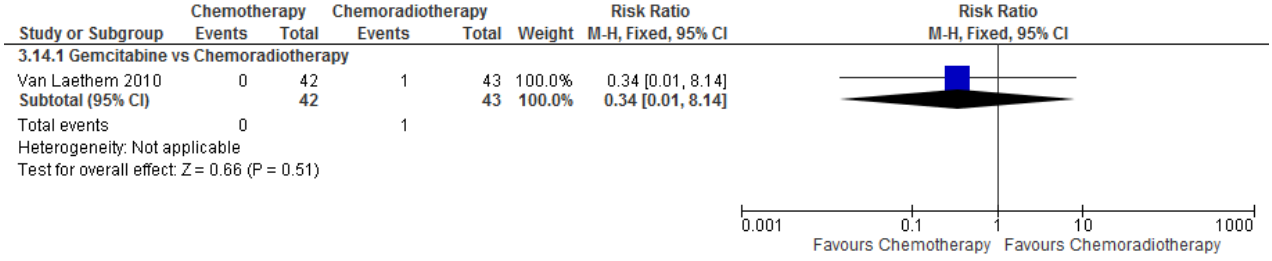


Figure 349: # patients with Grade 3 or 4 platelets

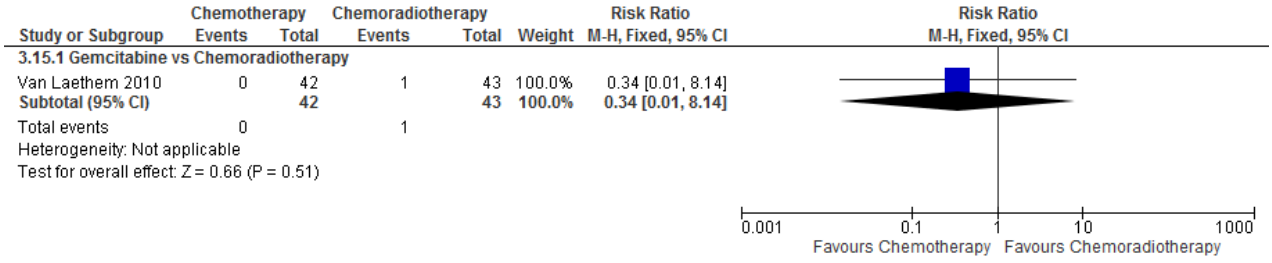


Figure 350: # patients with Grade 3 or 4 serum glutamicpyruvic transaminase

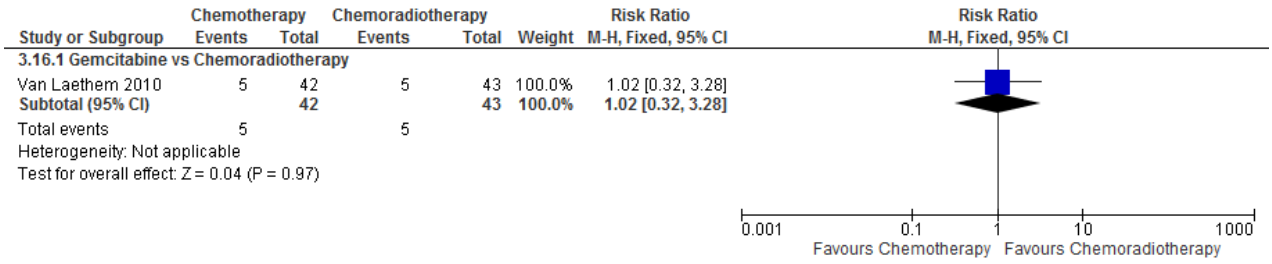


Figure 351: # patients with Grade 3 or 4 stomatitis

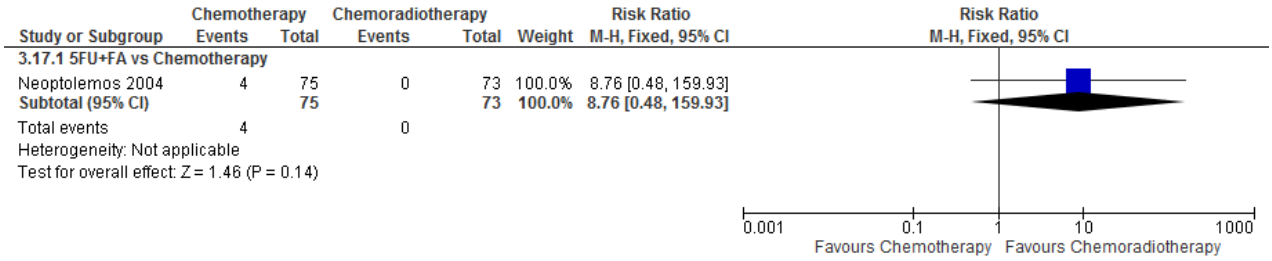


Figure 352: # patients with Grade 3 or 4 vomiting

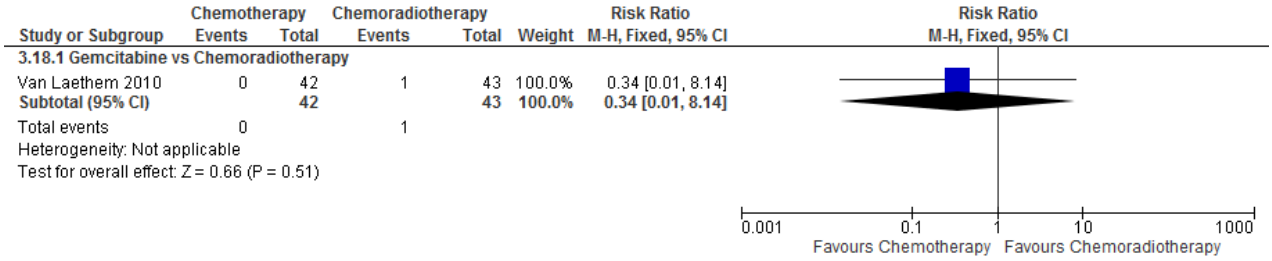


Figure 353: # patients with Grade 3 or 4 weight loss

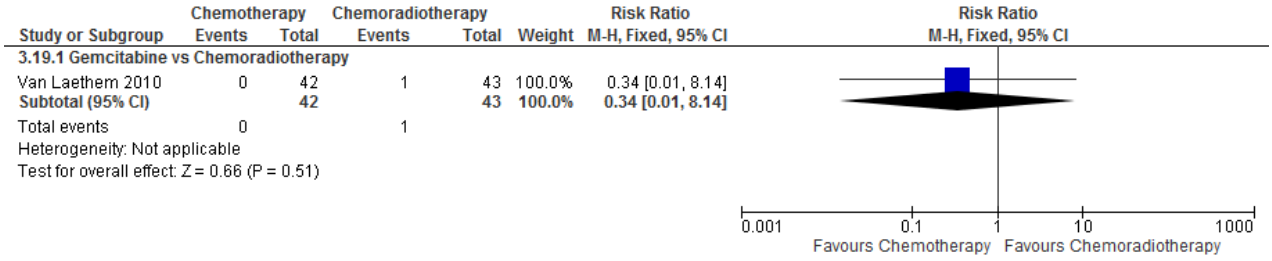
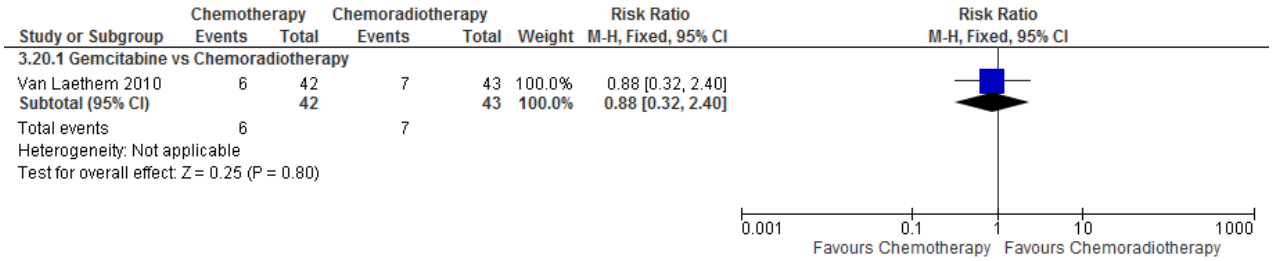


Figure 354: # patients with Grade 3 or 4 white blood cell count



H.14.49 Adjuvant chemotherapy versus adjuvant chemoimmunotherapy in resected pancreatic cancer patients

Figure 355: Overall survival

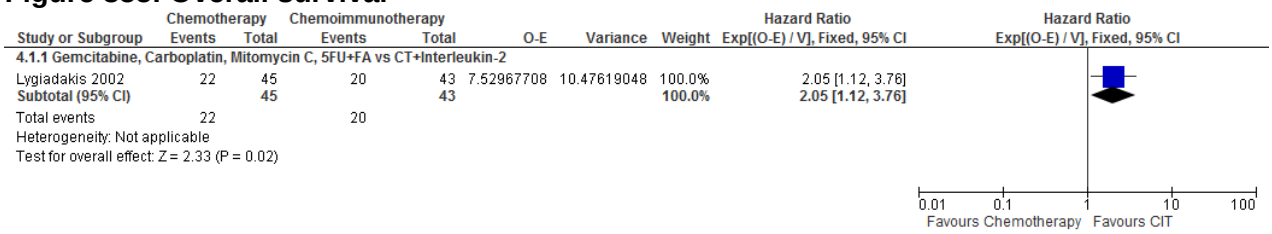


Figure 356: Disease-free survival

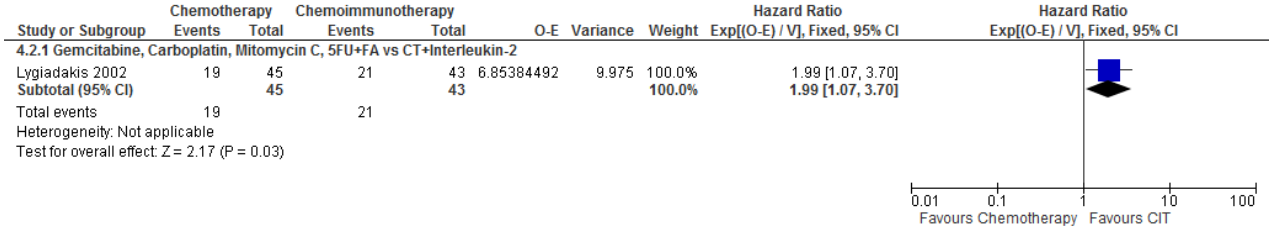


Figure 357: # patients with Grade 3 or 4 nausea

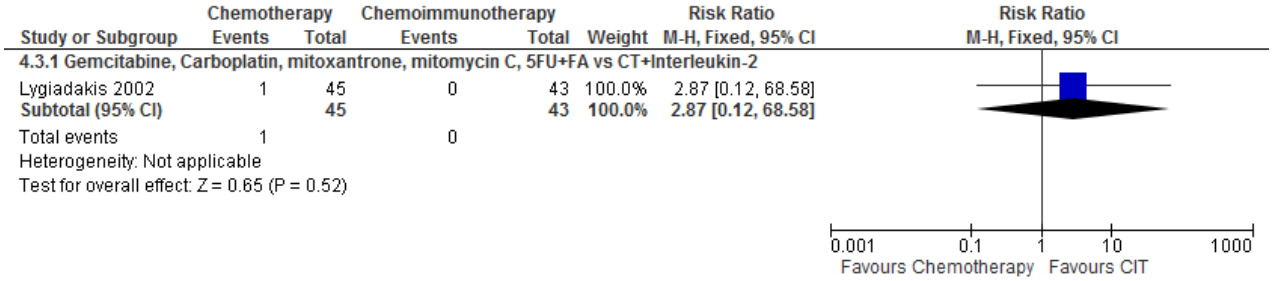
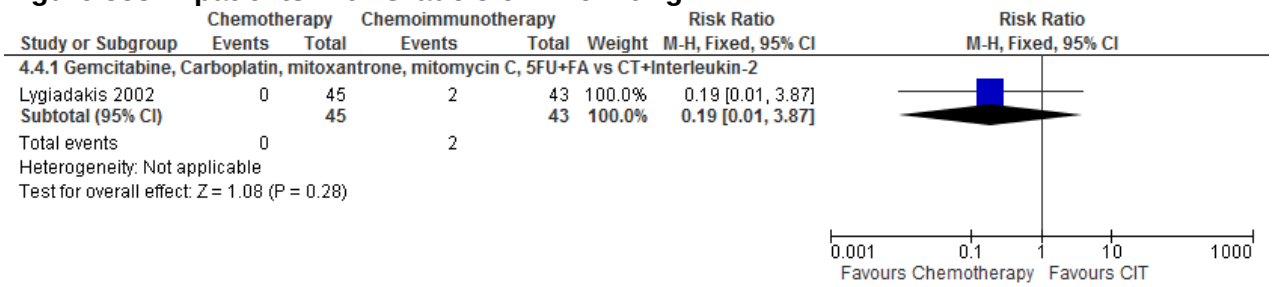


Figure 358: # patients with Grade 3 or 4 vomiting



H.14.5 Adjuvant chemotherapy versus adjuvant chemoradioimmunotherapy in resected pancreatic cancer patients

Figure 359: Overall survival

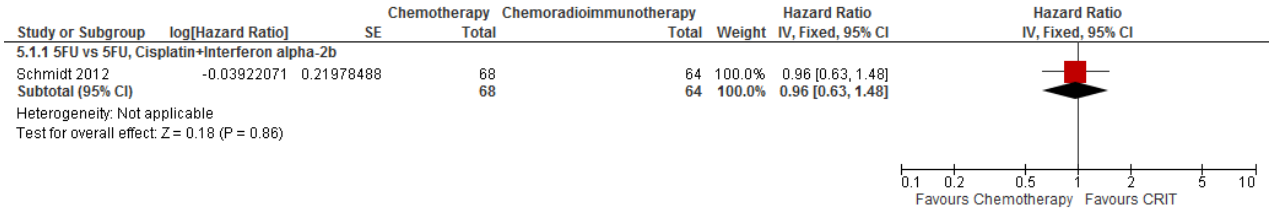


Figure 360: Disease-free survival

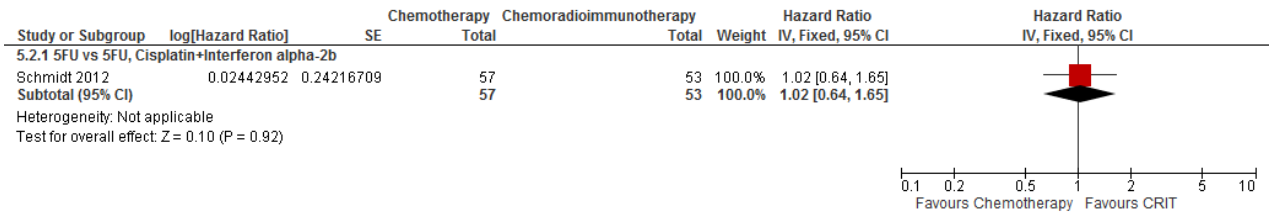


Figure 361: # patients with any Grade 3 or 4 toxicity

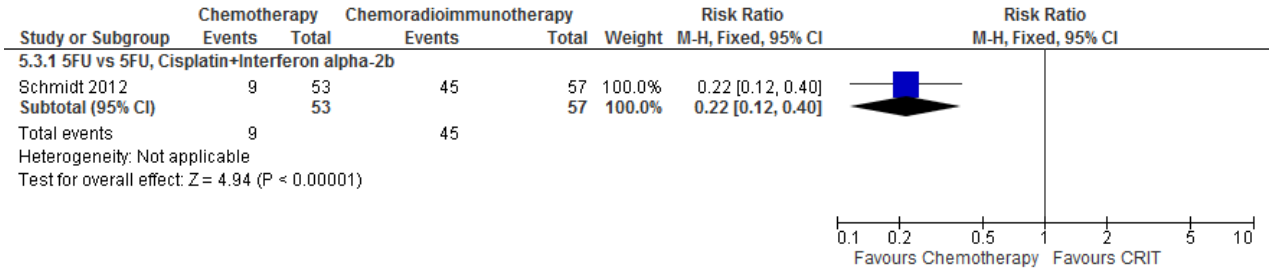
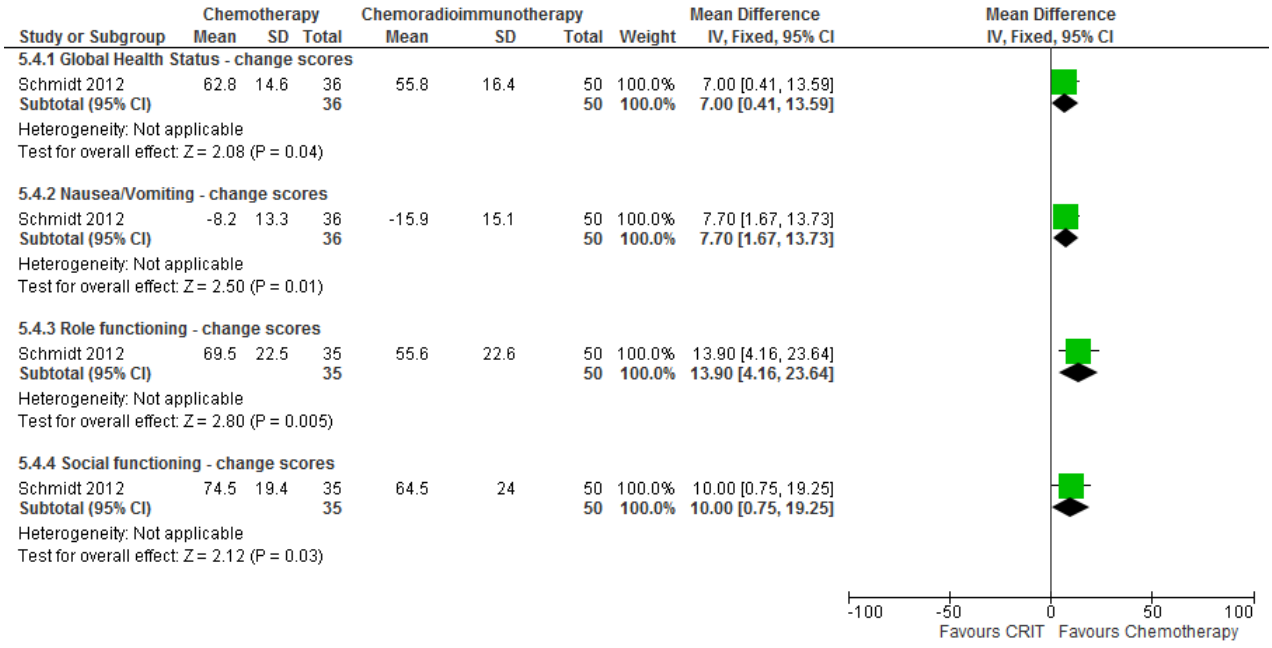


Figure 362: EORTC QLQ-C30 Quality of Life subscales – change scores



H.14.6 Adjuvant chemoradiotherapy followed by chemotherapy versus no adjuvant therapy in resected pancreatic cancer patients

Figure 363: # patients with any Grade 3 or 4 haematological toxicity

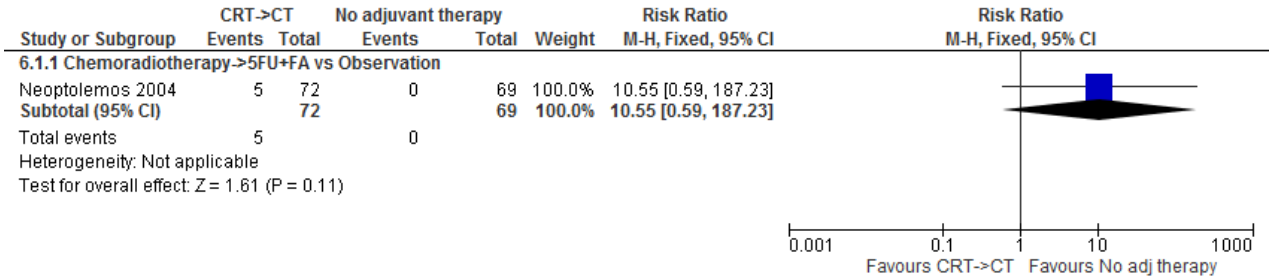


Figure 364: # patients with any Grade 3 or 4 haematological toxicity

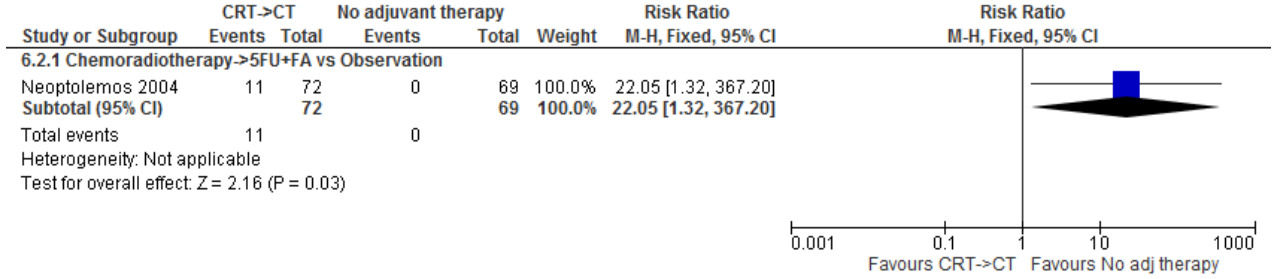


Figure 365: # patients with Grade 3 or 4 stomatitis

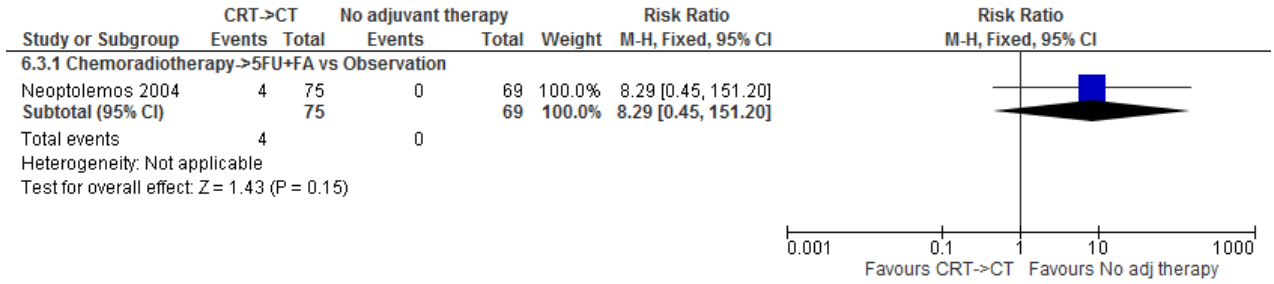
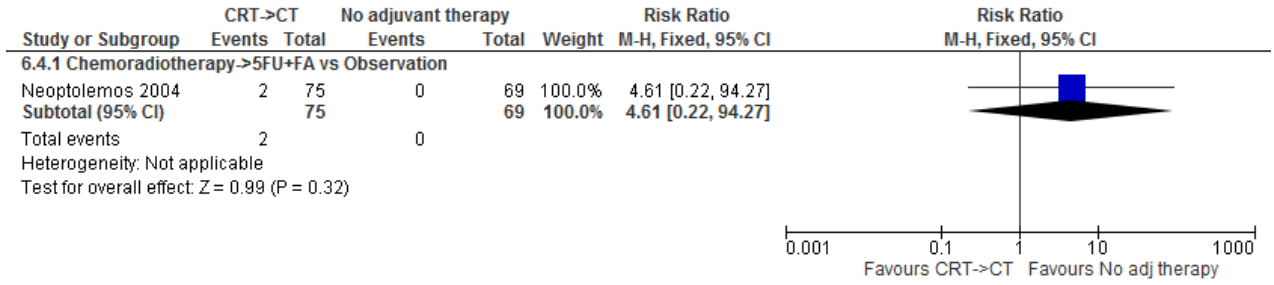


Figure 366: # patients with any Grade 3 or 4 diarrhoea



H.14.7 Adjuvant chemoradiotherapy followed by chemotherapy versus chemotherapy in resected pancreatic cancer patients

Figure 367: Overall survival

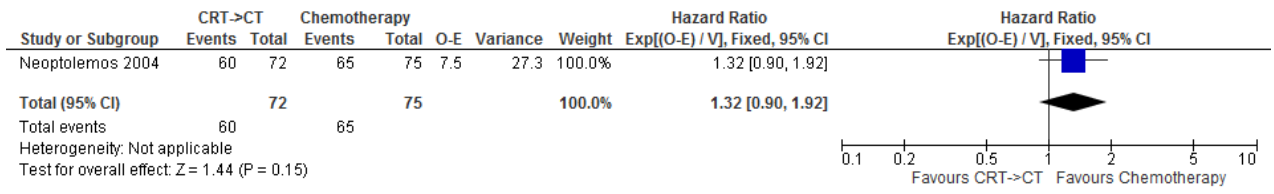


Figure 368: # patients with any Grade 3 or 4 haematological toxicity

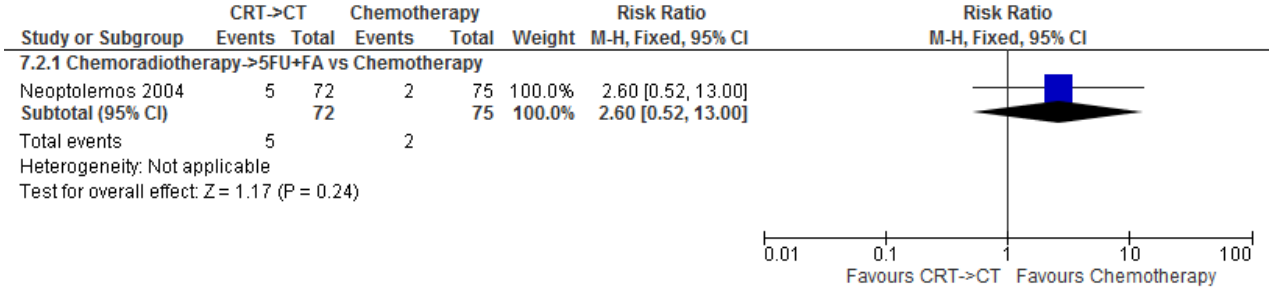


Figure 369: # patients with any Grade 3 or 4 non-haematological toxicity

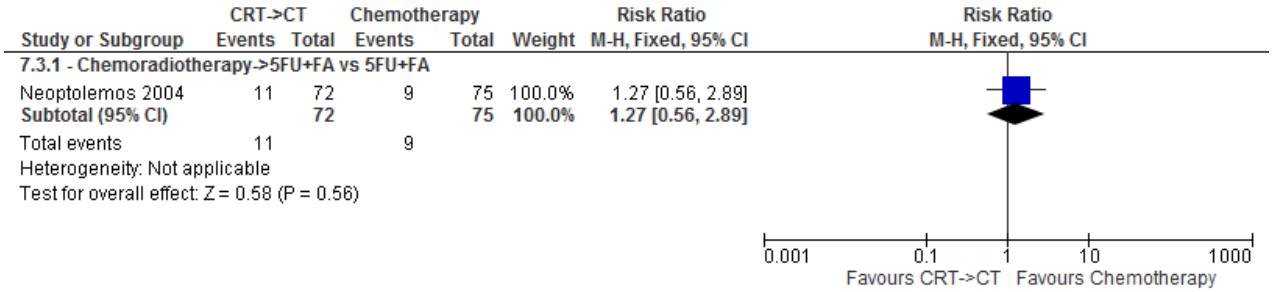


Figure 370: # patients with Grade 3 or 4 stomatitis

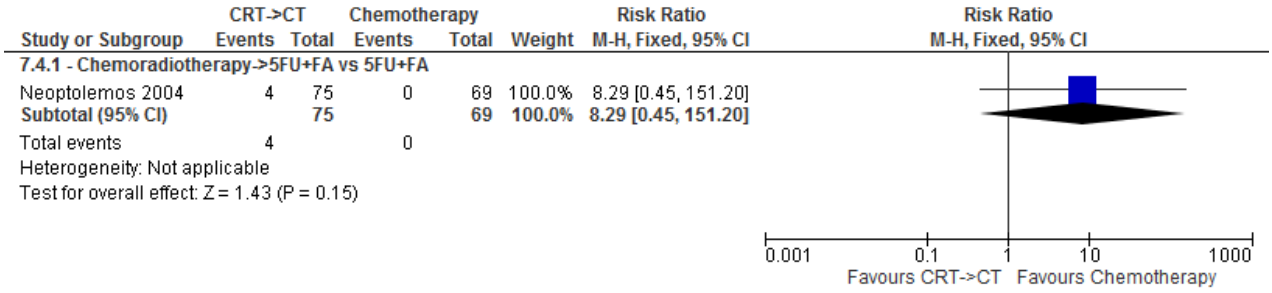
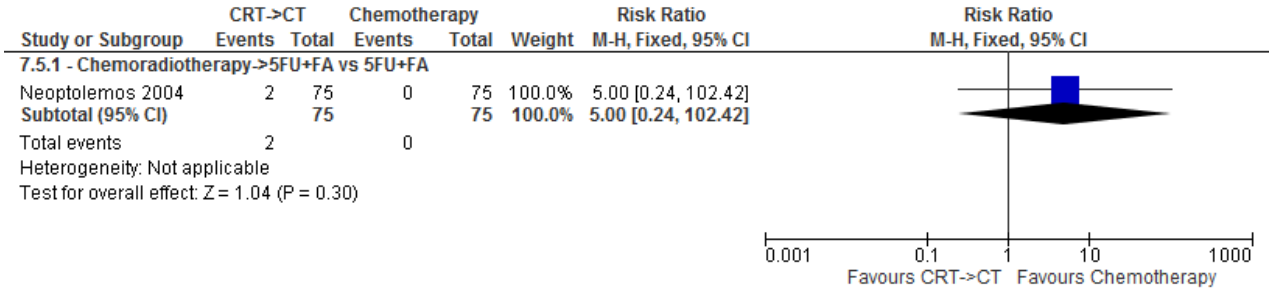


Figure 371: # patients with Grade 3 or 4 diarrhoea



H.14.81 Adjuvant chemoradiotherapy followed by chemotherapy versus chemoradiotherapy in resected pancreatic cancer patients

Figure 372: Overall survival

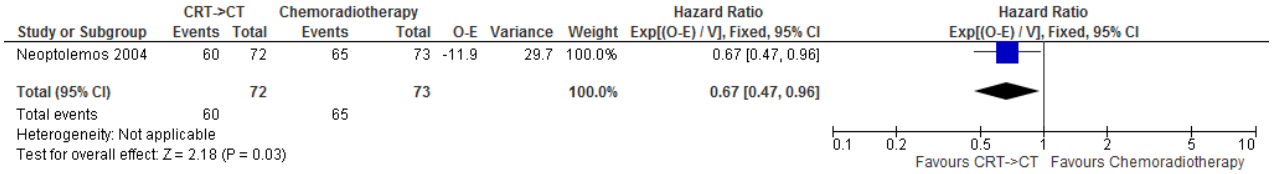


Figure 373: # patients with any Grade 3 or 4 haematological toxicity

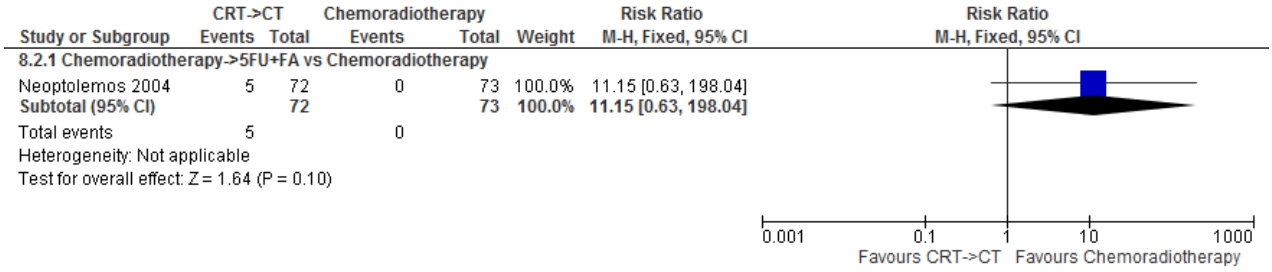


Figure 374: # patients with any Grade 3 or 4 non-haematological toxicity

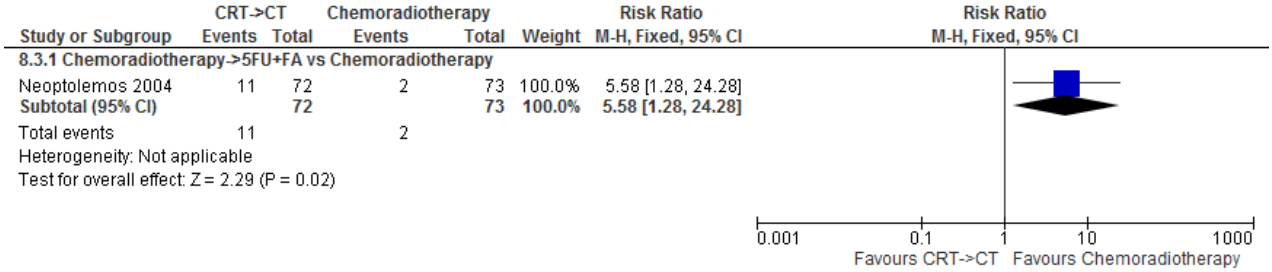


Figure 375: # patients with Grade 3 or 4 stomatitis

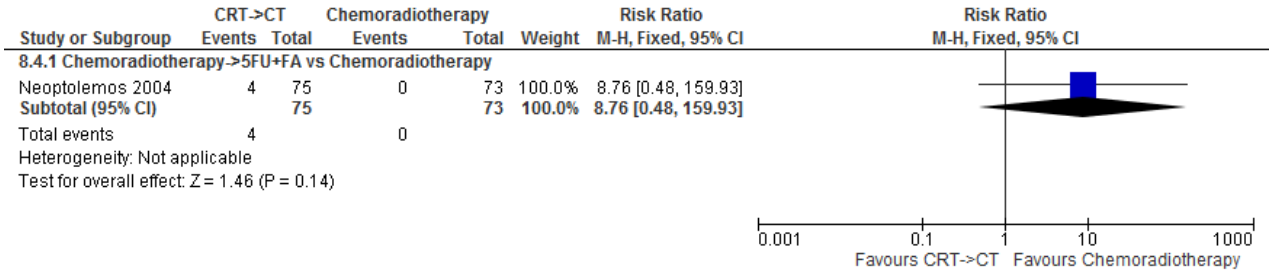
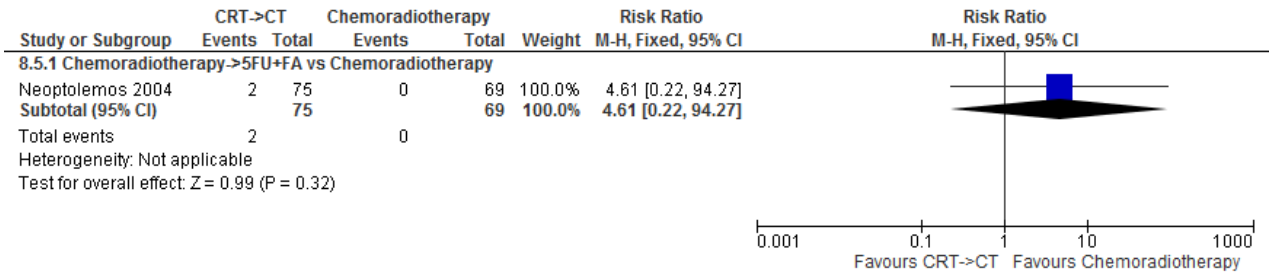


Figure 376: # patients with Grade 3 or 4 diarrhoea



H.14.9 Adjuvant chemotherapy-1 (gemcitabine) followed by chemoradiotherapy versus chemotherapy-2 (other) followed by chemoradiotherapy in resected pancreatic cancer patients

Figure 377: Overall survival

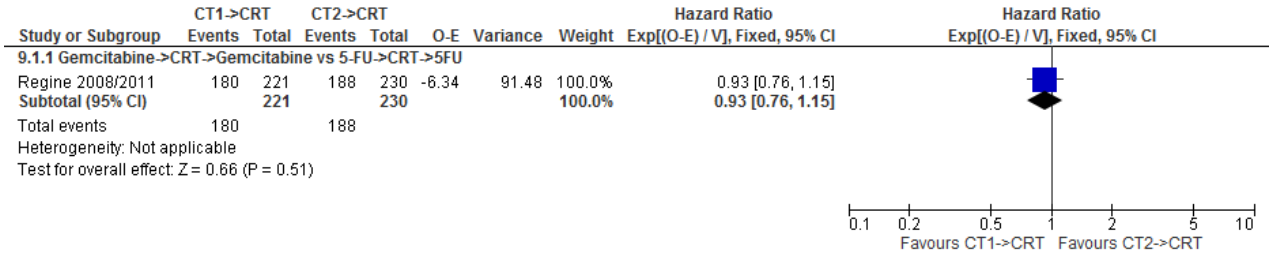


Figure 378: Disease-free survival

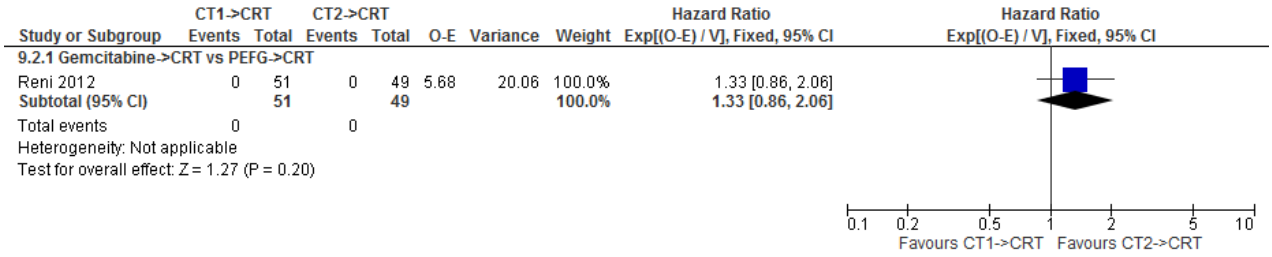


Figure 379: # patients with any Grade 4 toxicity

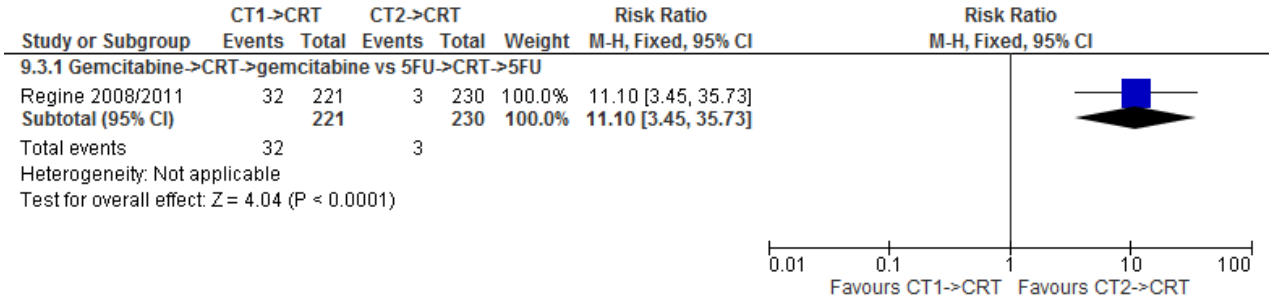


Figure 380: # patients with Grade 3 or 4 diarrhoea

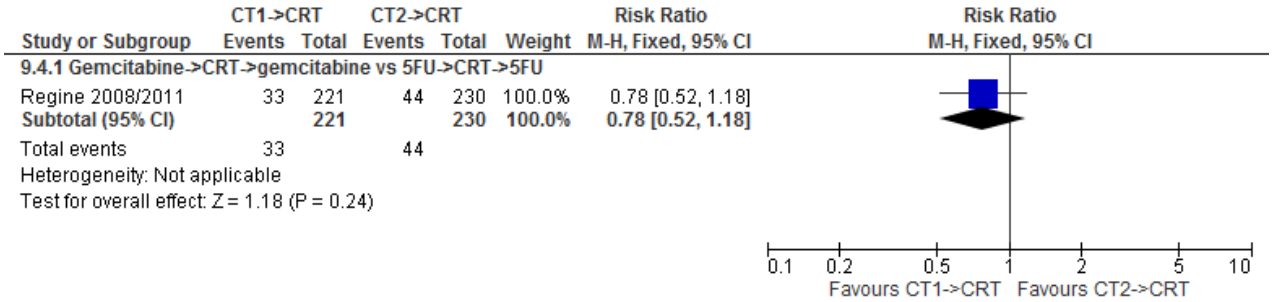


Figure 381: # patients with Grade 3 or 4 neutropenia

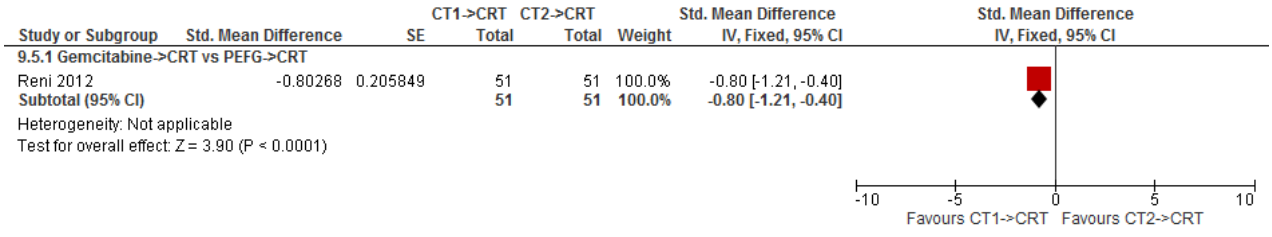


Figure 382: # patients with Grade 3 or 4 stomatitis

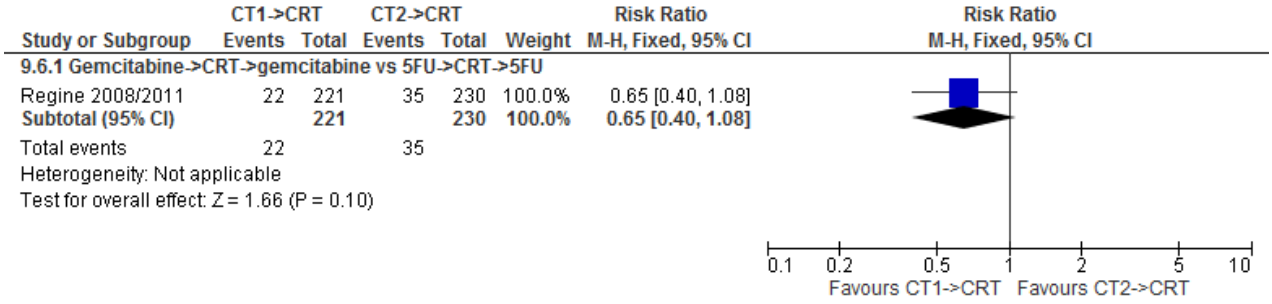


Figure 383: # patients with Grade 3 or 4 thrombocytopenia

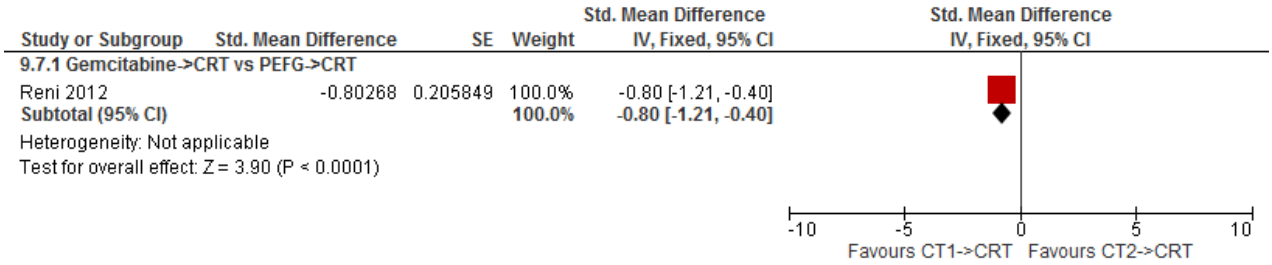


Figure 384: # patients with Grade 3 or 4 worst haematological toxicities

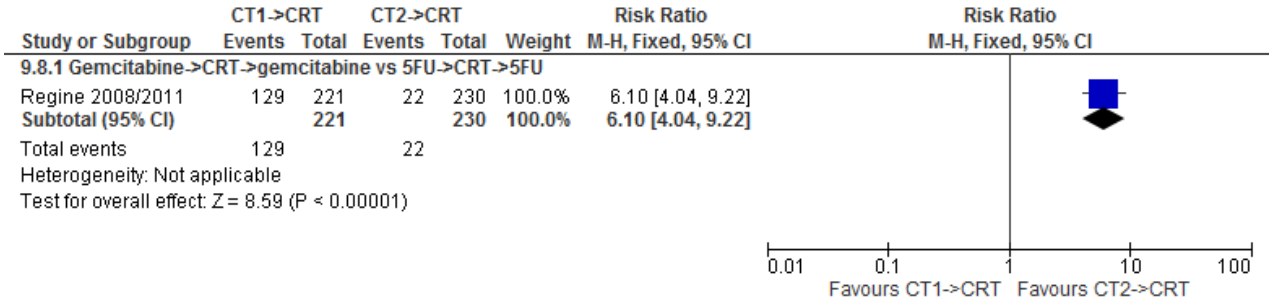


Figure 385: # patients with Grade 3 or 4 worst non-haematological toxicities

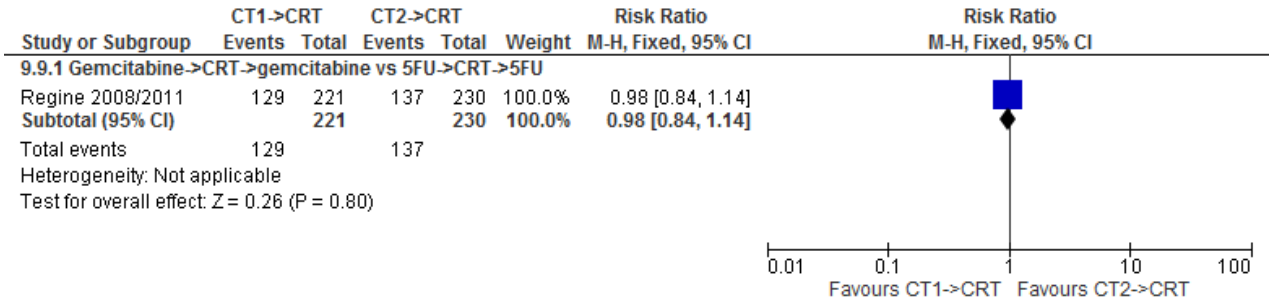
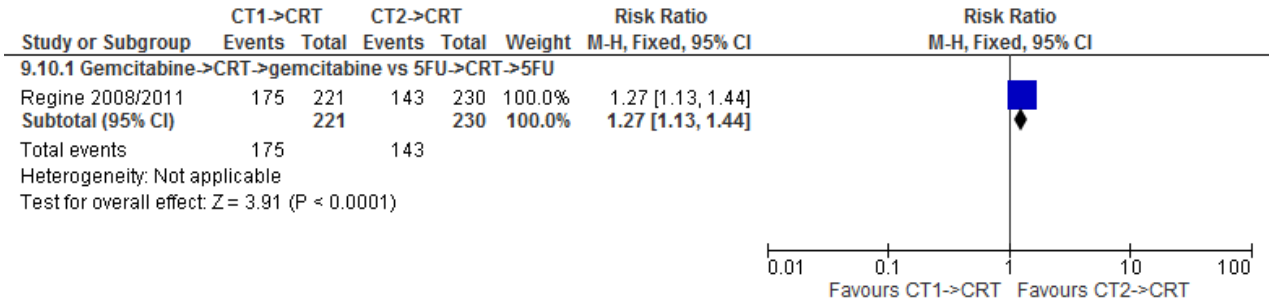


Figure 386: # patients with Grade 3 or 4 worst overall toxicities



H.14.10 Adjuvant immunotherapy versus no adjuvant therapy in resected pancreatic cancer patients

Figure 387: Overall survival

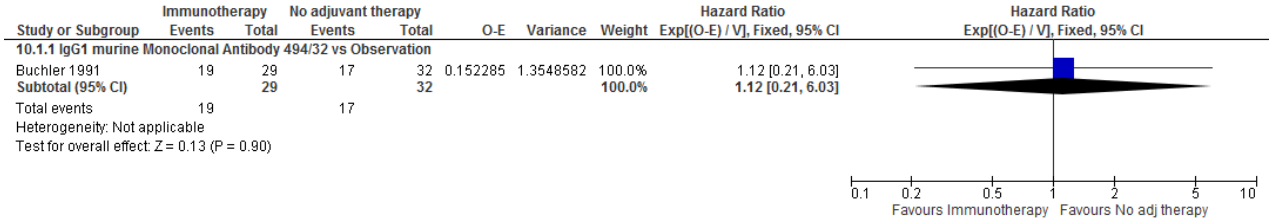
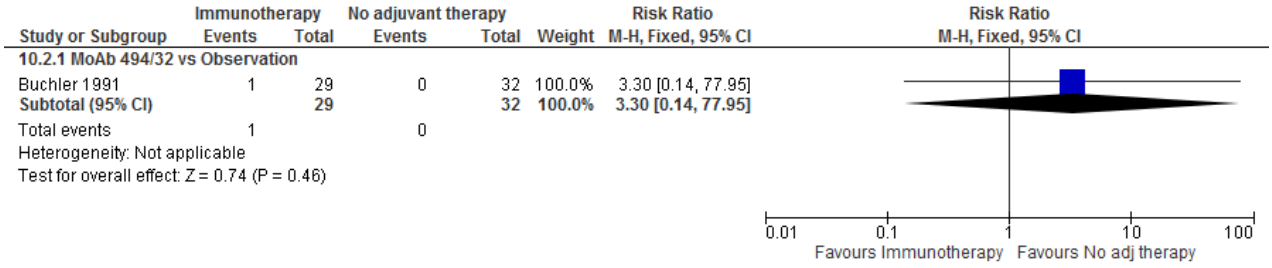


Figure 388: # patients with Grade 3 or 4 abdominal pain



H.14.11 Adjuvant chemoimmunotherapy versus no adjuvant therapy in resected pancreatic cancer patients

Figure 389: Overall survival

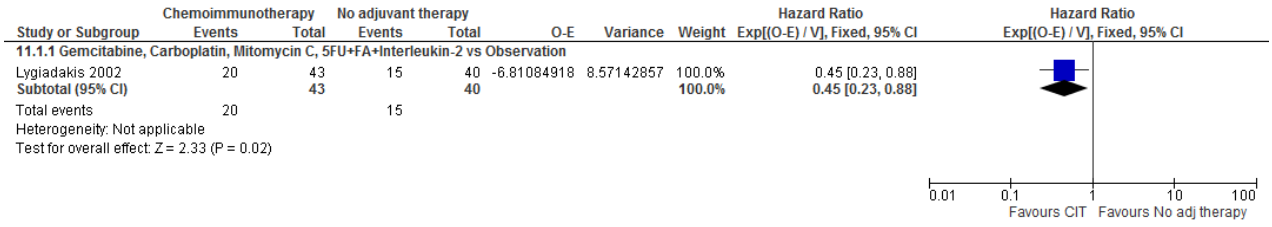


Figure 390: Disease-free survival

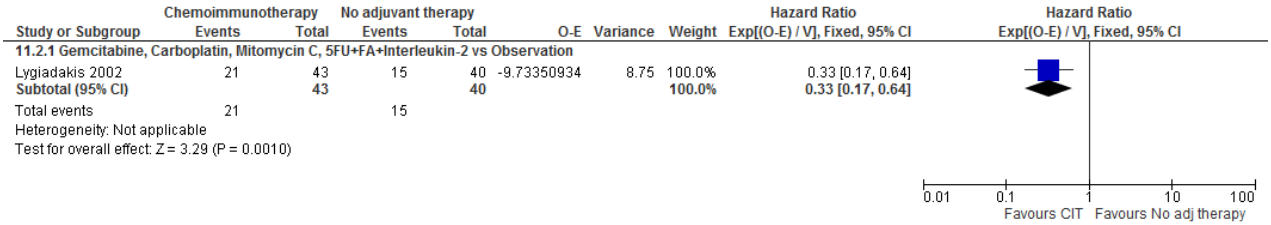
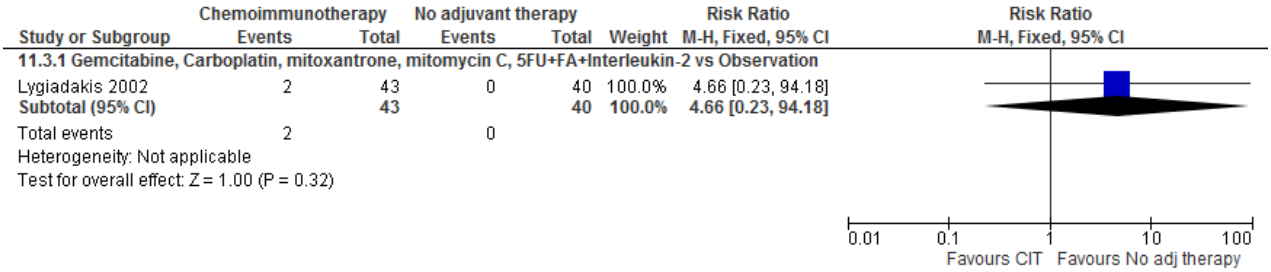


Figure 391: # patients with Grade 3 or 4 vomiting



H.15 Follow-up for people with resected pancreatic cancer

Figure 392: CT/MRI versus PET on mortality (time-varying exposure model) in "surgical group" of pancreatic cancer patients

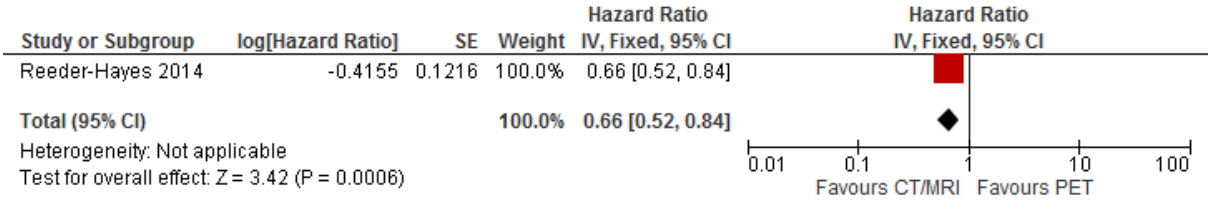


Figure 393: CT/MRI versus PET on mortality (time-varying exposure model) in "borderline group" of pancreatic cancer patients

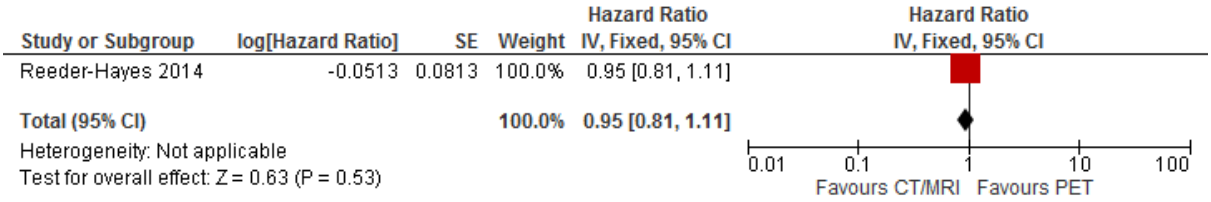


Figure 394: No follow-up versus PET on mortality (time-varying exposure model) in "surgical group" of pancreatic cancer patients

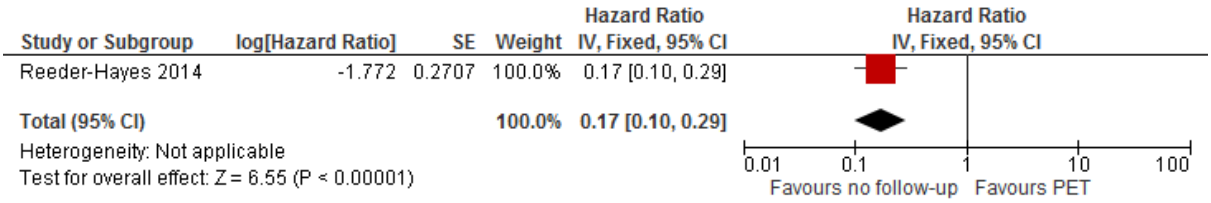


Figure 395: No follow-up versus PET on mortality (time-varying exposure model) in "borderline group" of pancreatic cancer patients

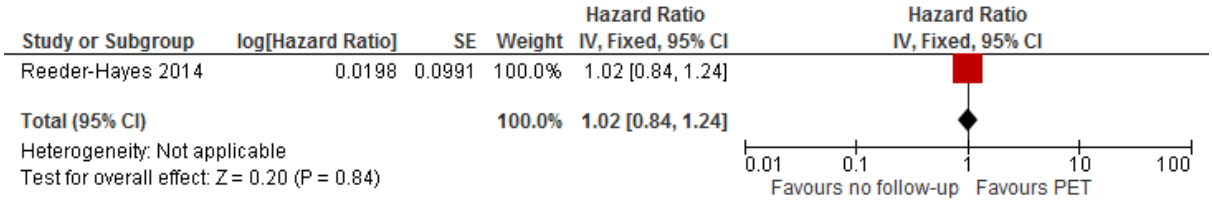


Figure 396: CT/MRI versus PET on survival beyond 180 days in "surgical group" of pancreatic cancer patients

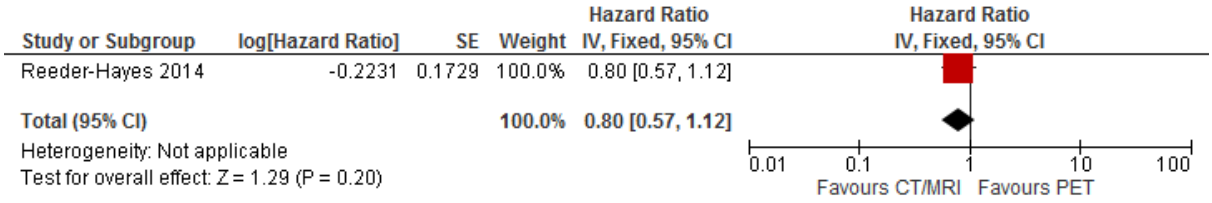


Figure 397: CT/MRI versus PET on survival beyond 180 days in "borderline group" of pancreatic cancer patients

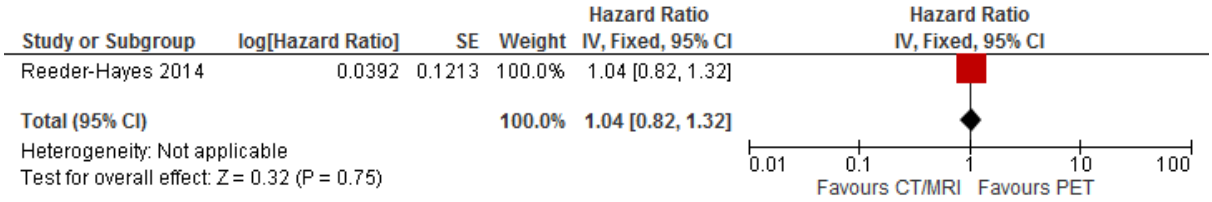


Figure 398: No follow-up versus PET on survival beyond 180 days in "surgical group" of pancreatic cancer patients

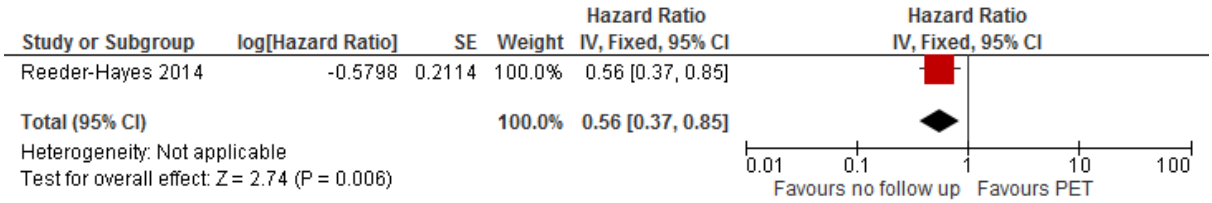
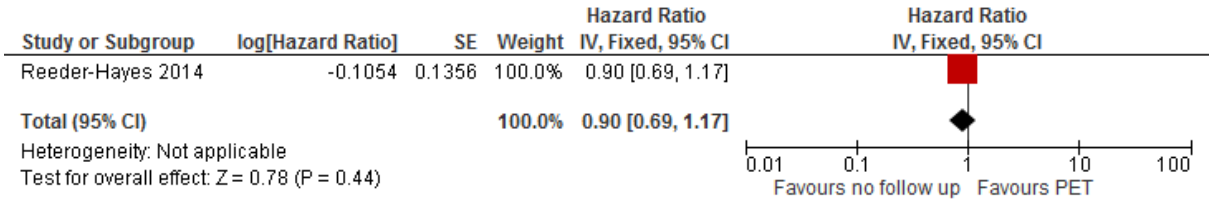


Figure 399: No follow-up versus PET on survival beyond 180 days in "borderline group" of pancreatic cancer patients



H.16 Management of locally advanced pancreatic cancer

H.16.1 Different chemoradiotherapy regimens

Figure 400: GEM-CRT versus paclitaxel-CRT – Overall response rates (CR+PR) at 1 month and 1 year follow-up

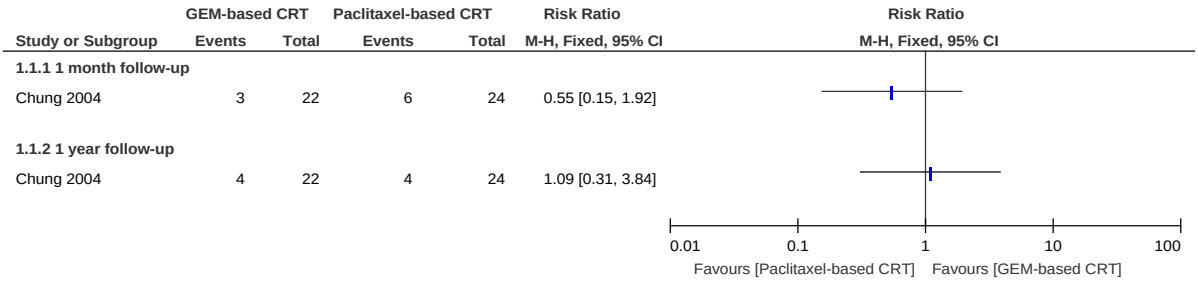


Figure 401: GEM-CRT versus paclitaxel-CRT – Adverse effects - Grade 3/4 toxicities

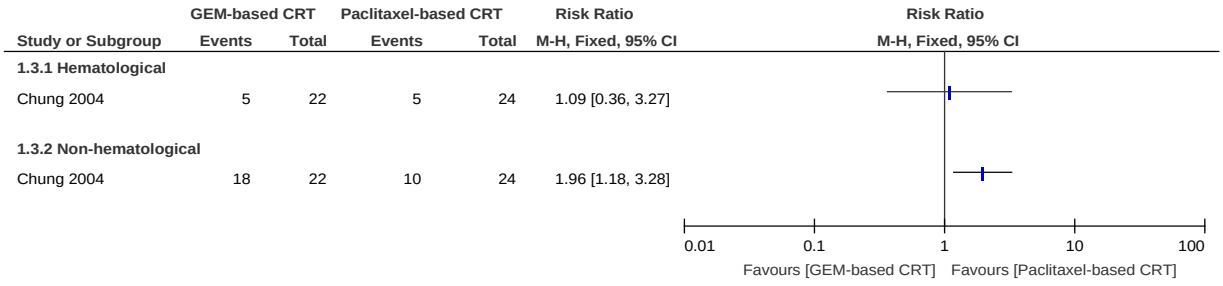


Figure 402: GEM-CRT versus 5FU-CRT – Overall pain control – follow-up not reported

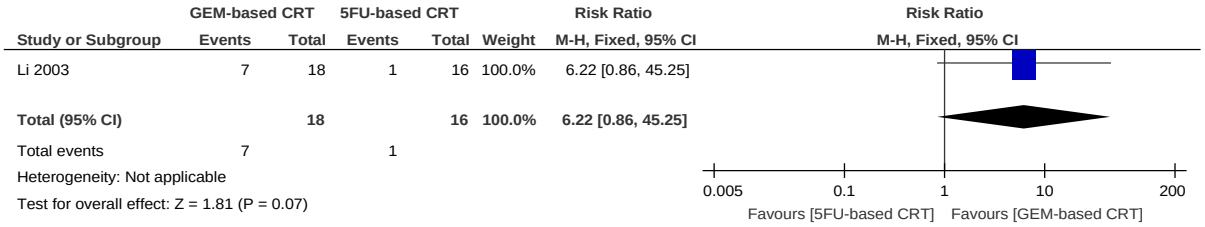


Figure 403: GEM-CRT versus 5FU-CRT – Adverse effects - Grade 3/4 toxicities

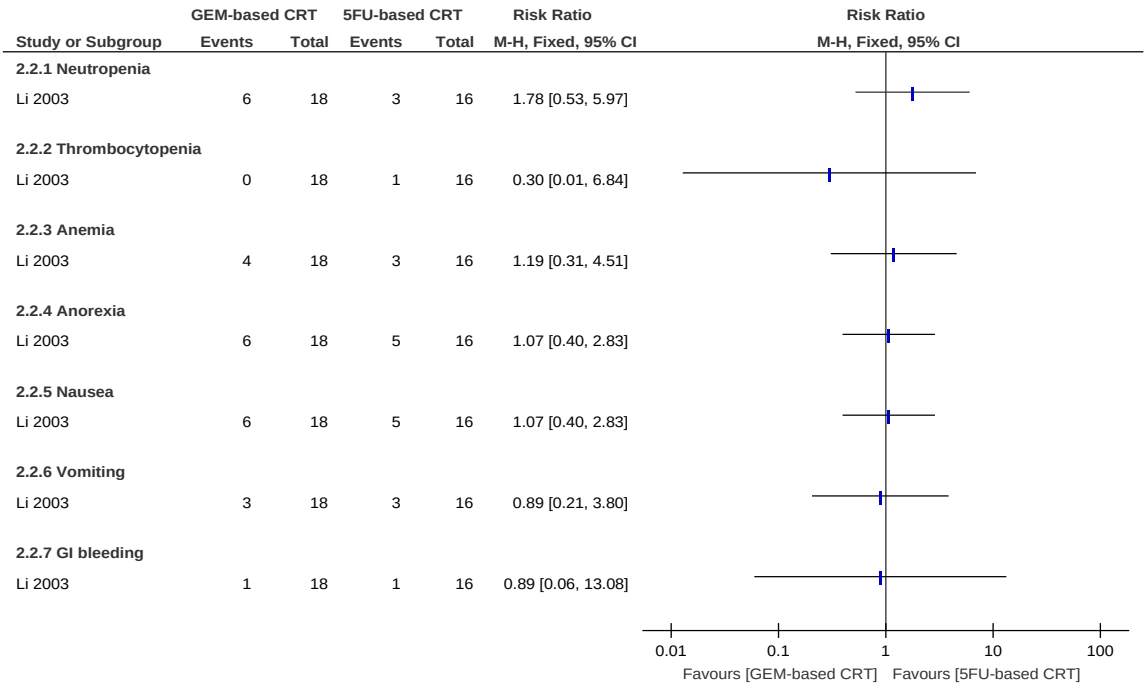


Figure 404: GEM/Cisplatin-CRT versus 5FU-CRT – HQRL: Average monthly Karnofsky performance score

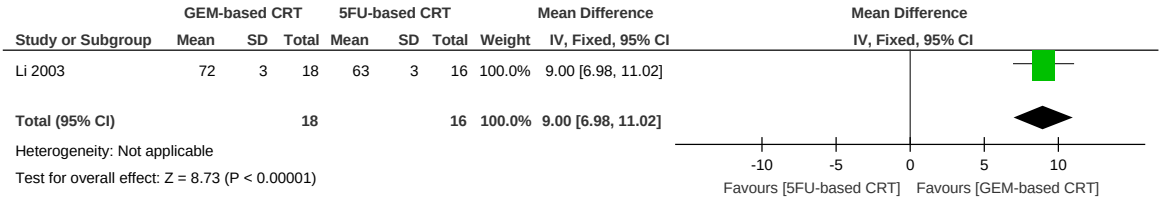
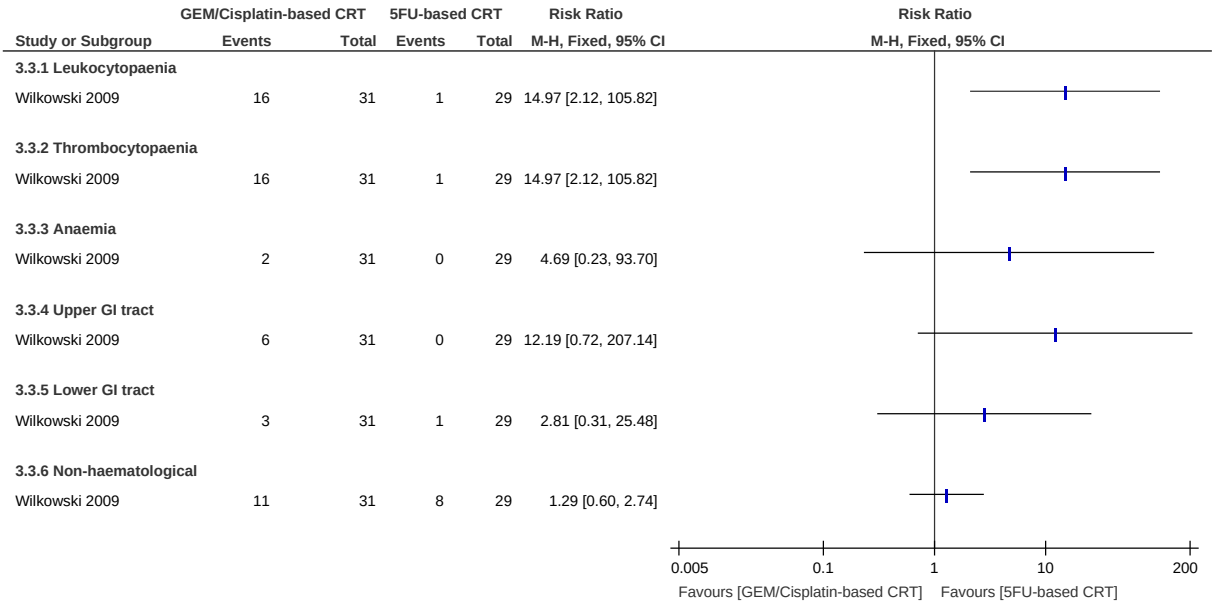


Figure 405: GEM/Cisplatin-CRT versus 5FU-CRT – Adverse effects, Grade 3/4 toxicities



H.16.21 Different chemoradiotherapy regimens after induction chemotherapy

Figure 406: GEM-CRT versus capecitabine-CRT after induction CT – Overall response rates (CR+PR)

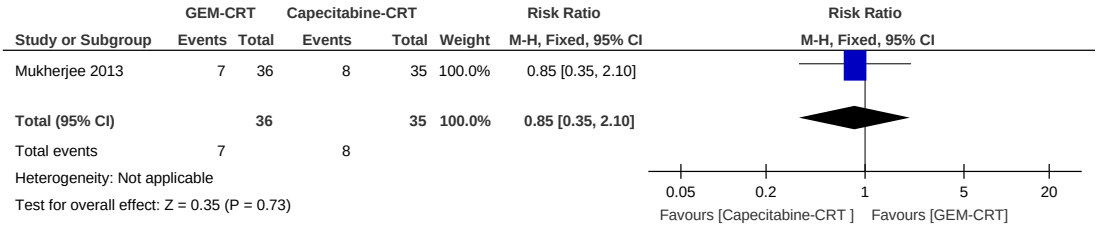


Figure 407: GEM-CRT versus capecitabine-CRT after induction CT – PFS

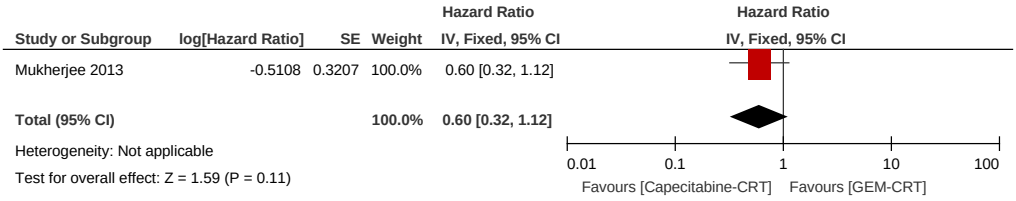


Figure 408: GEM-CRT versus capecitabine-CRT after induction CT – Overall Survival

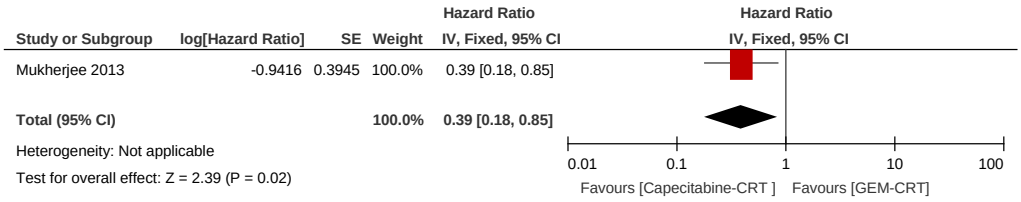


Figure 409: GEM-CRT versus capecitabine-CRT after induction CT – Adverse effects - Grade 3/4 toxicities

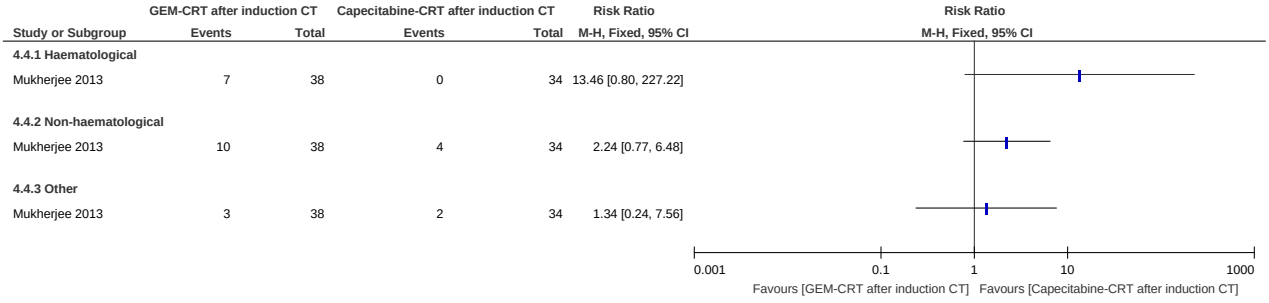


Figure 410: Capecitabine-CRT + cetuximab versus capecitabine-CRT alone after induction CT – Objective response rate

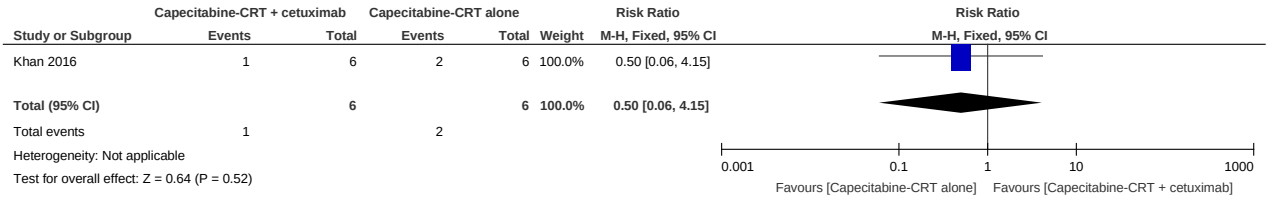
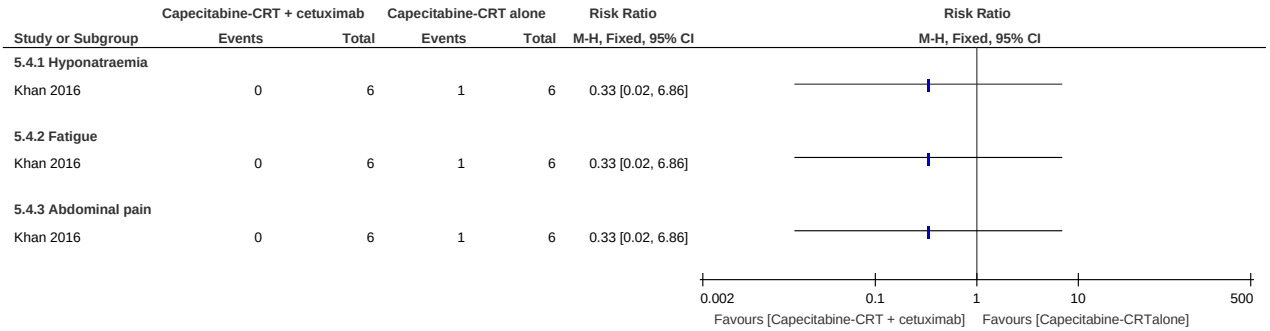
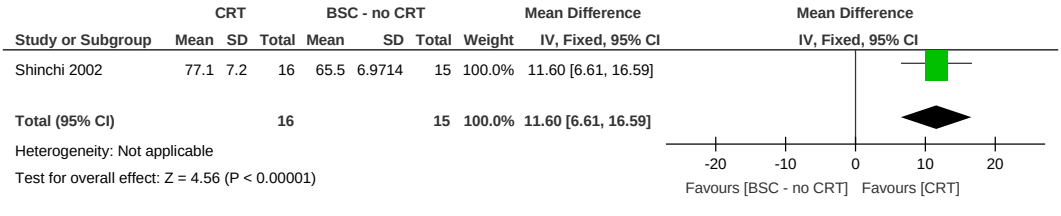


Figure 411: Capecitabine-CRT + cetuximab versus capecitabine-CRT alone after induction CT – Objective response rate



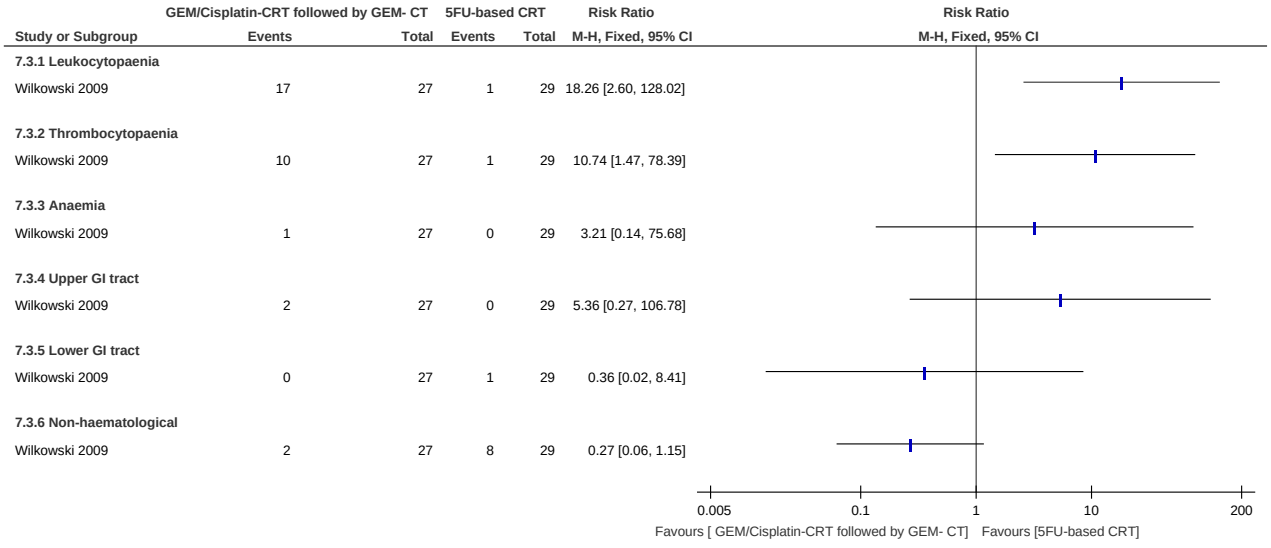
H.16.3 Chemoradiotherapy versus best supportive care

Figure 412: CRT versus best supportive care -no CRT– HQRL: Average of monthly Karnofsky scores



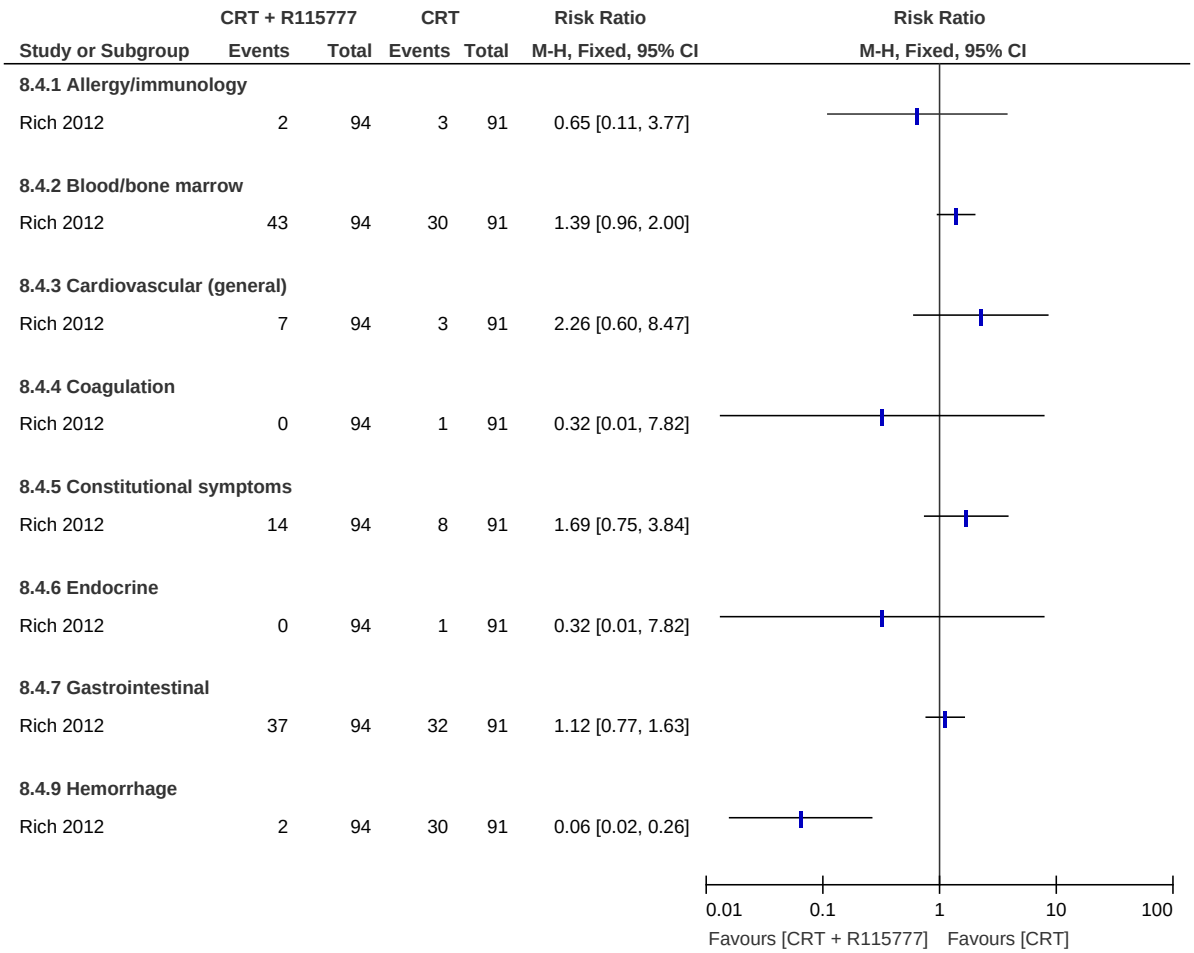
H.16.4 Chemoradiotherapy followed by chemotherapy versus chemoradiotherapy alone

Figure 413: CRT followed by CT versus CRT – Adverse effects - Grade 3/4 toxicities



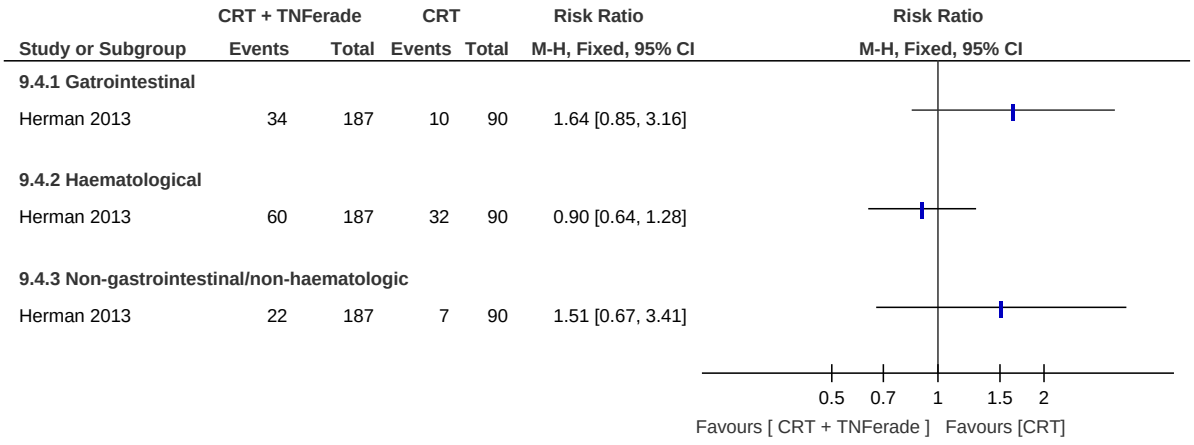
H.16.5 Chemoradiotherapy + R115777 versus chemoradiotherapy

Figure 414: CRT + R115777 versus CRT– Adverse effects - Grade 3/4 toxicities



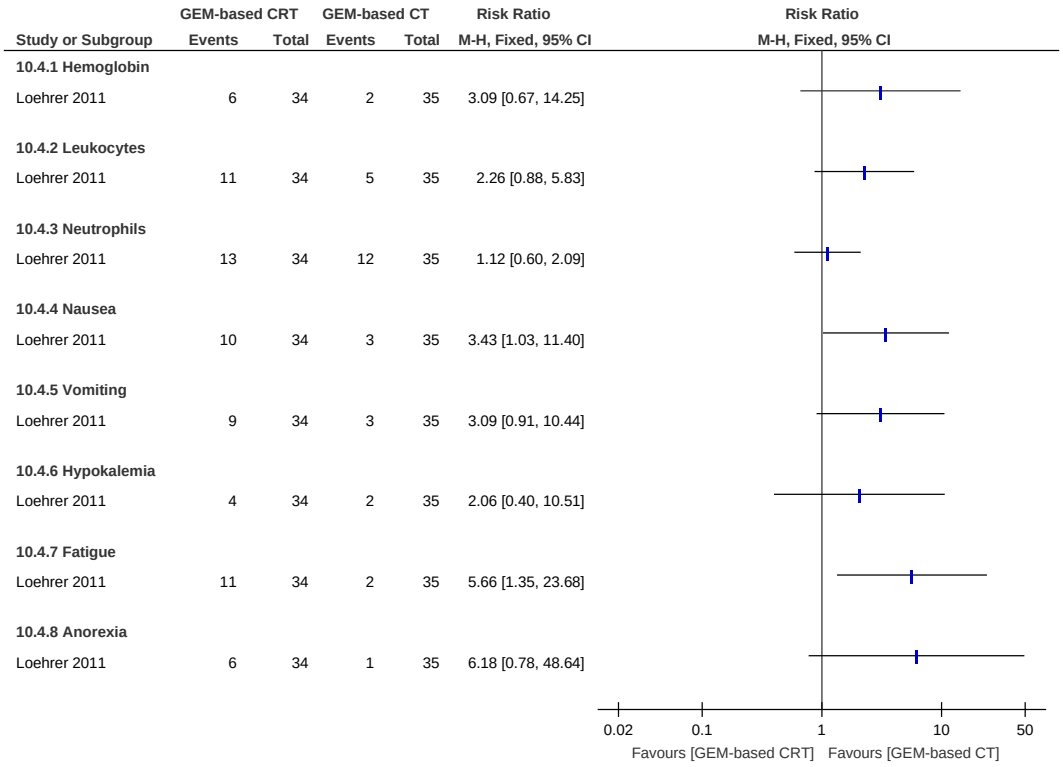
H.16.6 Chemoradiotherapy + TNFerade versus chemoradiotherapy

Figure 415: CRT + TNFerade versus CRT – Adverse effects - Grade 3/4 toxicities



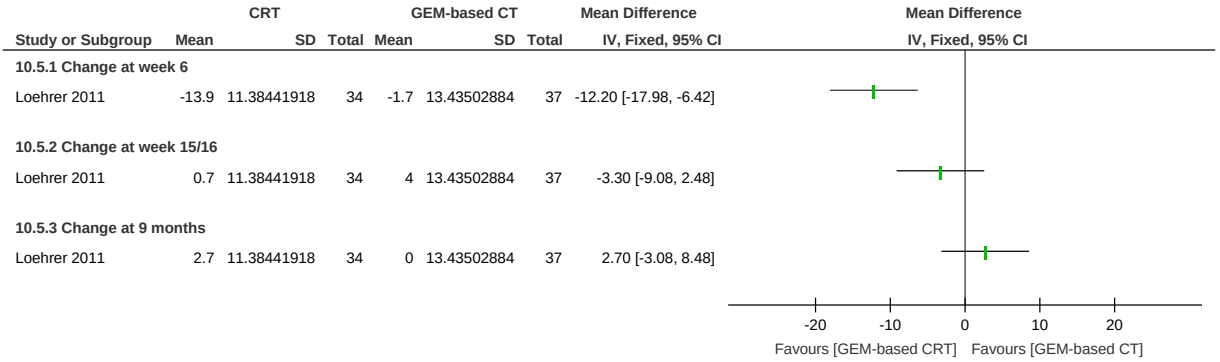
H.16.71 Chemoradiotherapy versus chemotherapy

2 Figure 416: CRT versus CT – Adverse effects - Grade 3/4 toxicities



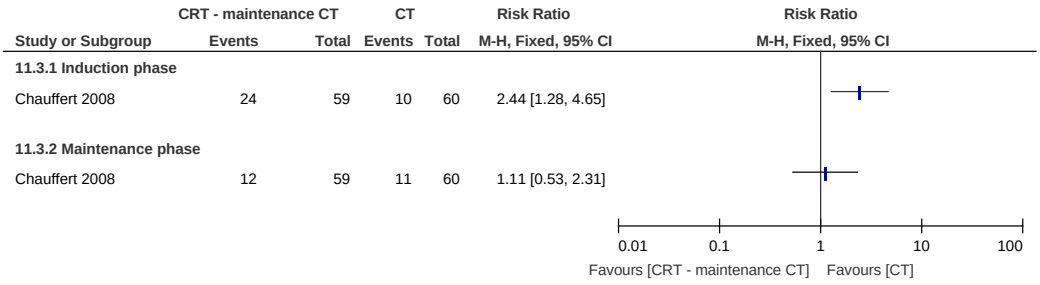
3

4 Figure 417: CRT versus CT – HQRL - Trial outcome index [mean difference of 5 change from baseline] at week 6, 15/16 and at 9 months follow-up



6

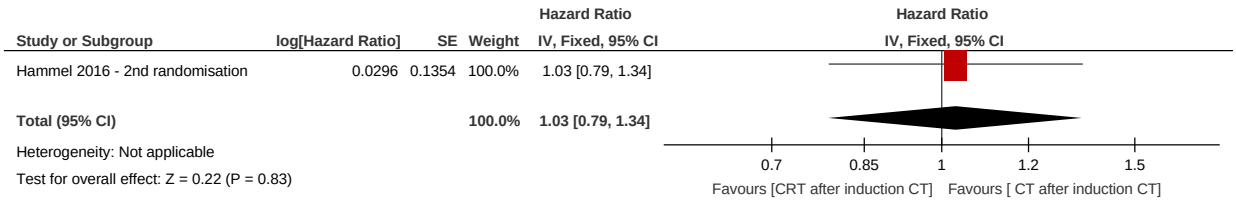
7 Figure 418: CRT versus CT followed by maintenance GEM-CT– Adverse effects - 8 Grade 3/4 toxicities



9

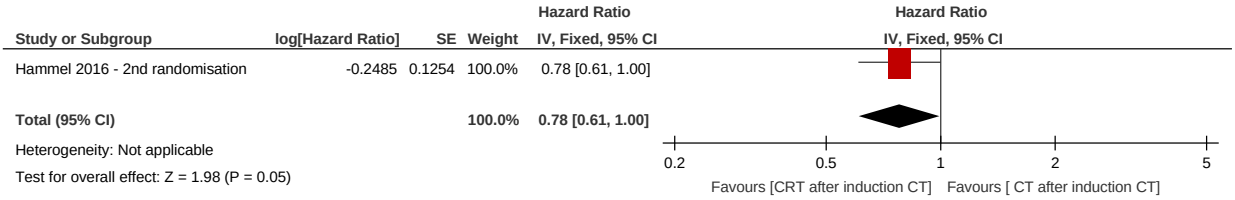
H.16.81 Chemoradiotherapy versus chemotherapy after induction chemotherapy

2 Figure 419: CRT versus CT after CT induction therapy – Overall survival



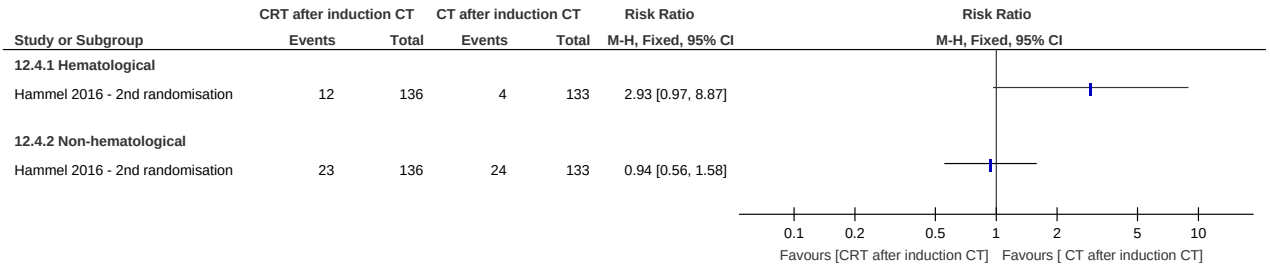
3

4 Figure 420: CRT versus CT after CT induction therapy – PFS



5

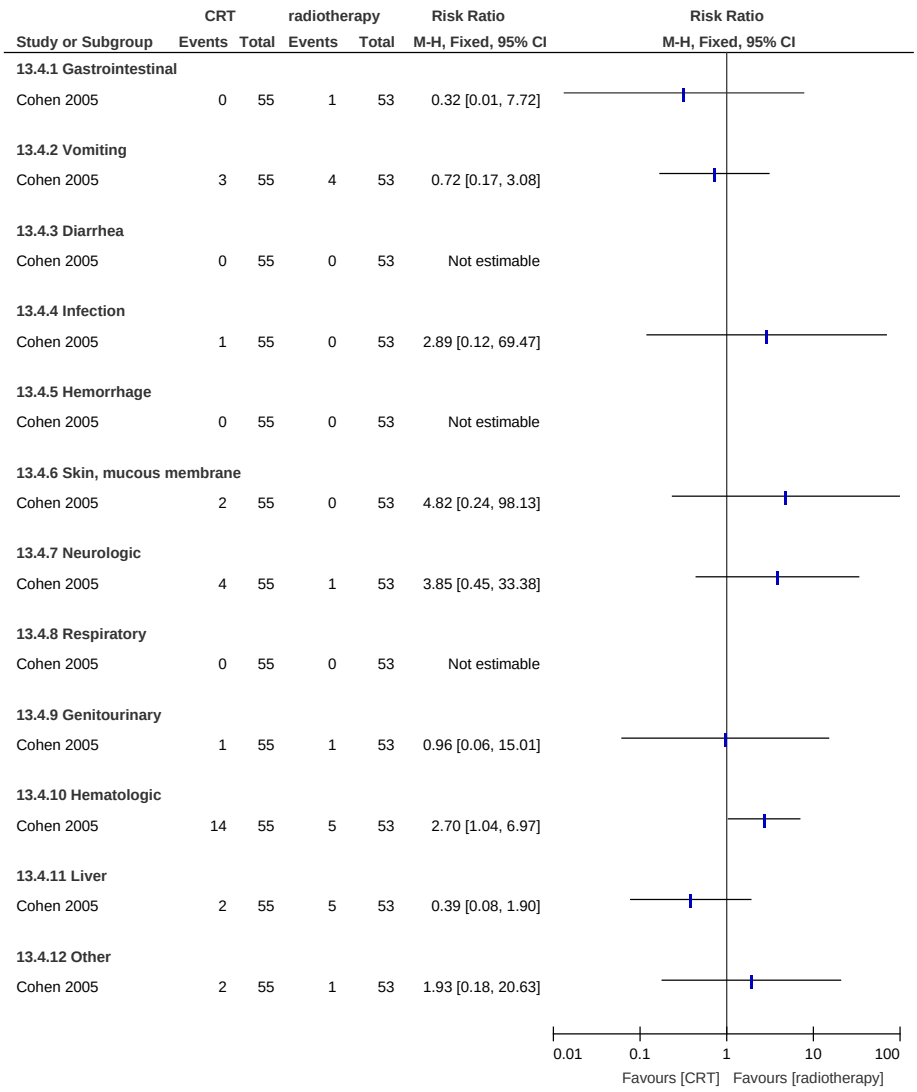
6 Figure 421: CRT versus CT after CT induction therapy – Adverse effects - Grade 3/4 7 toxicities



8

H.16.91 Chemoradiotherapy versus radiotherapy

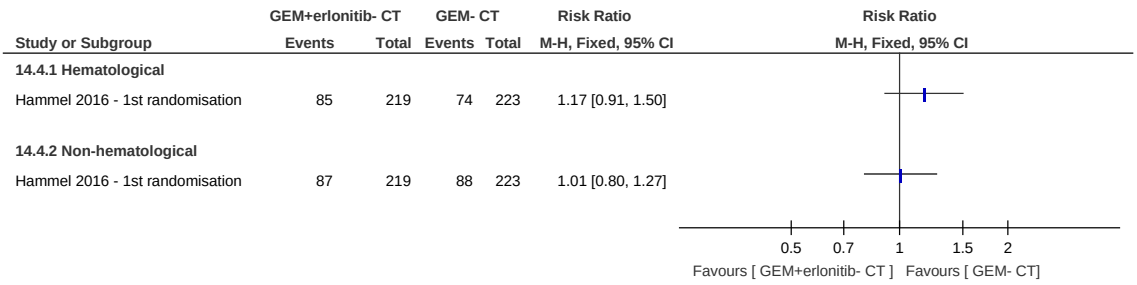
2 Figure 422: CRT versus radiotherapy – Adverse effects - Grade 3/4 toxicities



3

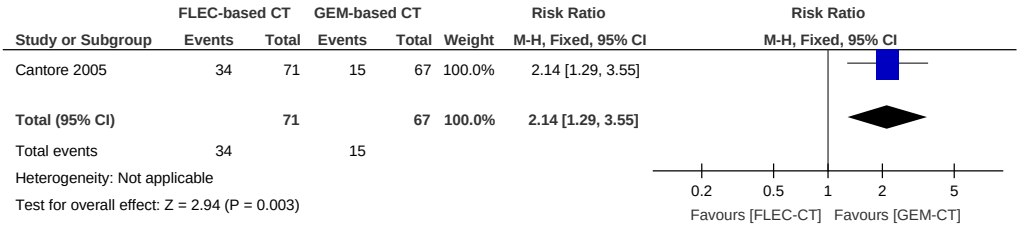
H.16.104 Different chemotherapy regimens

5 Figure 423: GEM+erlonitib-CT versus GEM-CT – Adverse effects - Grade 3/4
6 toxicities



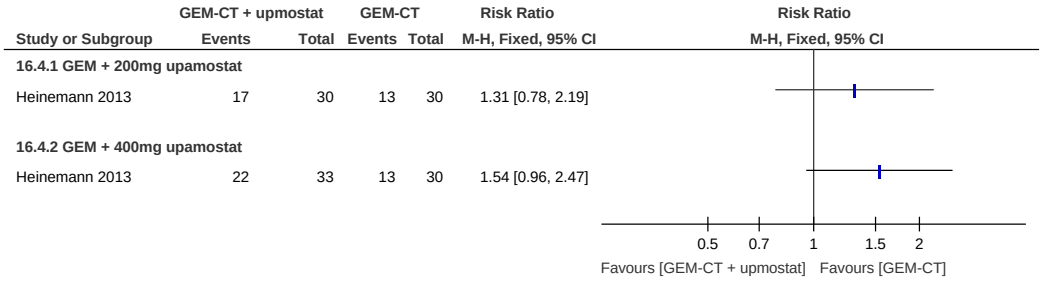
7

Figure 424: FLEC-CT versus GEM-CT – Adverse effects - Grade 3/4 toxicities



H.16.11 GEM-CT + upmostat versus GEM-CT

Figure 26: GEM-CT + upmostat versus GEM-CT – Adverse effects - Grade 3/4 toxicities



H.16.12 Radiotherapy + PR-350 versus Radiotherapy + Placebo

Figure 425: Radiotherapy + PR-350 versus Radiotherapy + Placebo – Objective Response - Effective response

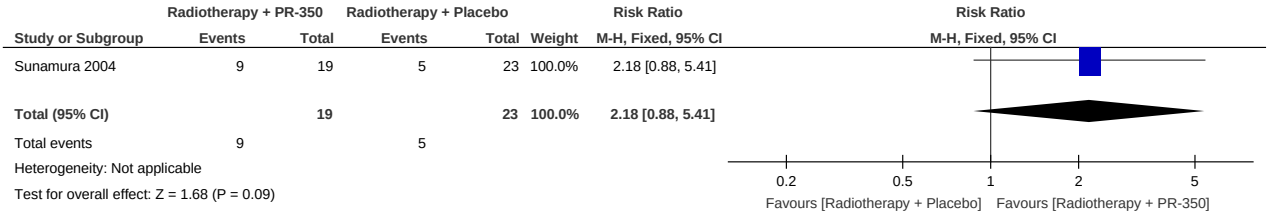
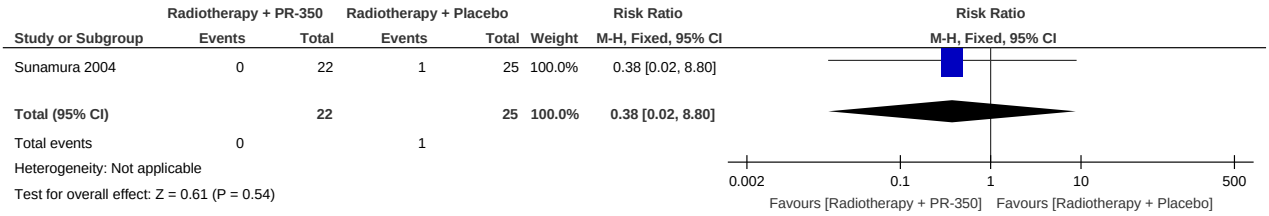


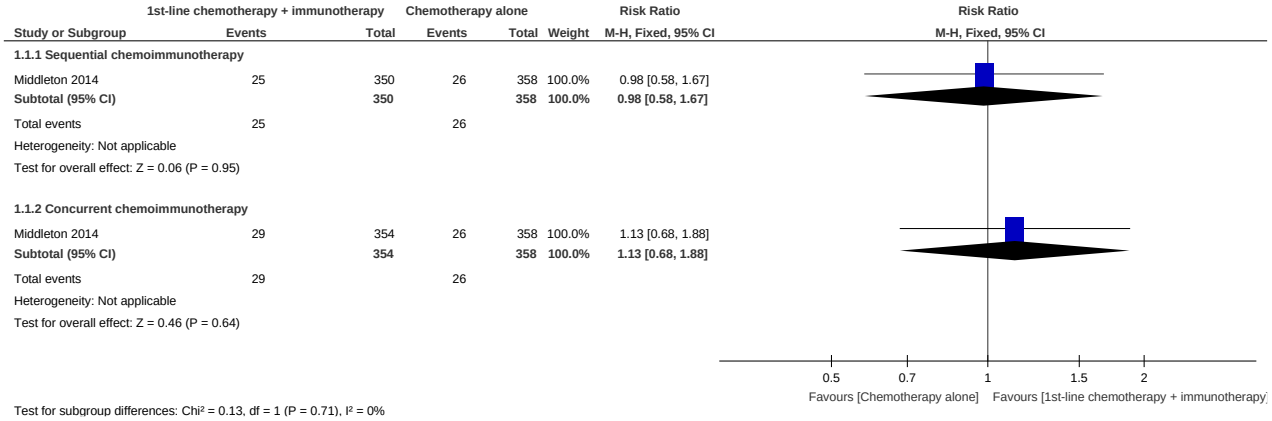
Figure 426: Radiotherapy + PR-350 versus Radiotherapy + Placebo – Adverse effects - Grade 3/4 toxicities



H.17 Management of metastatic pancreatic cancer

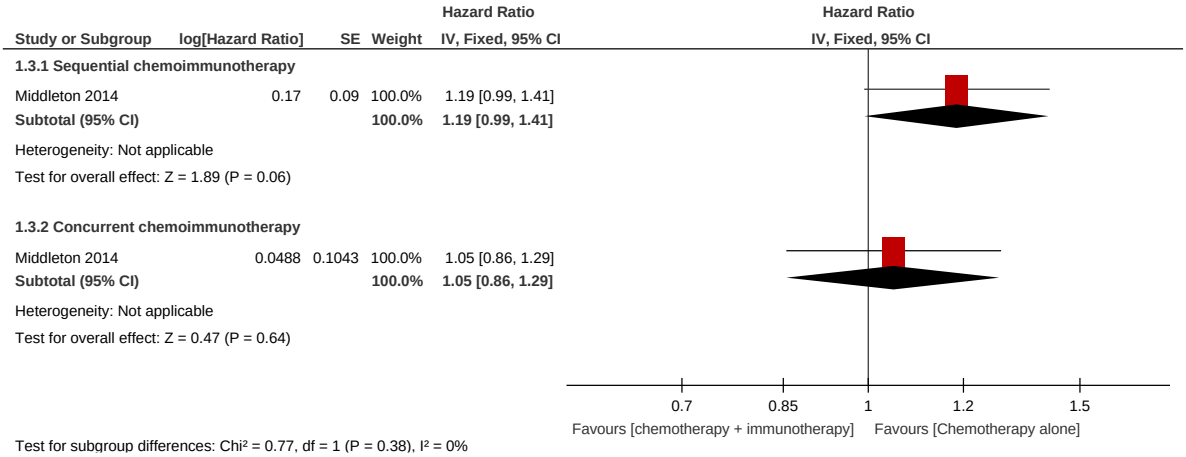
H.17.1 Chemotherapy versus chemoimmunotherapy in adults with locally advanced or metastatic pancreatic cancer

Figure 427: Overall response rate (CR + PR) at 8 weeks



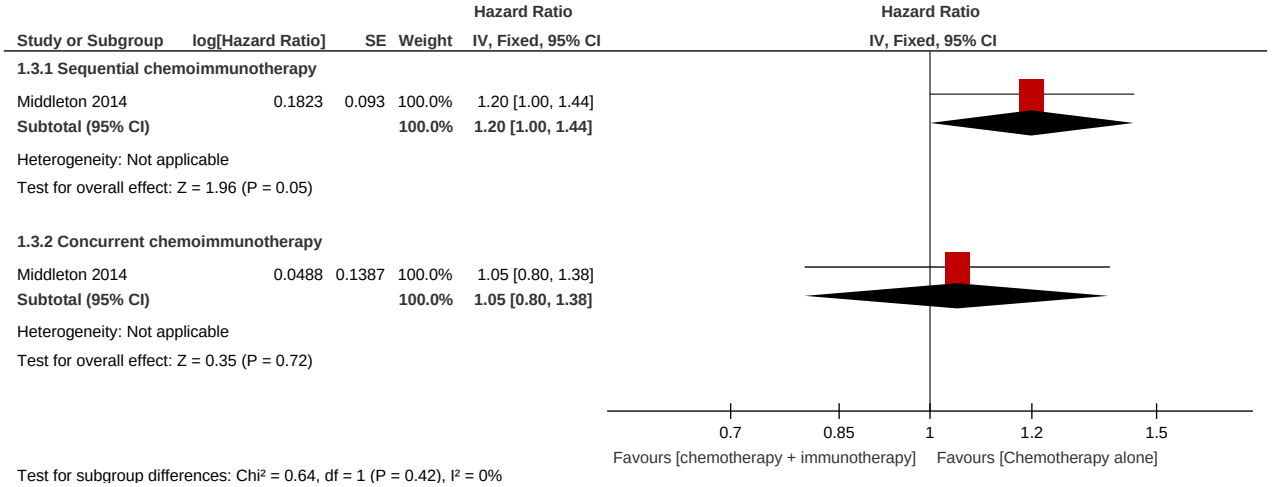
Test for subgroup differences: Chi² = 0.13, df = 1 (P = 0.71), I² = 0%

Figure 428: Time to progression



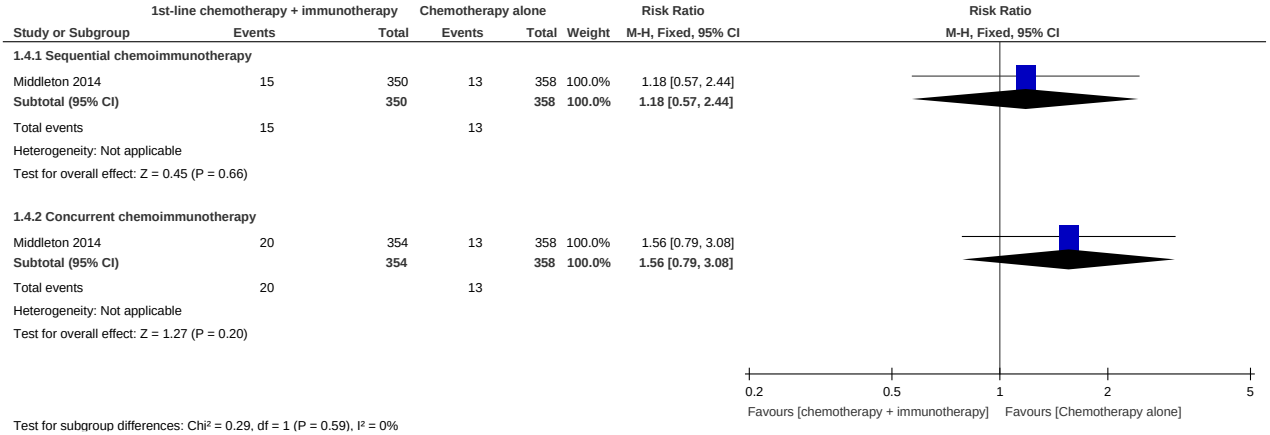
Test for subgroup differences: Chi² = 0.77, df = 1 (P = 0.38), I² = 0%

Figure 429: Overall survival



Test for subgroup differences: Chi² = 0.64, df = 1 (P = 0.42), I² = 0%

Figure 430: Grade 3/4/5 toxicities: Nausea



Test for subgroup differences: Chi² = 0.29, df = 1 (P = 0.59), I² = 0%

Figure 431: Grade 3/4/5 toxicities: Vomiting

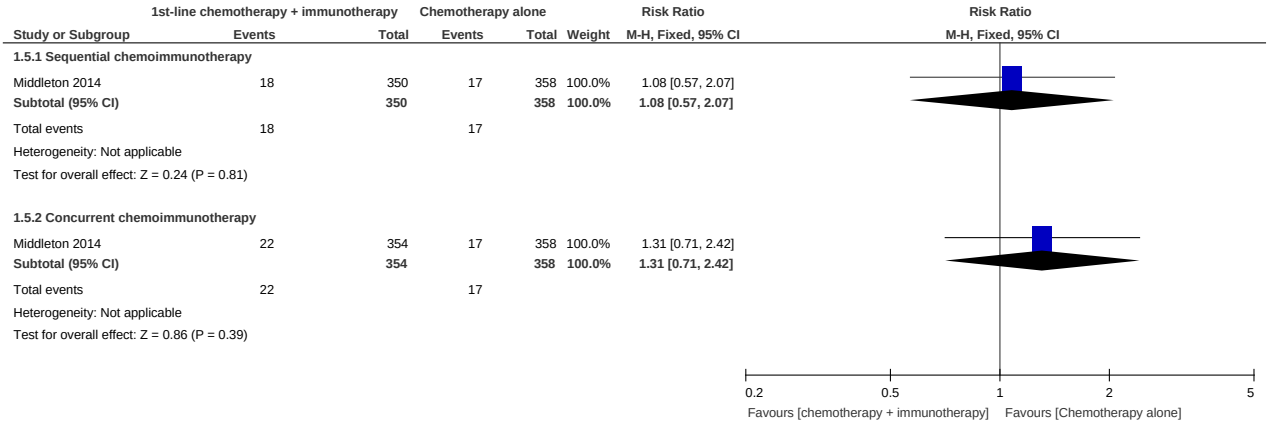


Figure 432: Grade 3/4/5 toxicities: Diarrhoea

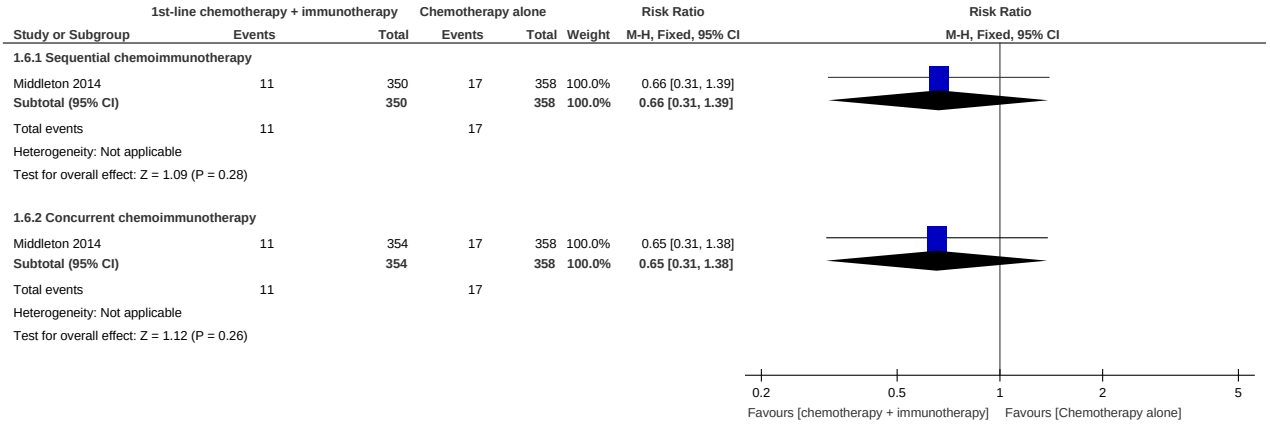


Figure 433: Grade 3/4/5 toxicities: Fatigue

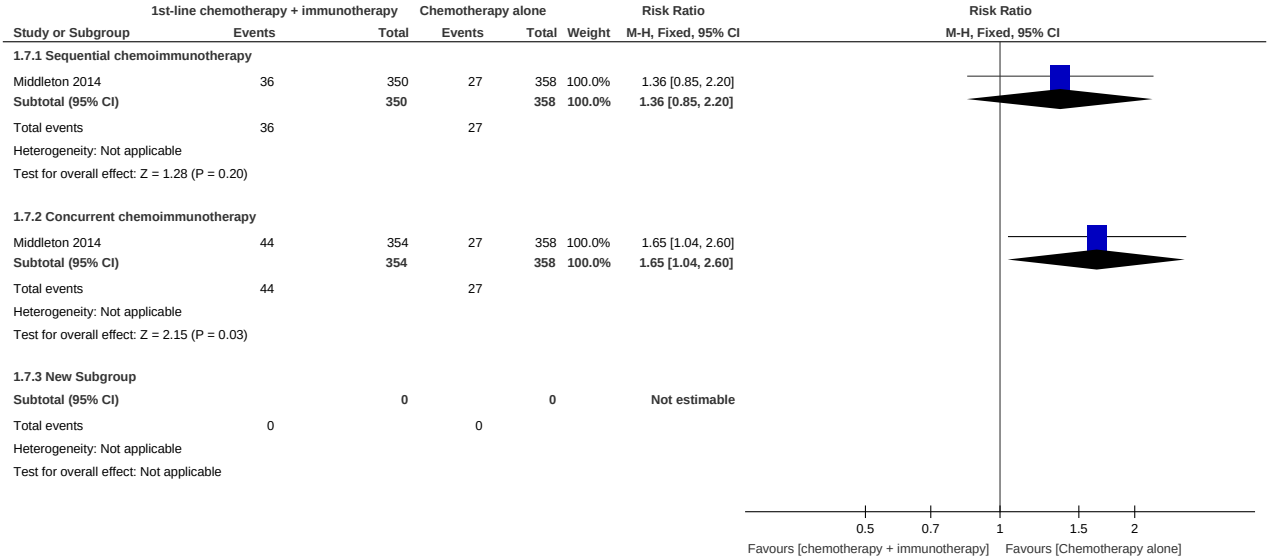
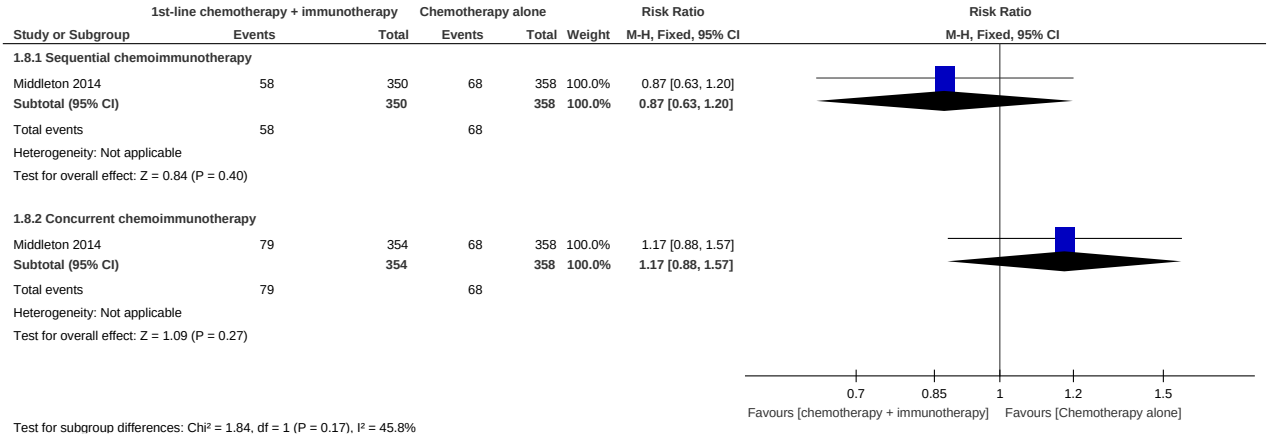
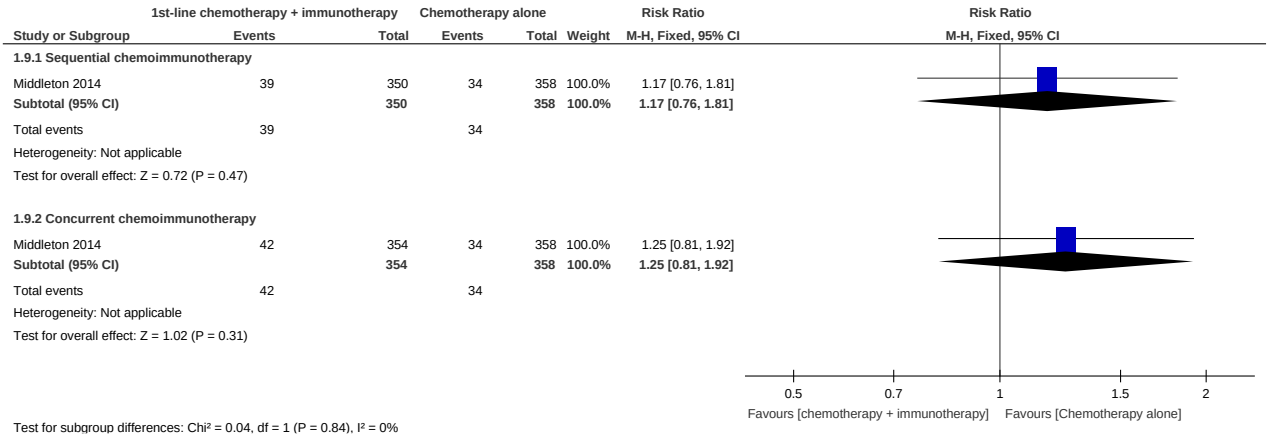


Figure 434: Grade 3/4/5 toxicities: Neutropenia



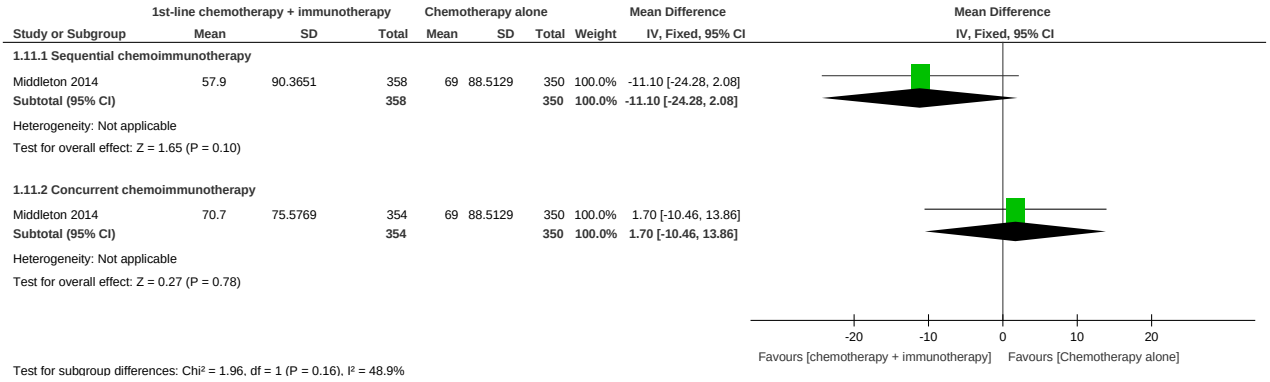
Test for subgroup differences: Chi² = 1.84, df = 1 (P = 0.17), I² = 45.8%

Figure 435: Grade 3/4/5 toxicities: Pain



Test for subgroup differences: Chi² = 0.04, df = 1 (P = 0.84), I² = 0%

Figure 436: Health-related Quality of Life at 20 weeks (EORTC QLQ-C30)



Test for subgroup differences: Chi² = 1.96, df = 1 (P = 0.16), I² = 48.9%

Figure 437: Overall response rate (CR + PR): unclear follow-up

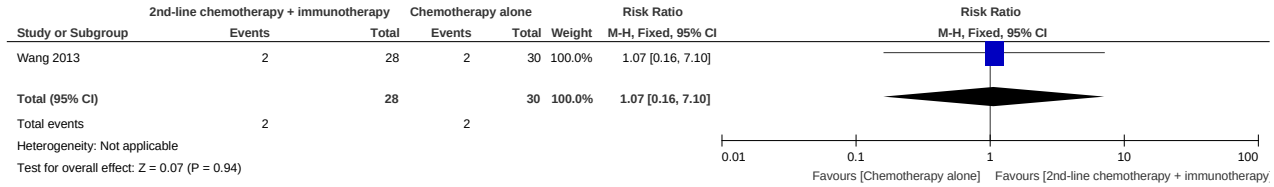
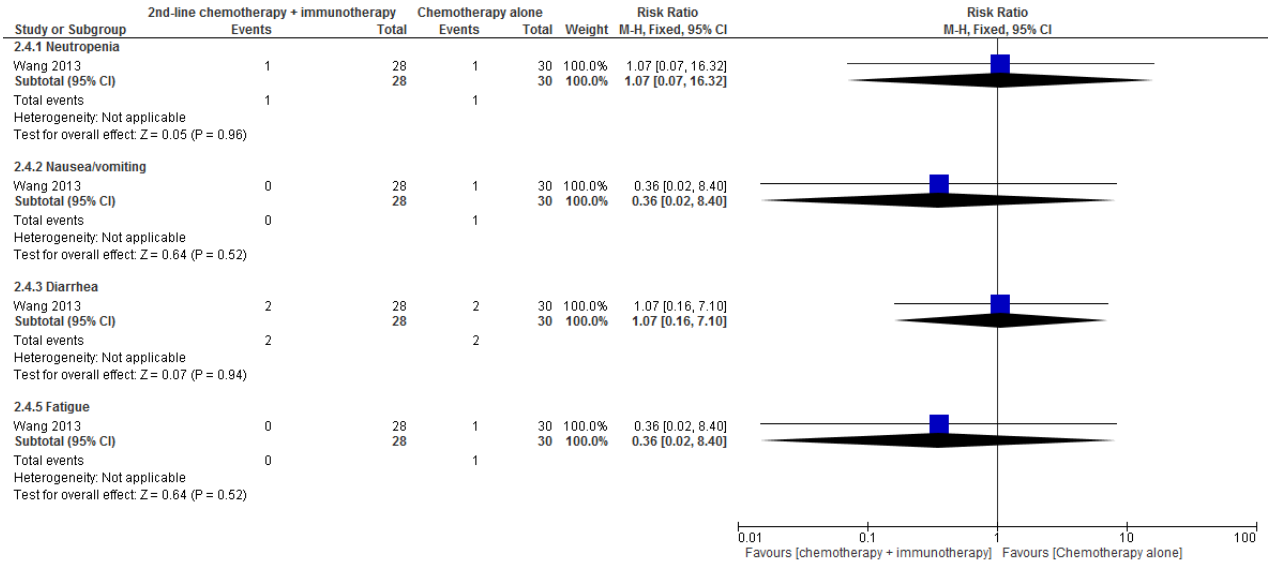


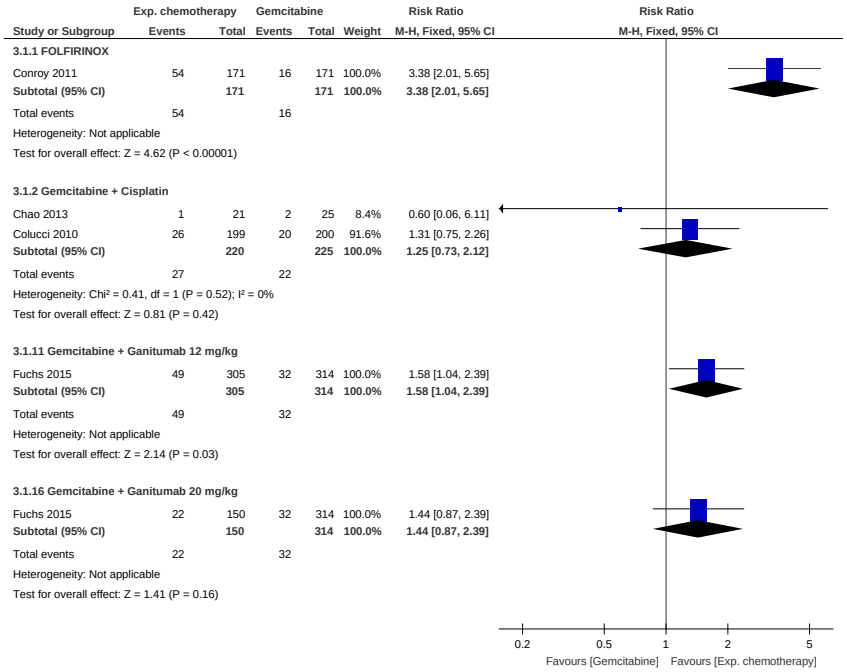
Figure 438: Grade 3/4 toxicities



H.17.21 Gemcitabine versus other chemotherapy

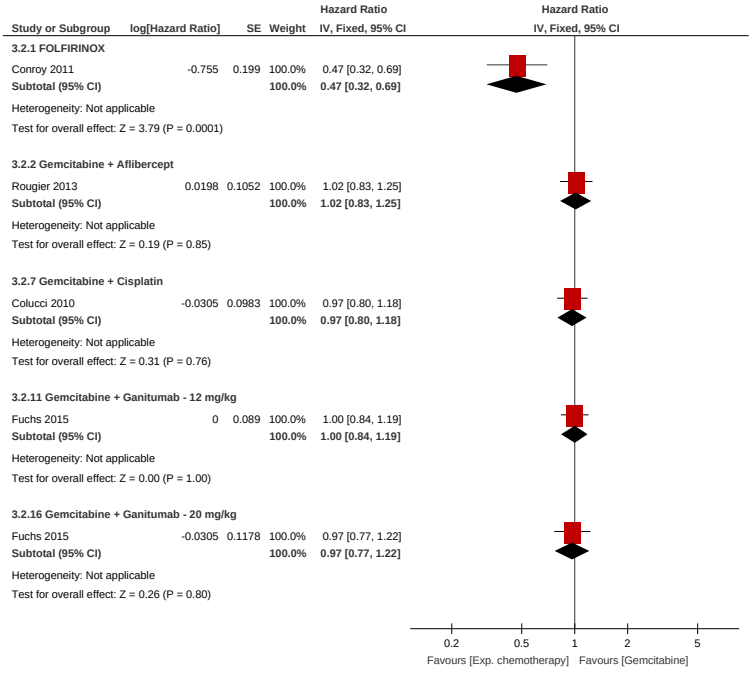
H.17.2.12 In adults with metastatic pancreatic cancer

3 Figure 439: overall response rate (CR+RP)



4

5 Figure 440: Progression-free survival



6

Figure 441: Overall survival

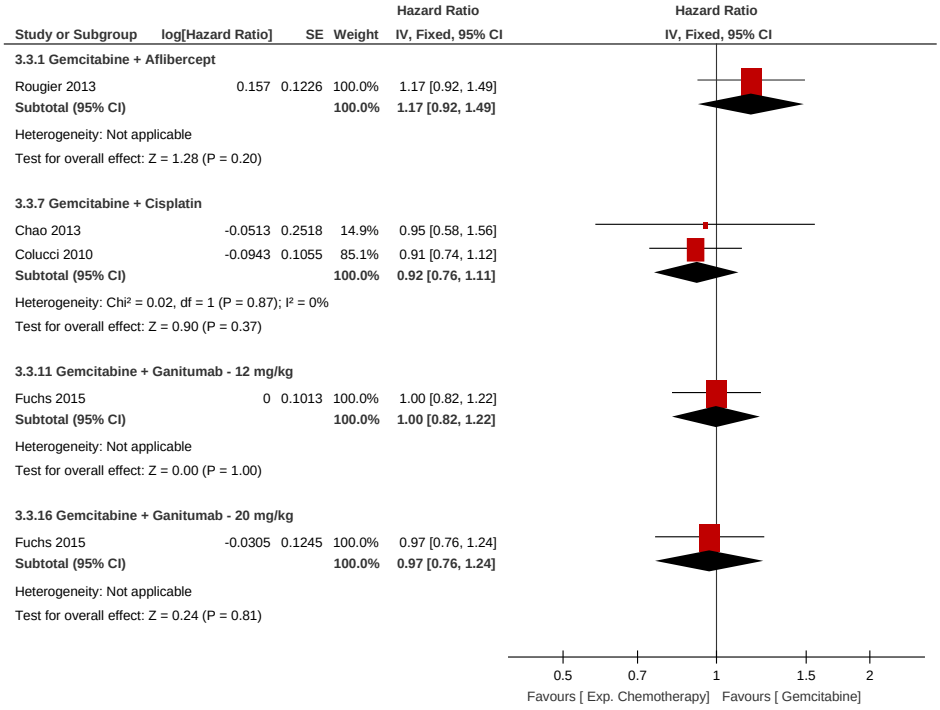


Figure 442: Grade 3/4 toxicities: Diarrhoea

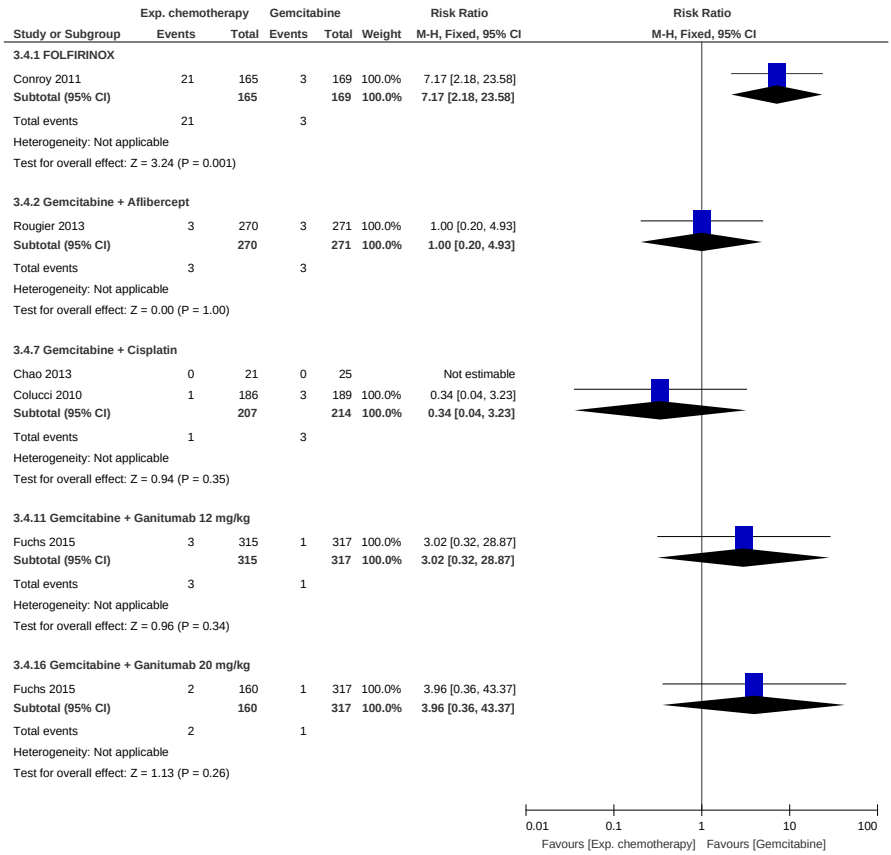


Figure 443: Grade 3/4 toxicities: Fatigue

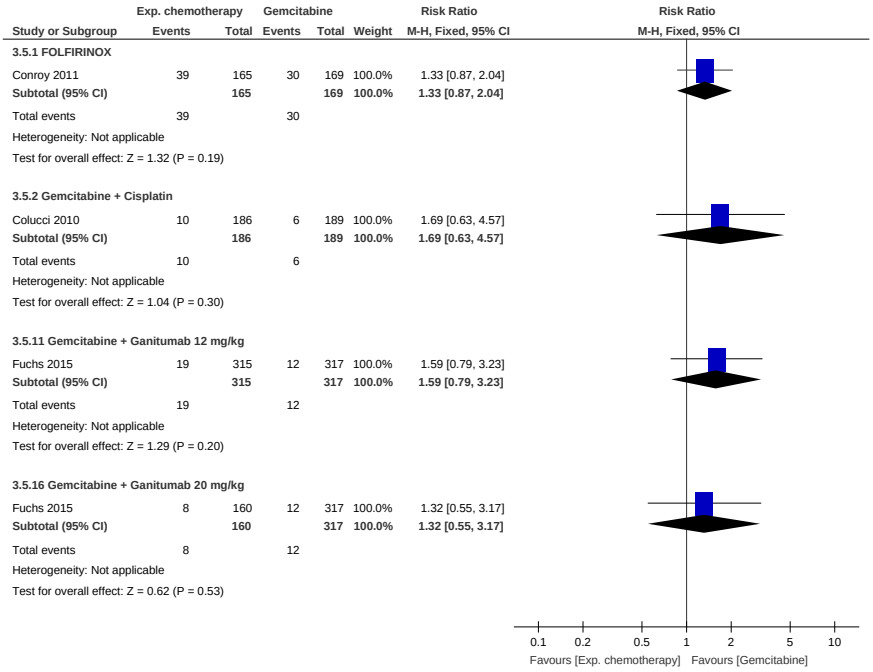


Figure 444: Grade 3/4 toxicities: Nausea/vomiting

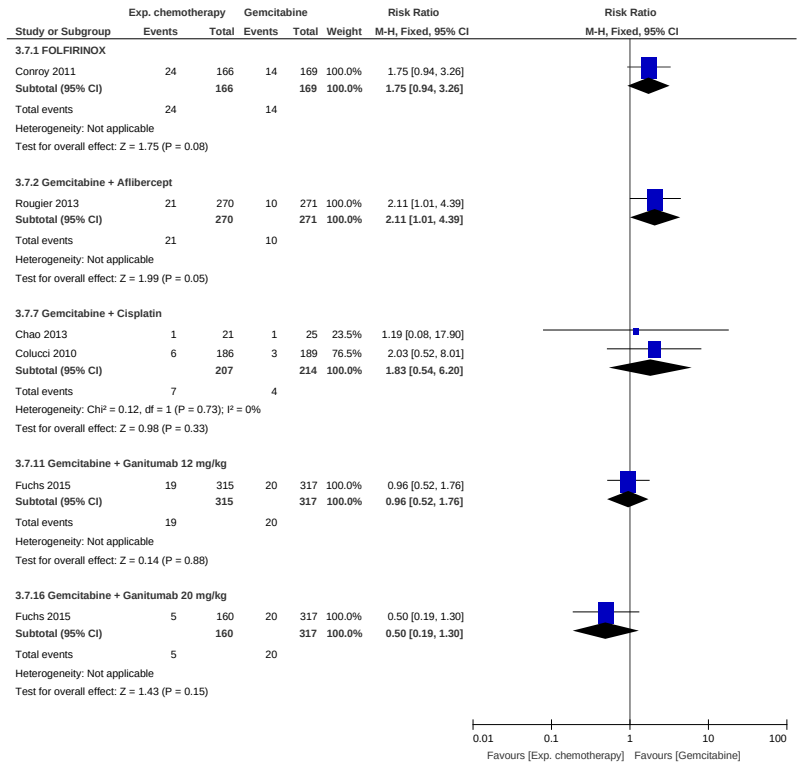


Figure 445: Grade 3/4 toxicities: Neutropenia

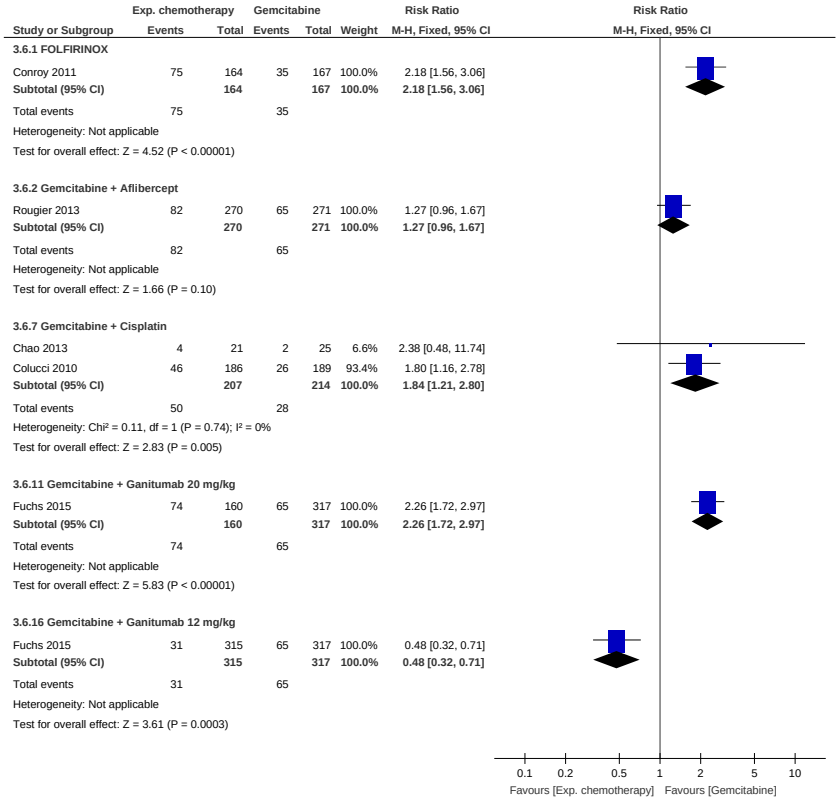


Figure 446: Grade 3/4 toxicities: Thrombocytopenia

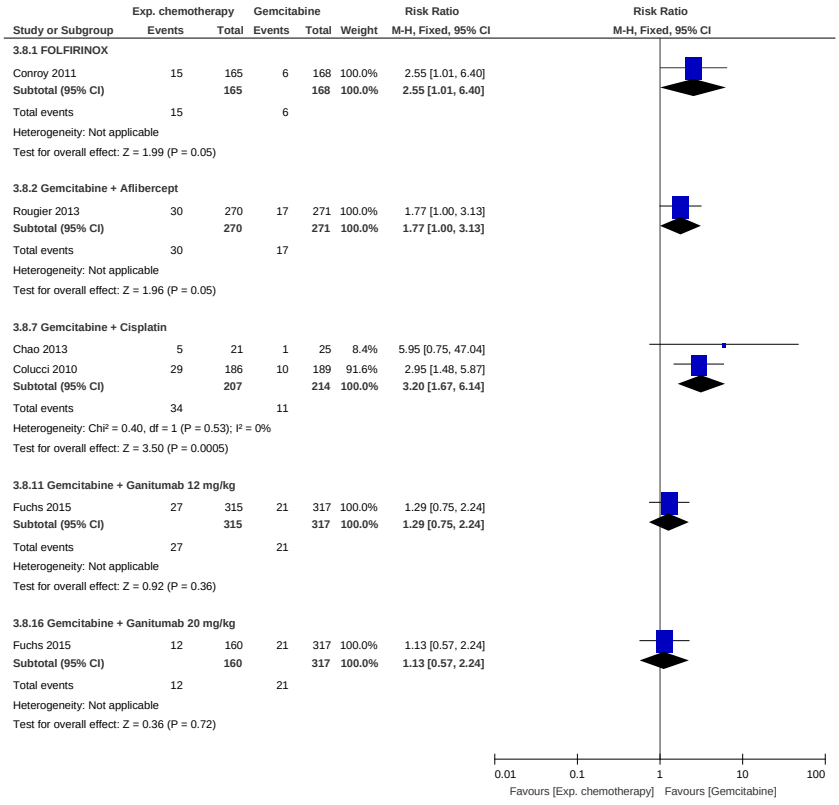


Figure 447: Grade 3/4 toxicities: Leucopoenia

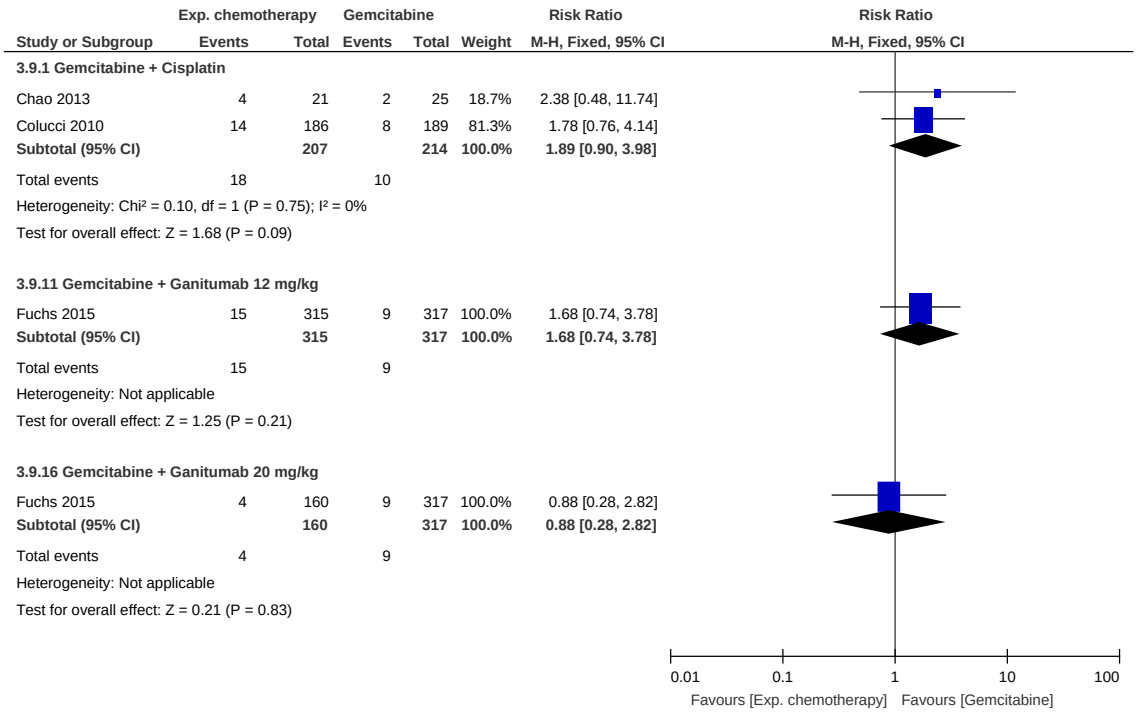
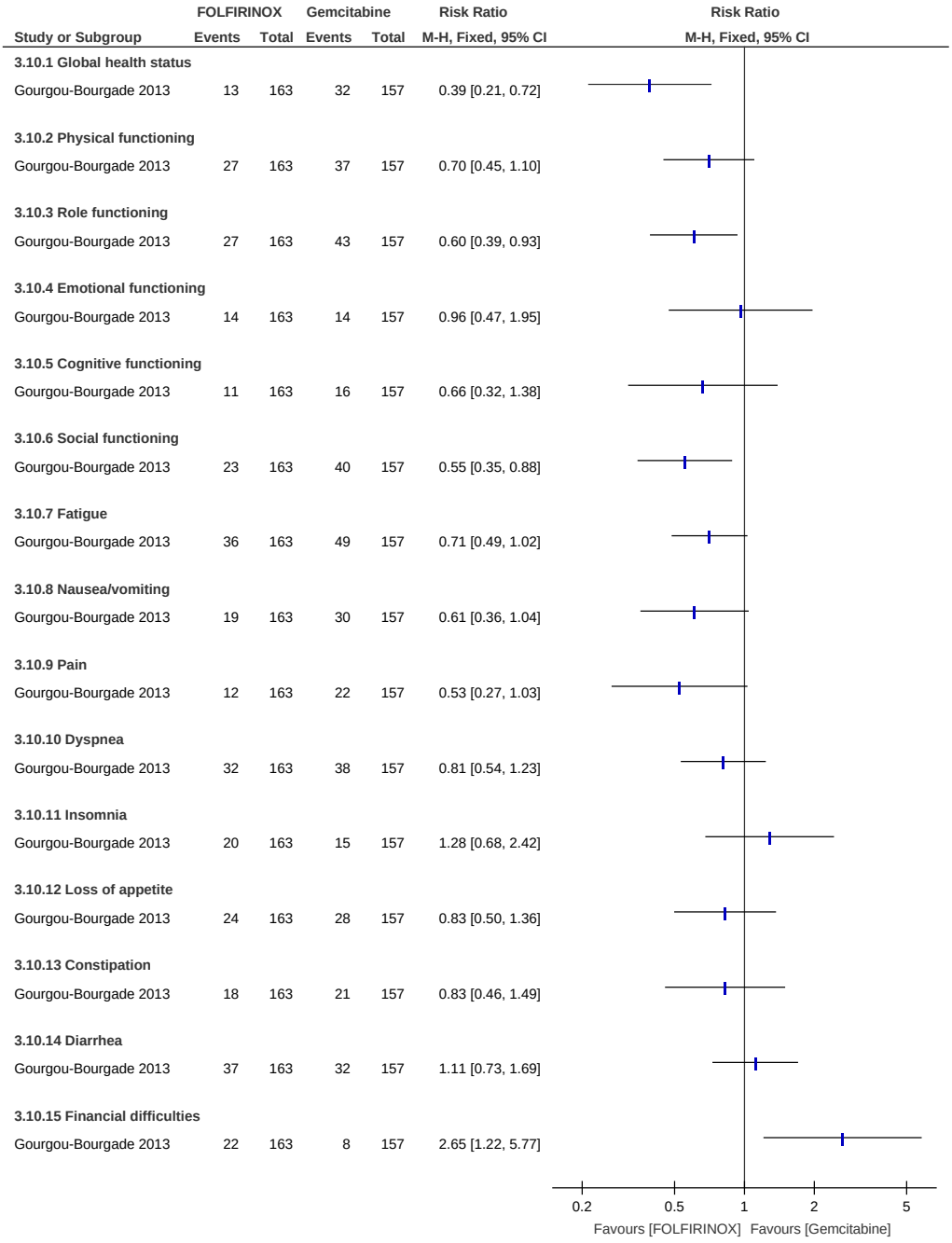
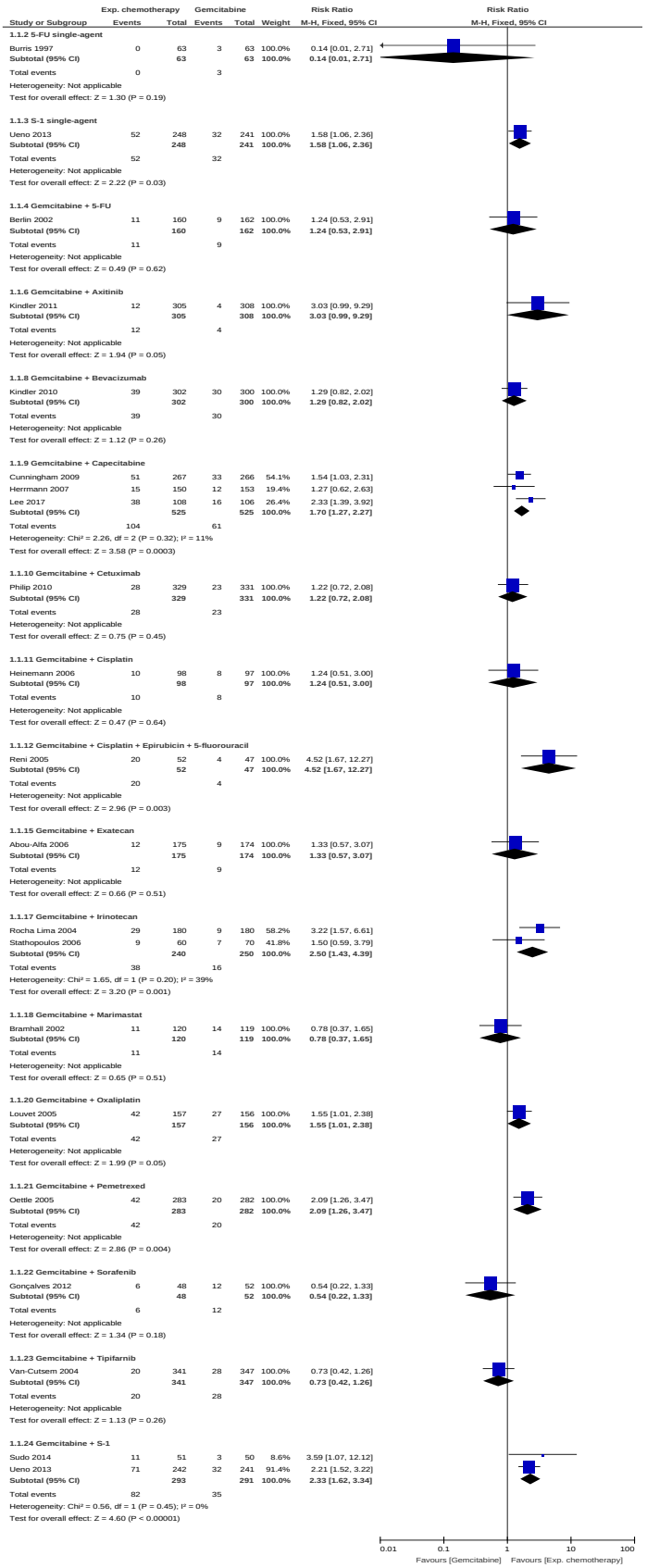


Figure 448: HRQL - Number of patients with a clinically significant (10 point) deterioration QLQ-C30 [between baseline and the end of treatment (6 months)]



H.17.2.21 In adults with locally advanced or metastatic pancreatic cancer

2 Figure 449: Overall response rate



3

Figure 450: Progression-free survival

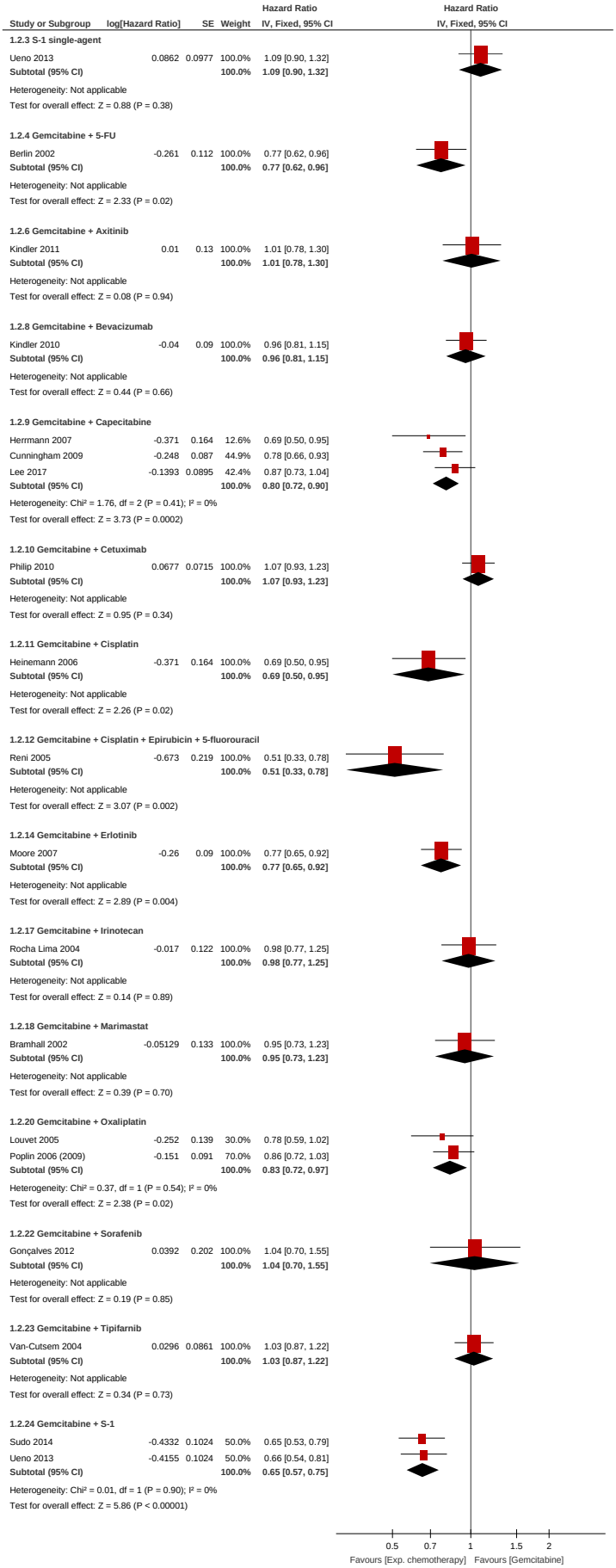
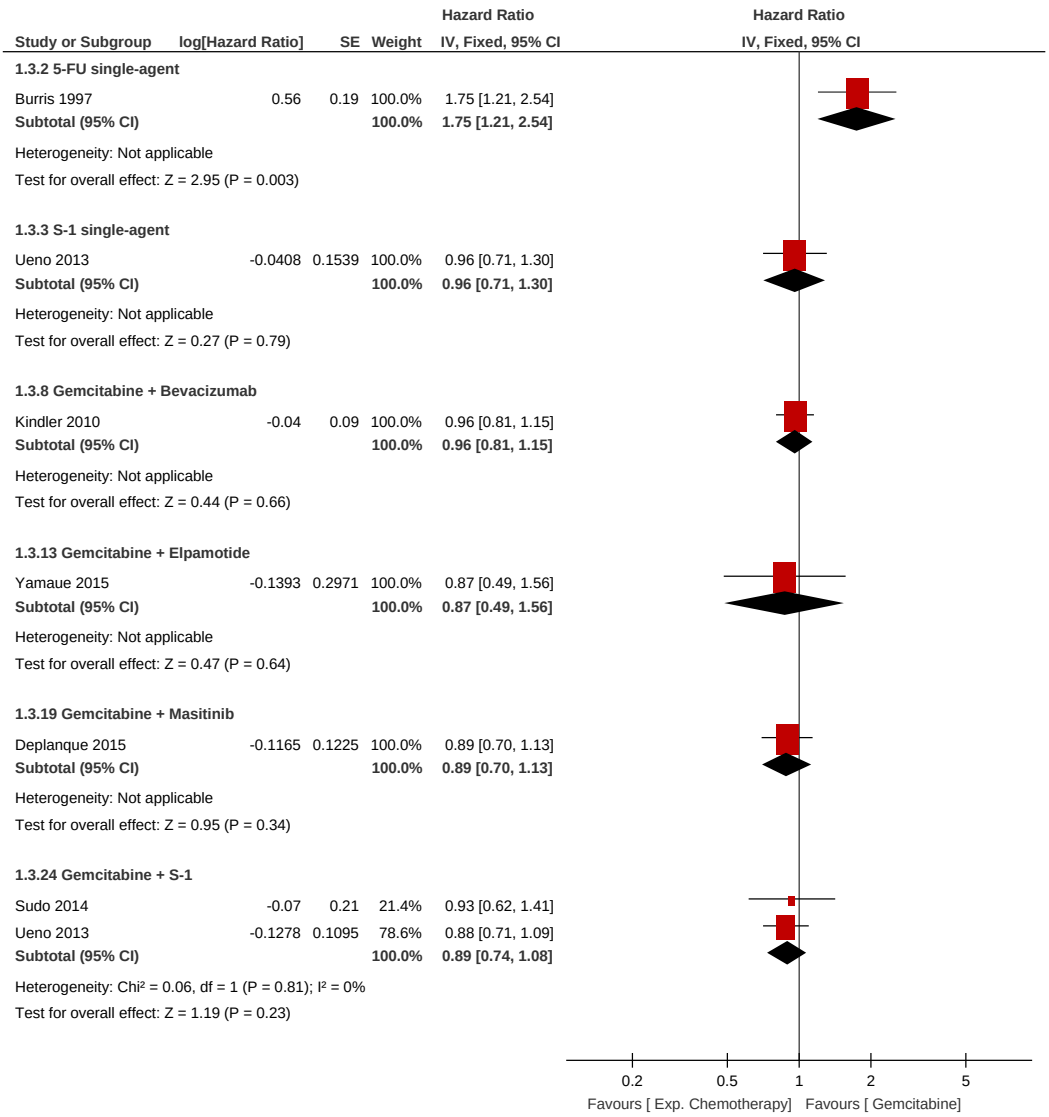
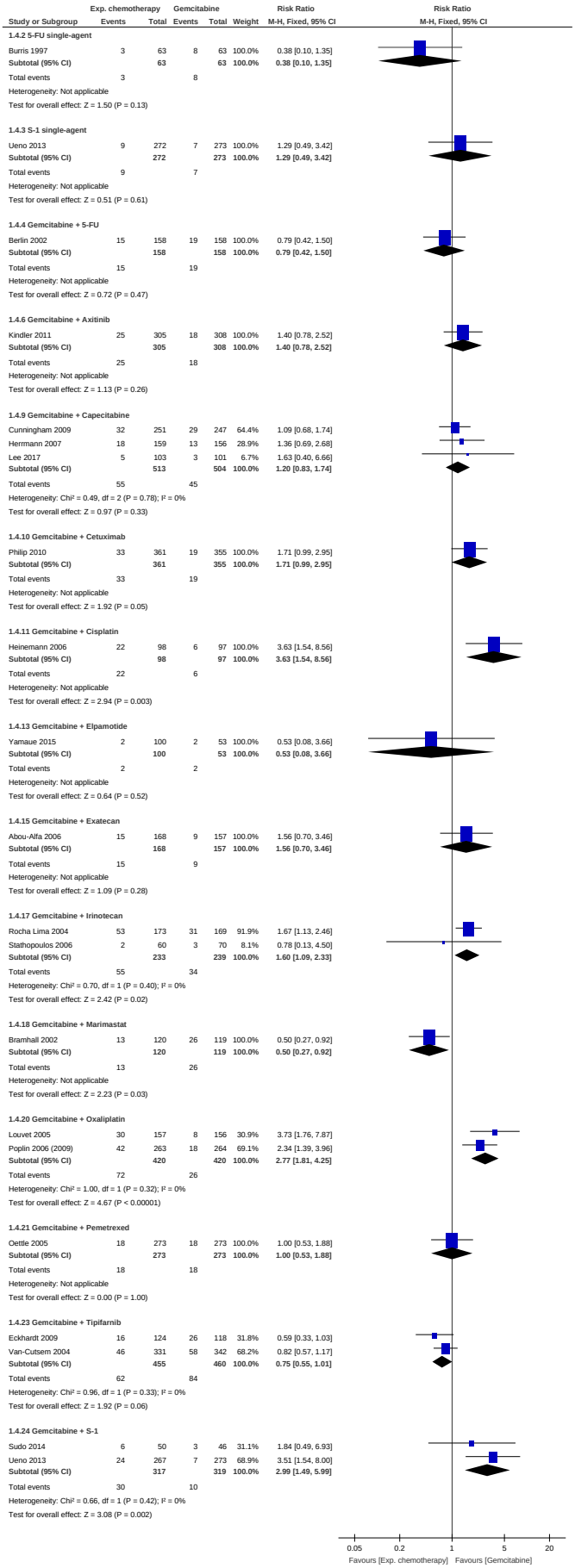


Figure 451: Overall survival

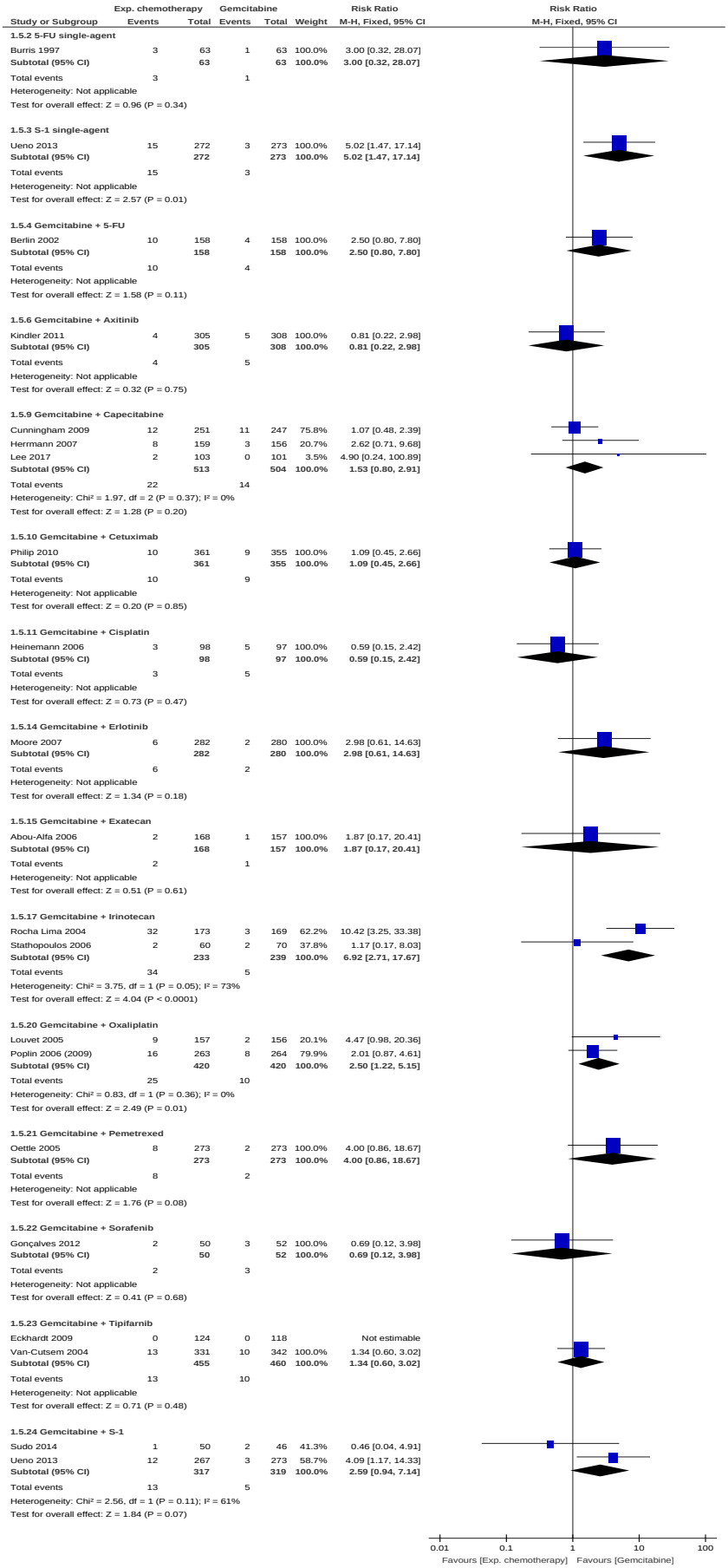


1 **Figure 452: Grade 3/4 toxicities - Nausea/Vomiting**



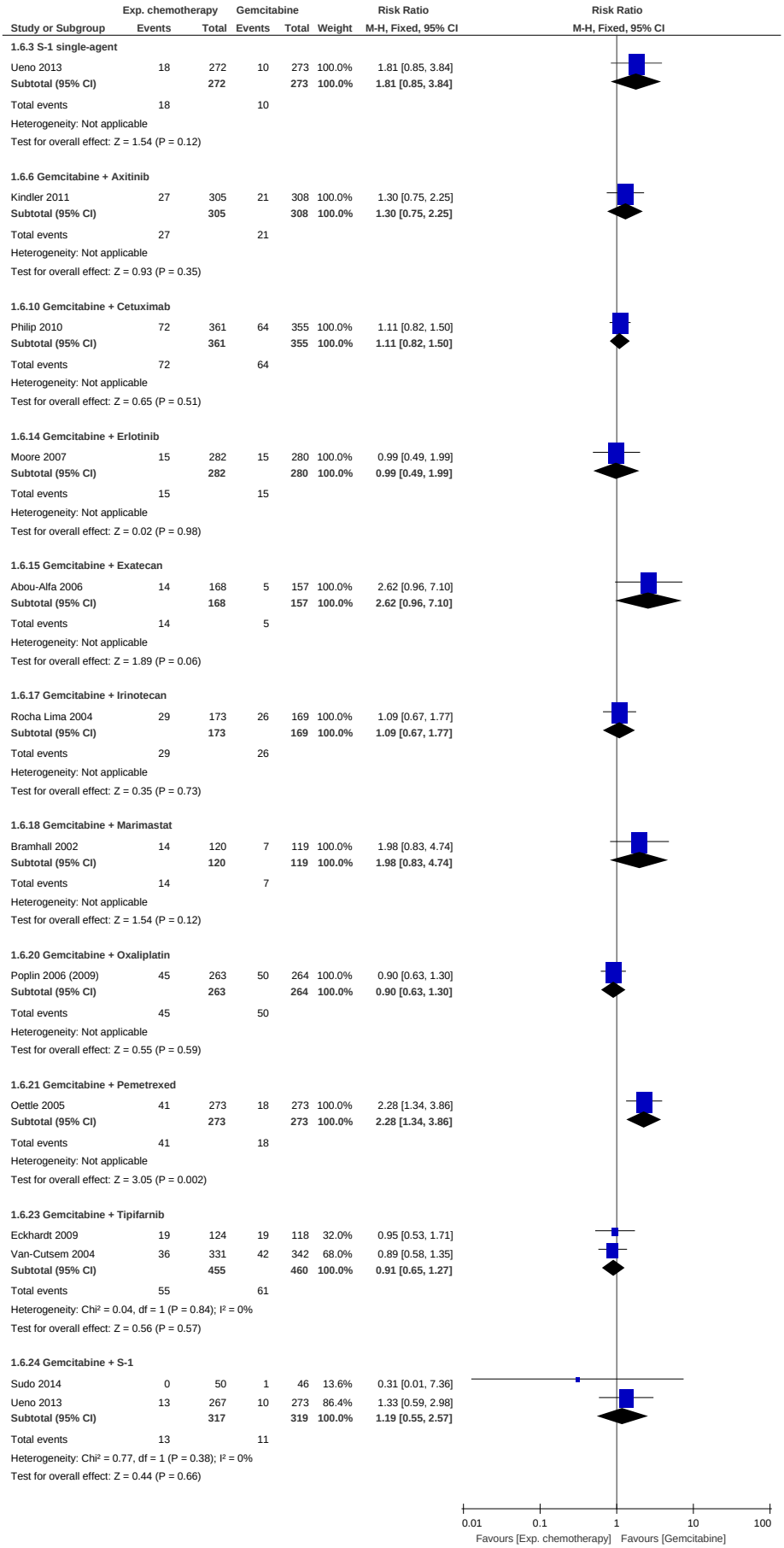
2

1 **Figure 453: Grade 3/4 toxicities – Diarrhoea**



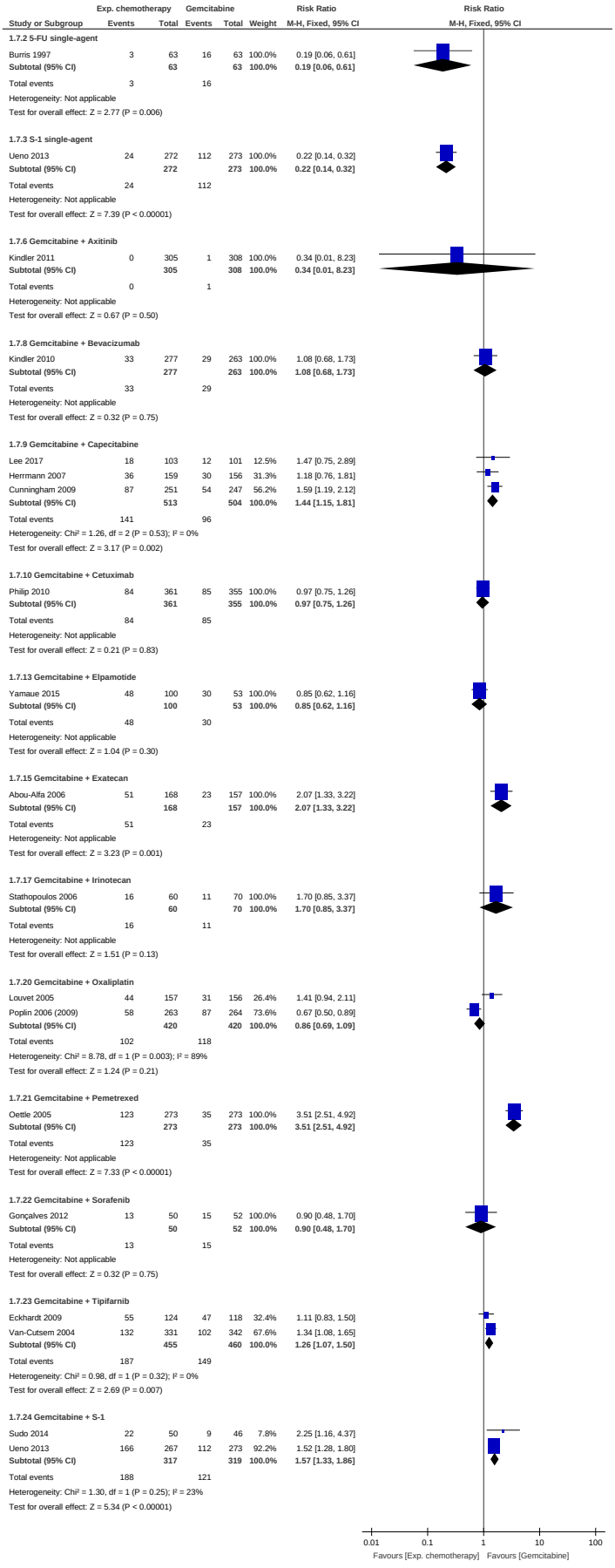
2

1 **Figure 454: Grade 3/4: Fatigue**



2

1 Figure 455: Grade 3/4: Neutropenia



2

Figure 456: Grade 3/4: Thrombocytopenia

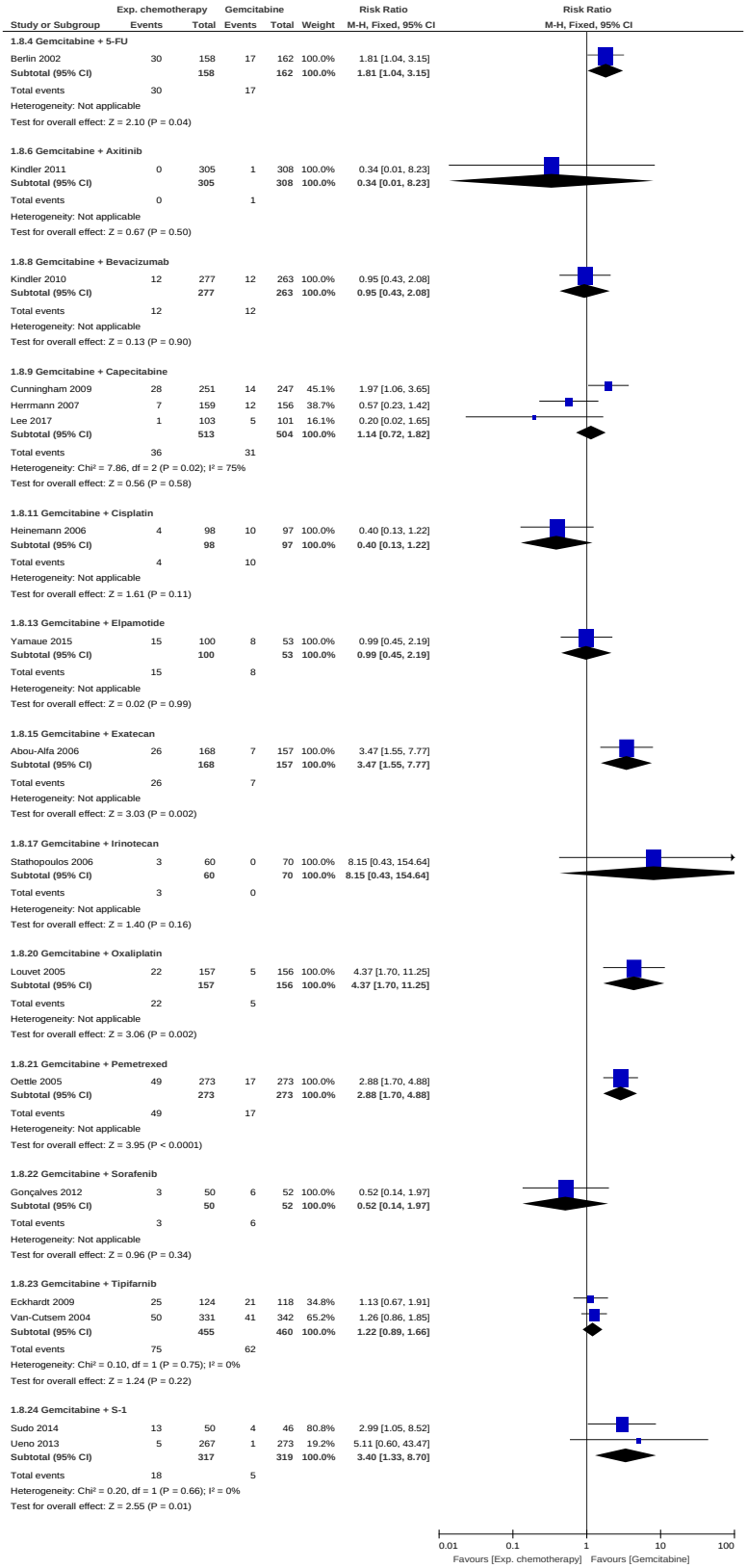


Figure 457: Grade 3/4: Leucopoenia

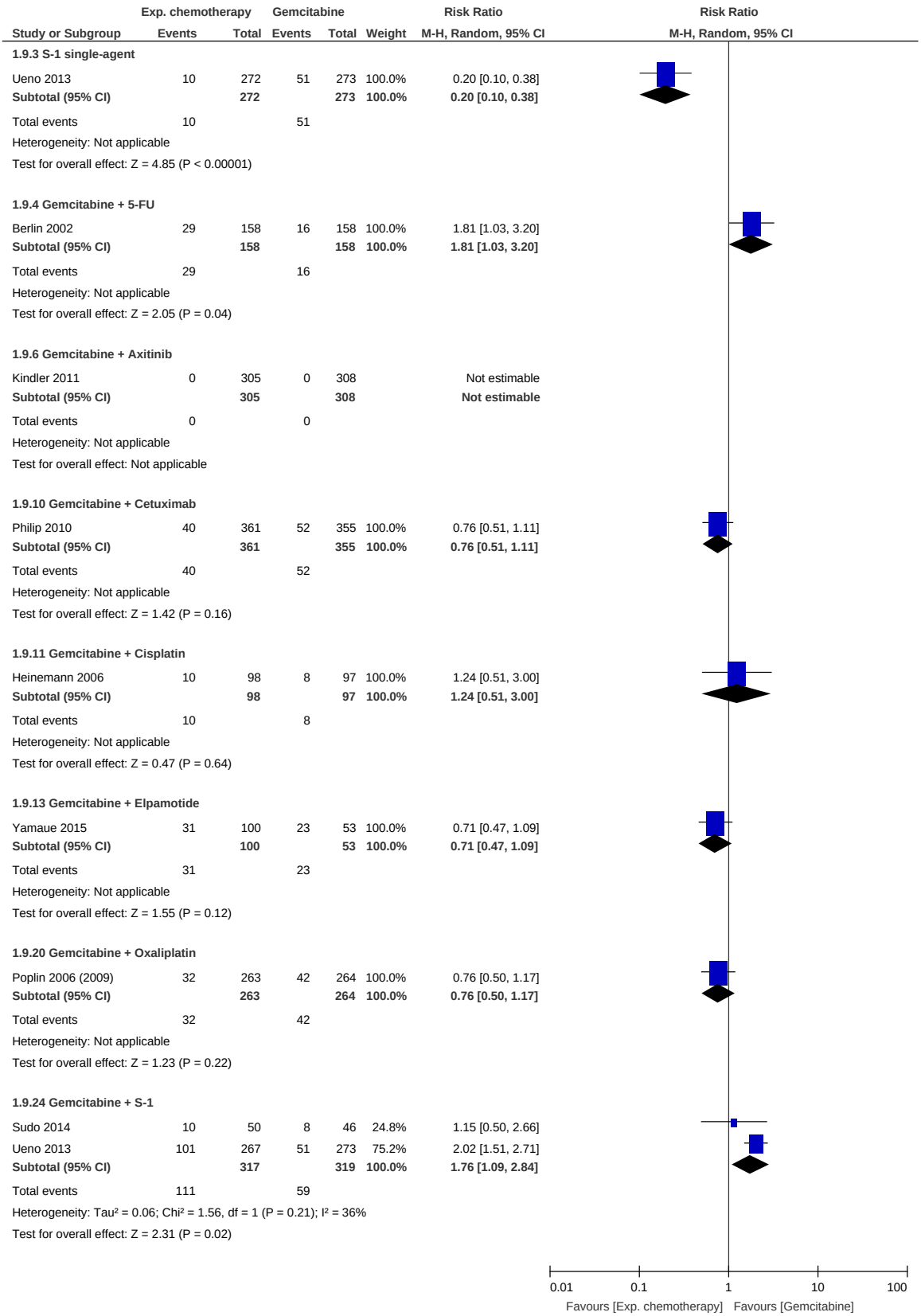


Figure 458: HRQL*(*mean score difference at 6 months -linear-analogy-self-assessment [LASA]indicators)

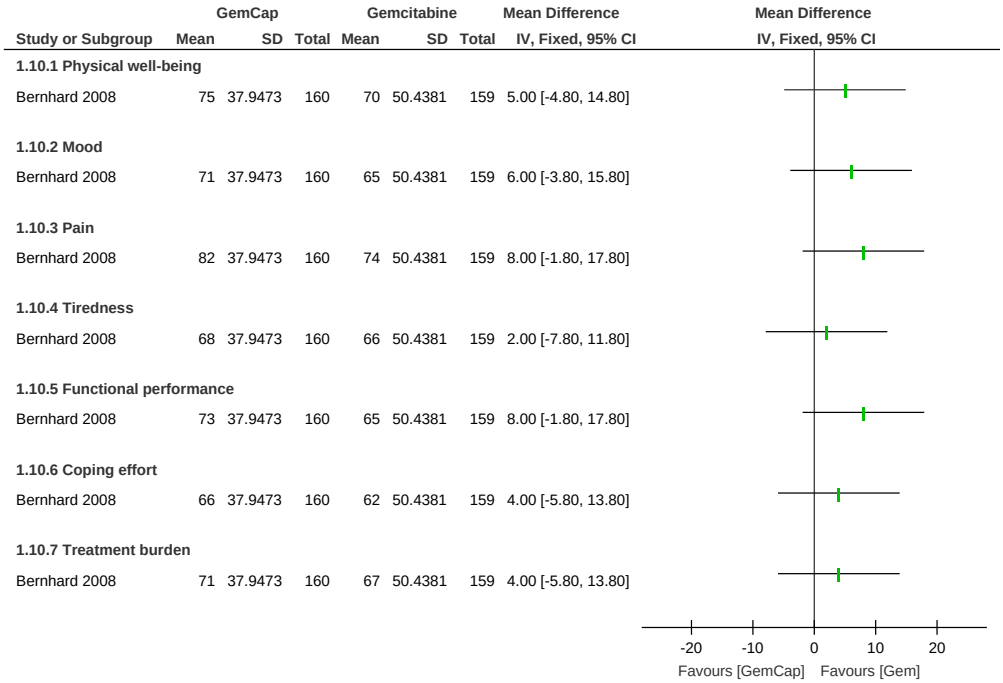


Figure 459: HRQL*(Emotional Well-Being Score at 5, 13, and 17 weeks follow-up)

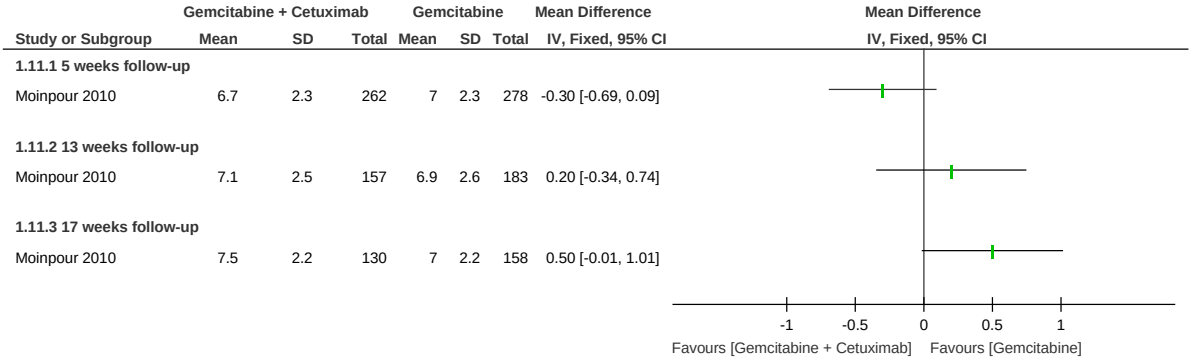


Figure 460: HRQL*(follow-up at at 6 treatment cycles-Spitzer 5-Item Index)

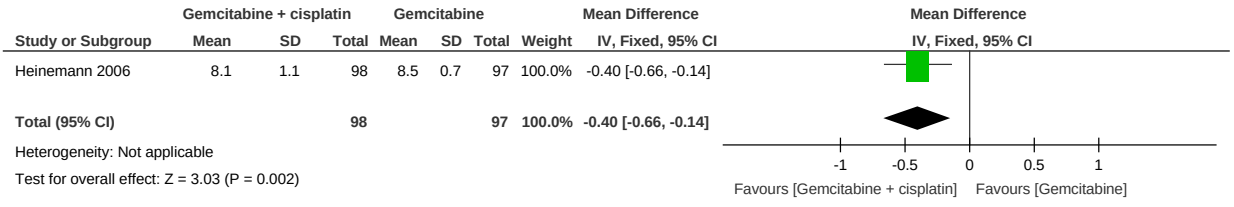


Figure 461: HRQL*(Number of patients with a clinically significant improvement QLQ-C30 at one cycle)

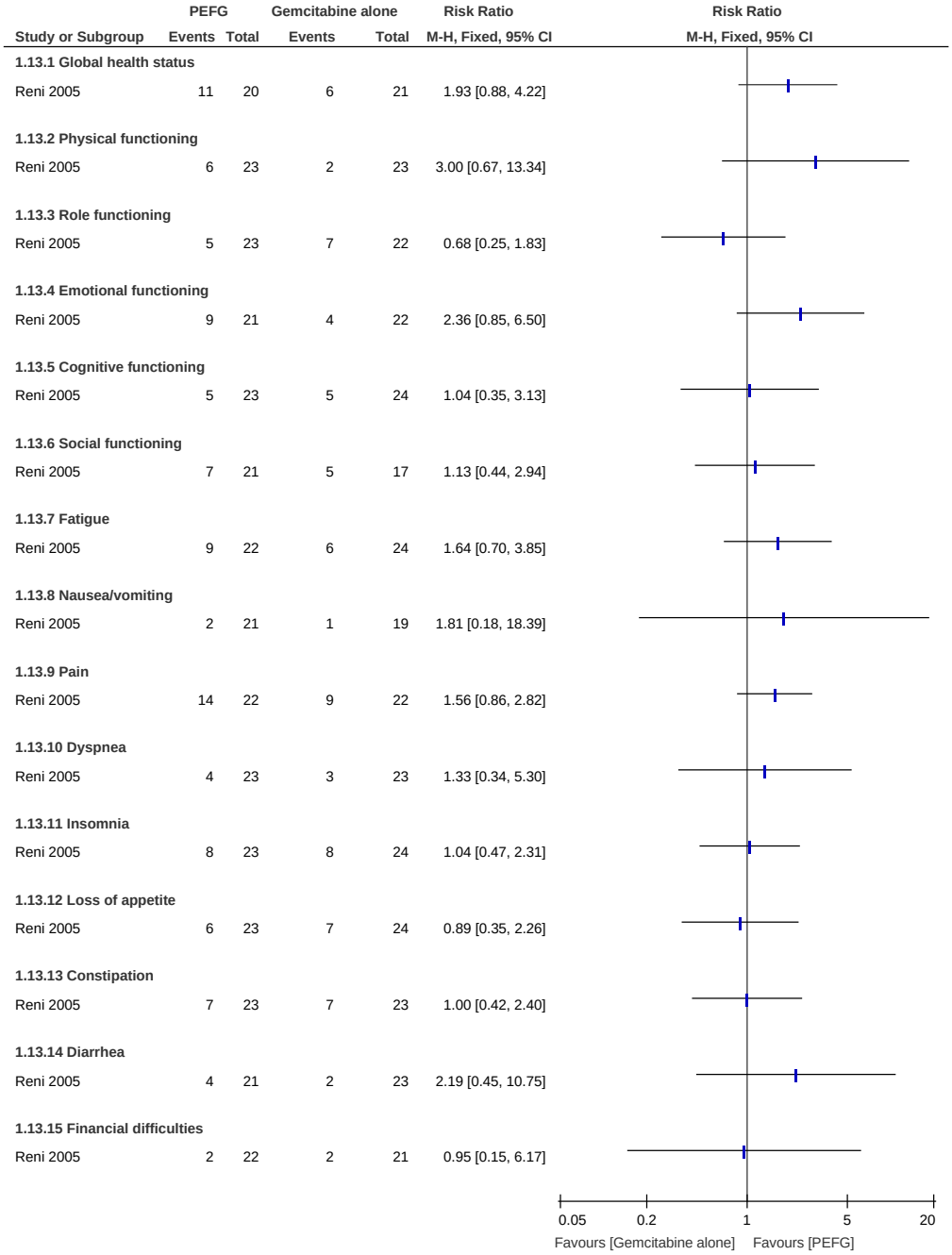


Figure 462: GEM + erlotinib *versus* capecitabine + erlotinib - Overall response rate (CR + PR)

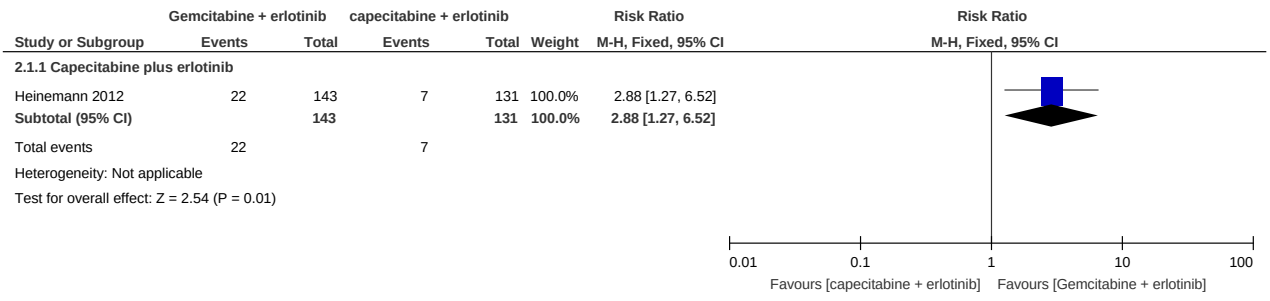


Figure 463: GEM + erlotinib *versus* capecitabine + erlotinib - Grade 3/4 toxicities

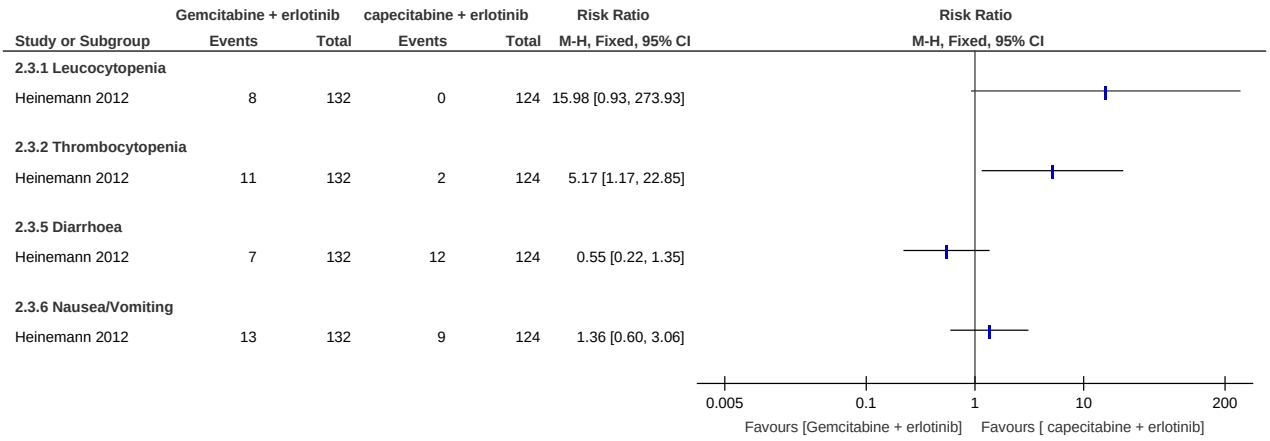


Figure 464: GEM + erlotinib *versus* GEM + erlotinib + bevacizumab - Overall response rate (CR + PR)

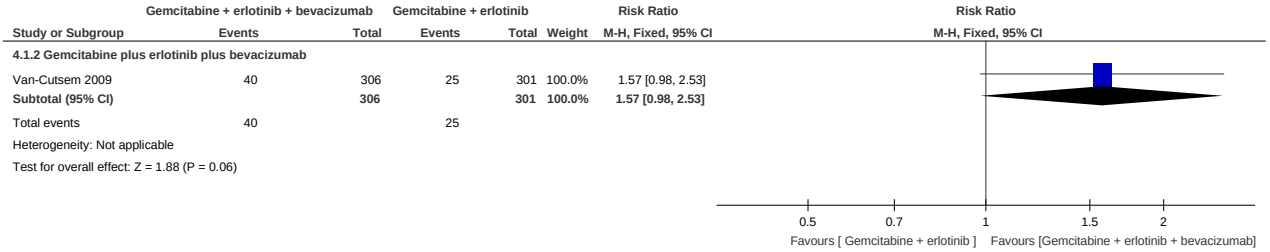


Figure 465: GEM + erlotinib *versus* GEM + erlotinib + bevacizumab – Progression-free survival

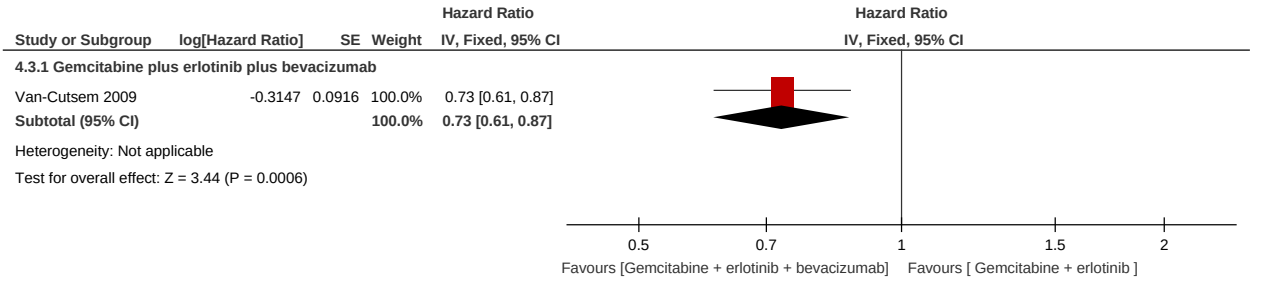
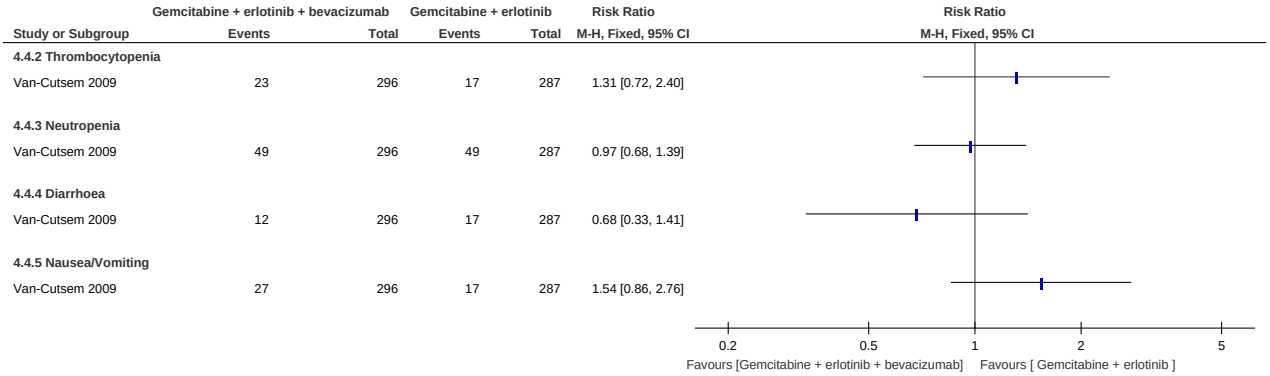
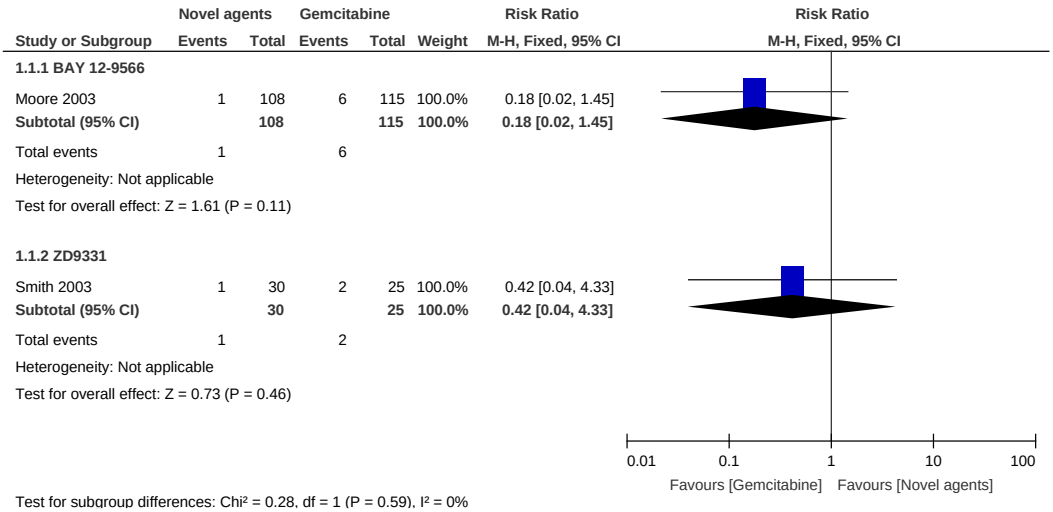


Figure 466: GEM + erlotinib *versus* GEM + erlotinib + bevacizumab - Grade 3/4 toxicities



H.17.3 Gemcitabine versus novel agents in adults with locally advanced or metastatic pancreatic cancer

Figure 467: Overall response rate (CR + PR) at 8 weeks of therapy



Test for subgroup differences: Chi² = 0.28, df = 1 (P = 0.59), I² = 0%

Figure 468: Progression-free survival

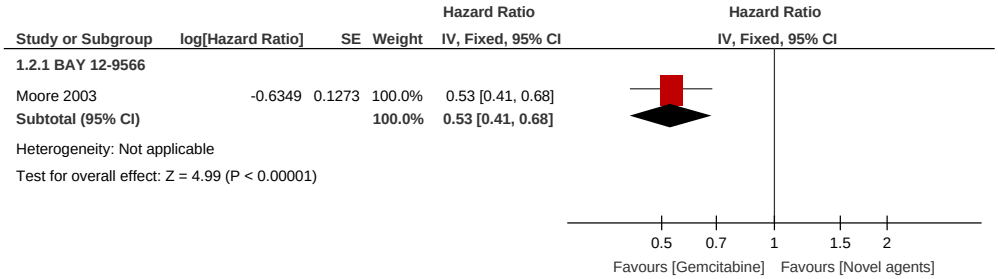


Figure 469: Overall survival

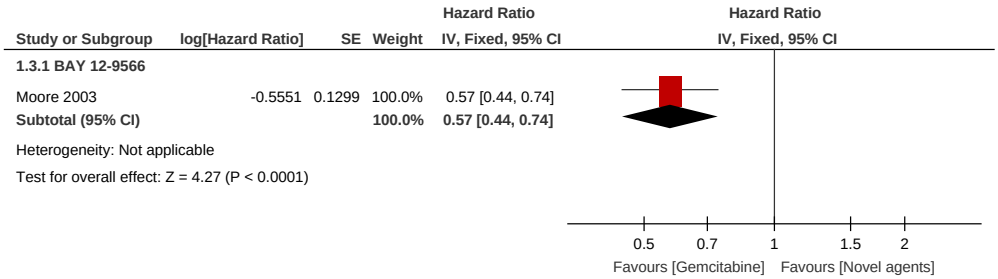
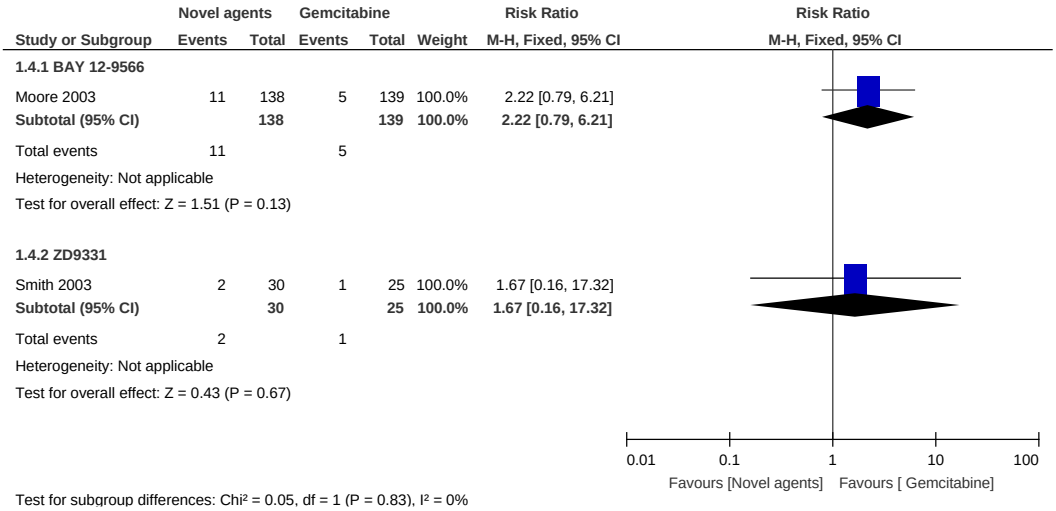
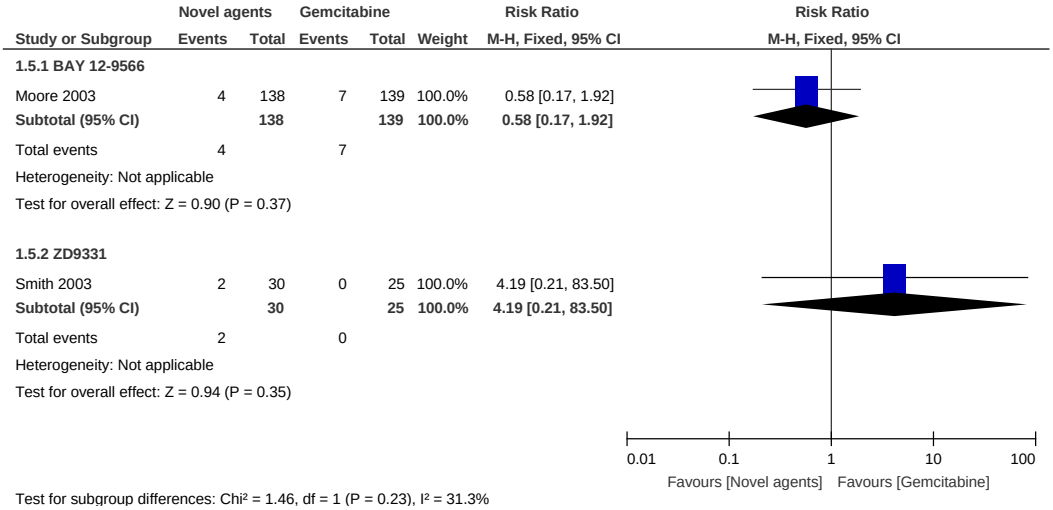


Figure 470: Grade 3/4 toxicities: Nausea



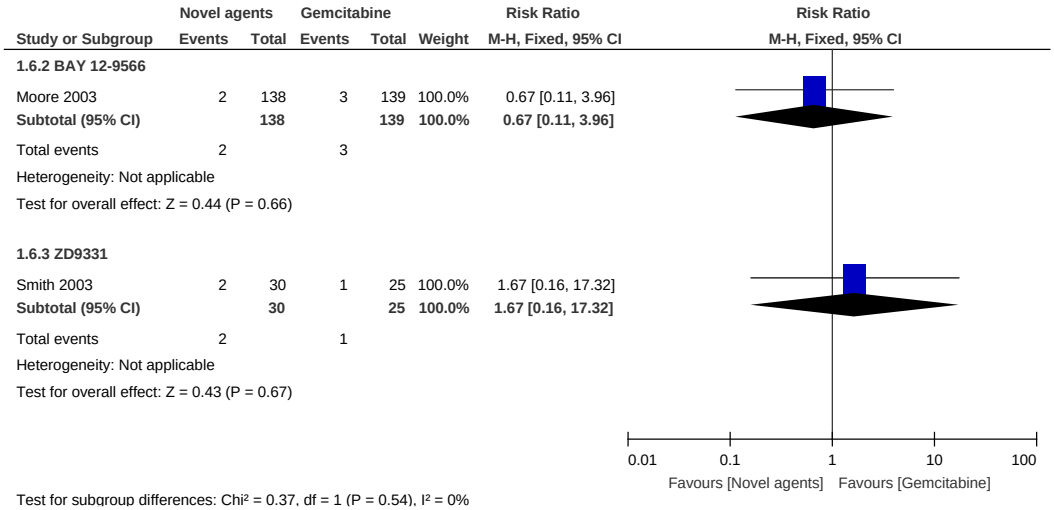
Test for subgroup differences: Chi² = 0.05, df = 1 (P = 0.83), I² = 0%

Figure 471: Grade 3/4 toxicities: Vomiting



Test for subgroup differences: Chi² = 1.46, df = 1 (P = 0.23), I² = 31.3%

Figure 472: Grade 3/4 toxicities: Diarrhoea



Test for subgroup differences: Chi² = 0.37, df = 1 (P = 0.54), I² = 0%

Figure 473: Grade 3/4 toxicities: Fatigue

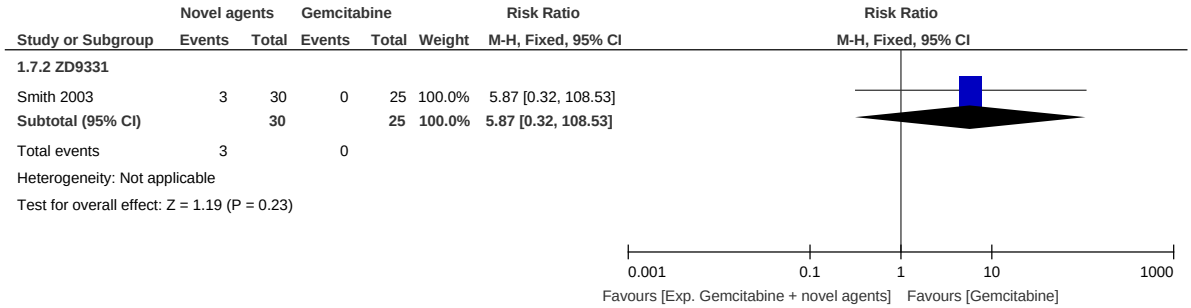


Figure 474: Grade 3/4 toxicities: Neutropenia

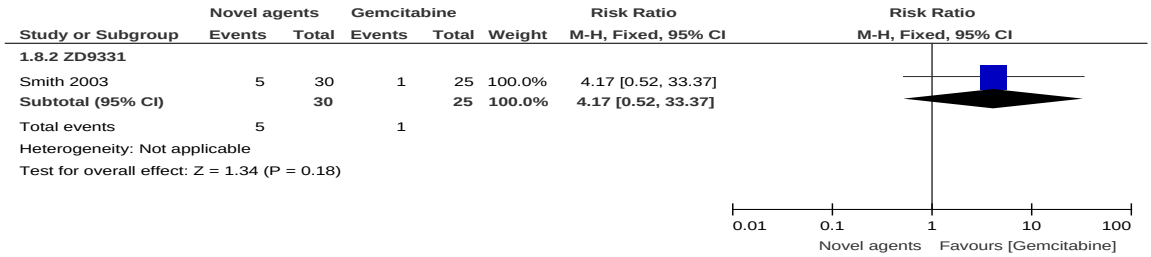


Figure 475: HRQL (EORTC C-30: Domains) - Mean change from Baseline at 8 weeks follow-up

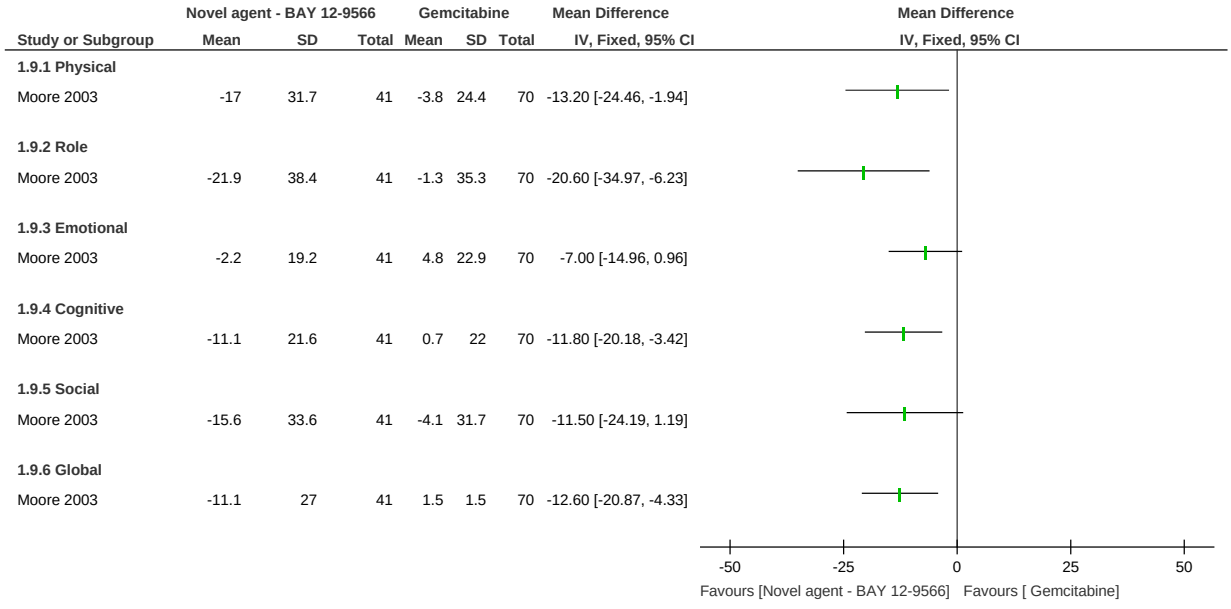
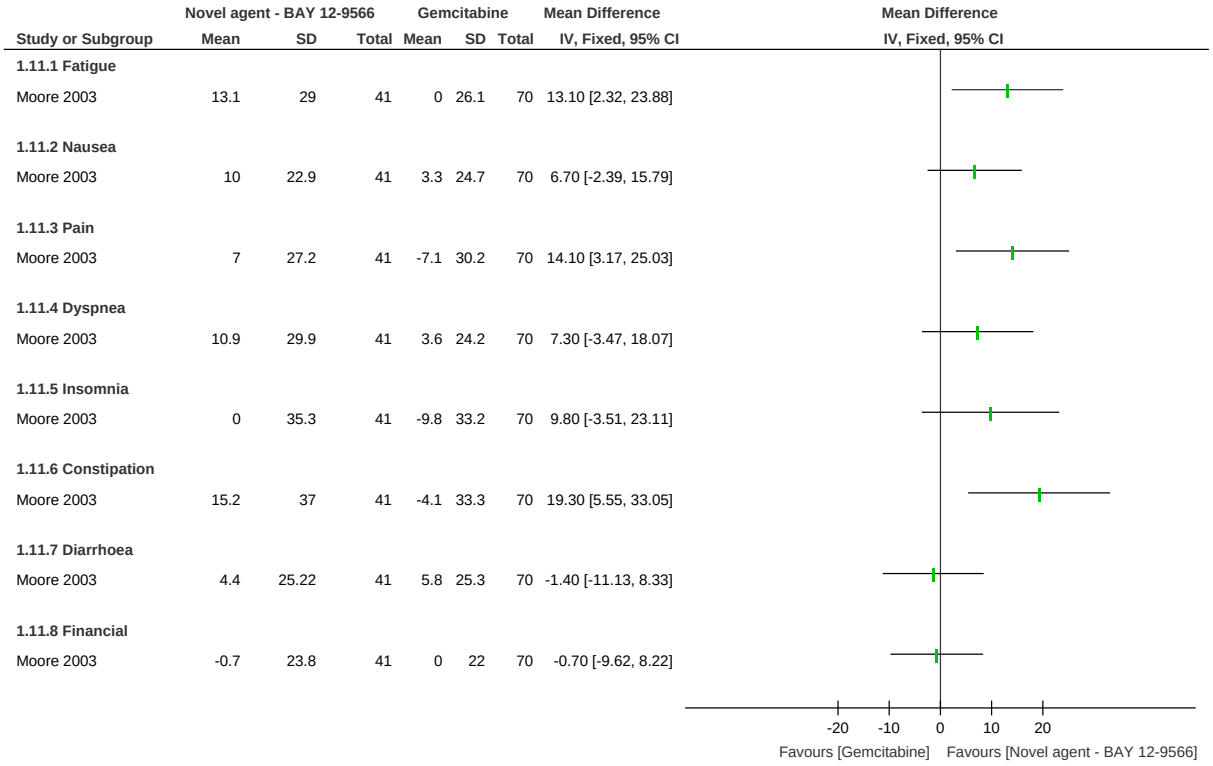


Figure 476: HRQL (EORTC C-30: Symptoms) - Mean change From Baseline at 8 weeks follow-up



H.17.4 Standard-dose gemcitabine versus low-dose gemcitabine in adults with locally advanced or metastatic pancreatic cancer

Figure 477: Overall response rate (CR + PR)

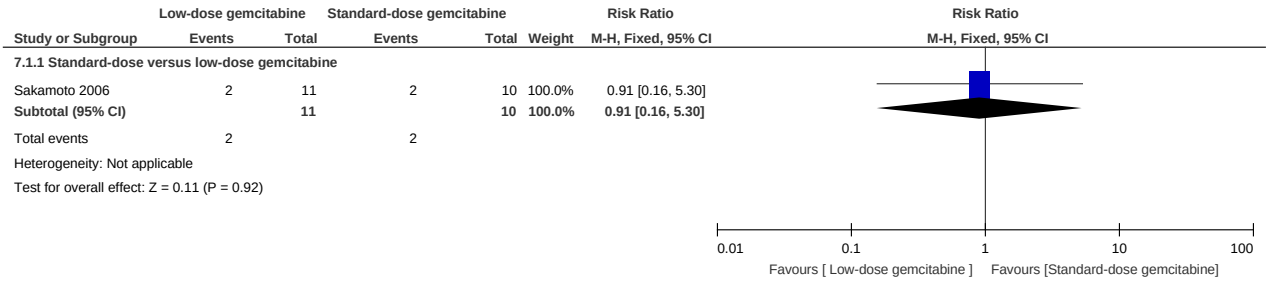
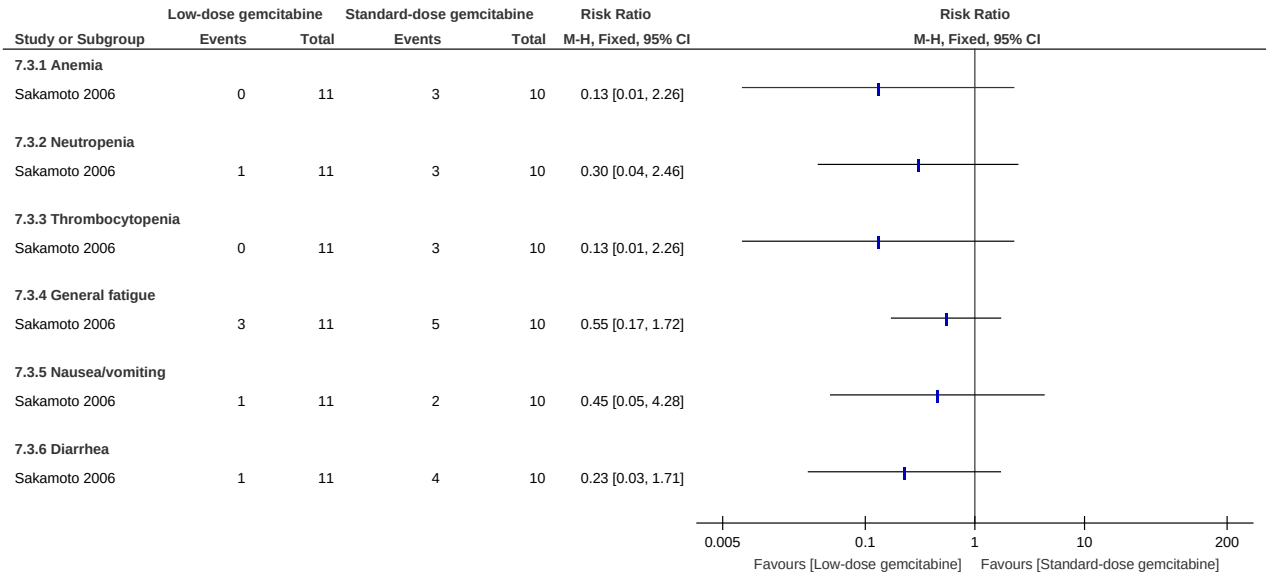


Figure 478: Grade 3/4 toxicities



H.17.5 5-FU versus combination 5-FU

H.17.5.1 In adults with metastatic pancreatic cancer

Figure 479: Overall response rate (CR + PR)

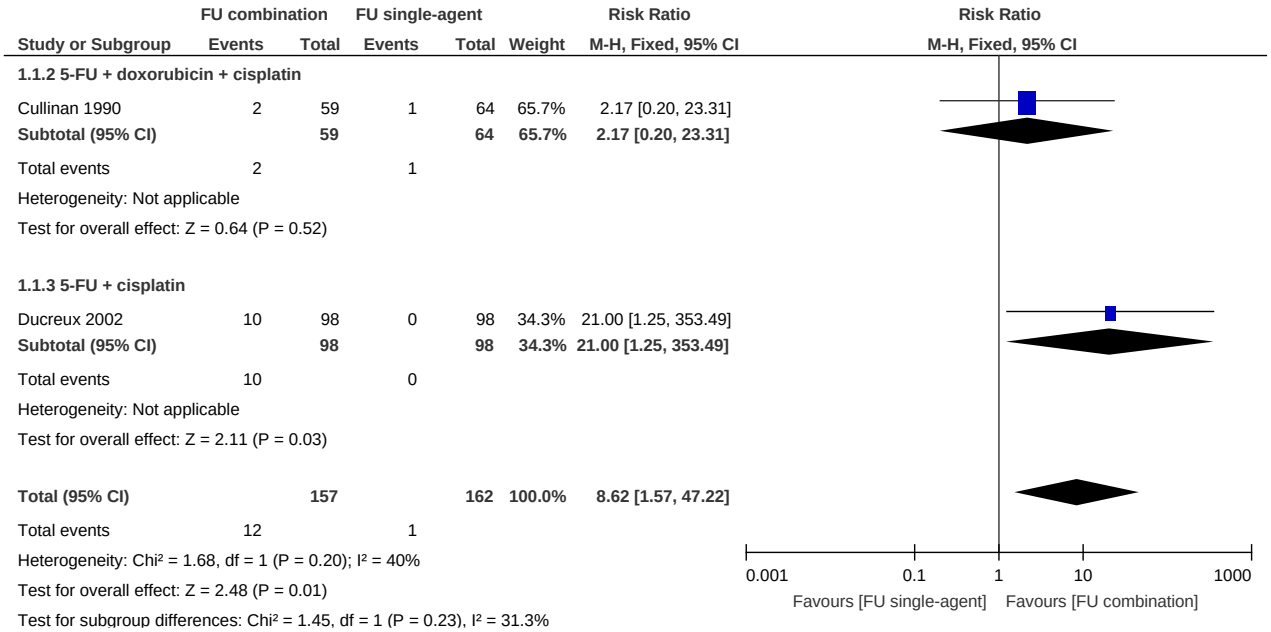


Figure 480: Progression-free survival

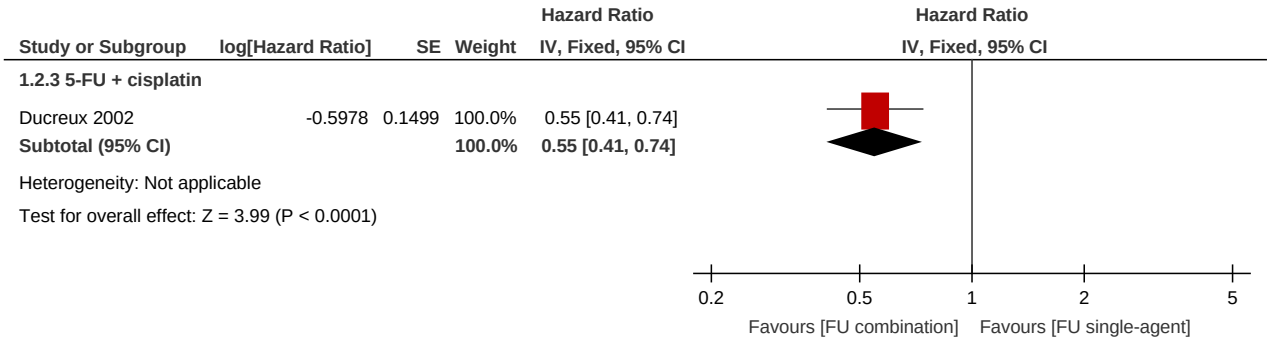


Figure 481: Overall survival

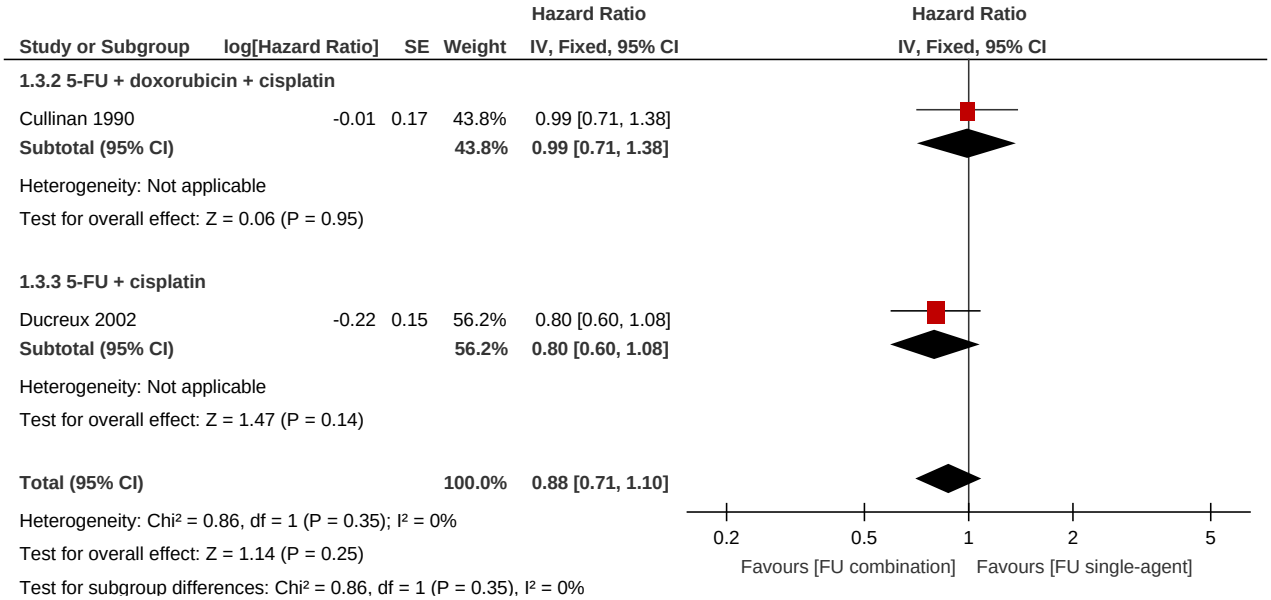


Figure 482: Grade 3/4 toxicities: Nausea

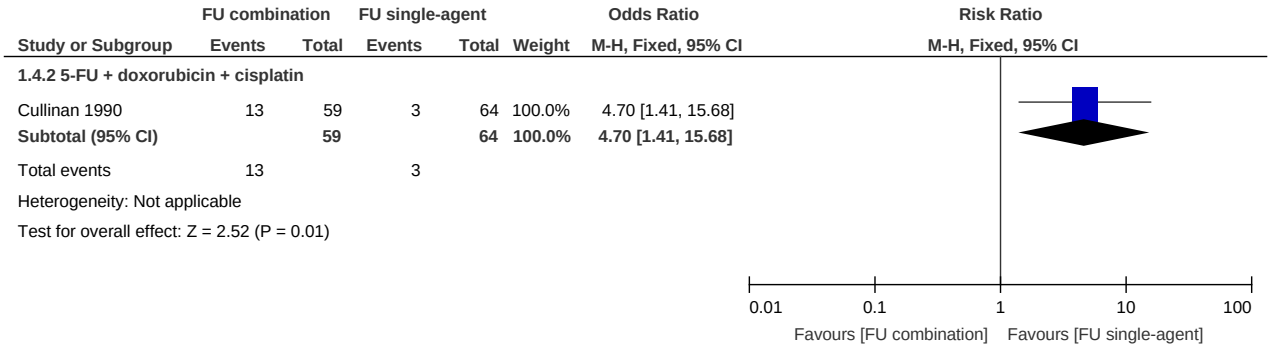


Figure 483: Grade 3/4 toxicities: Vomiting

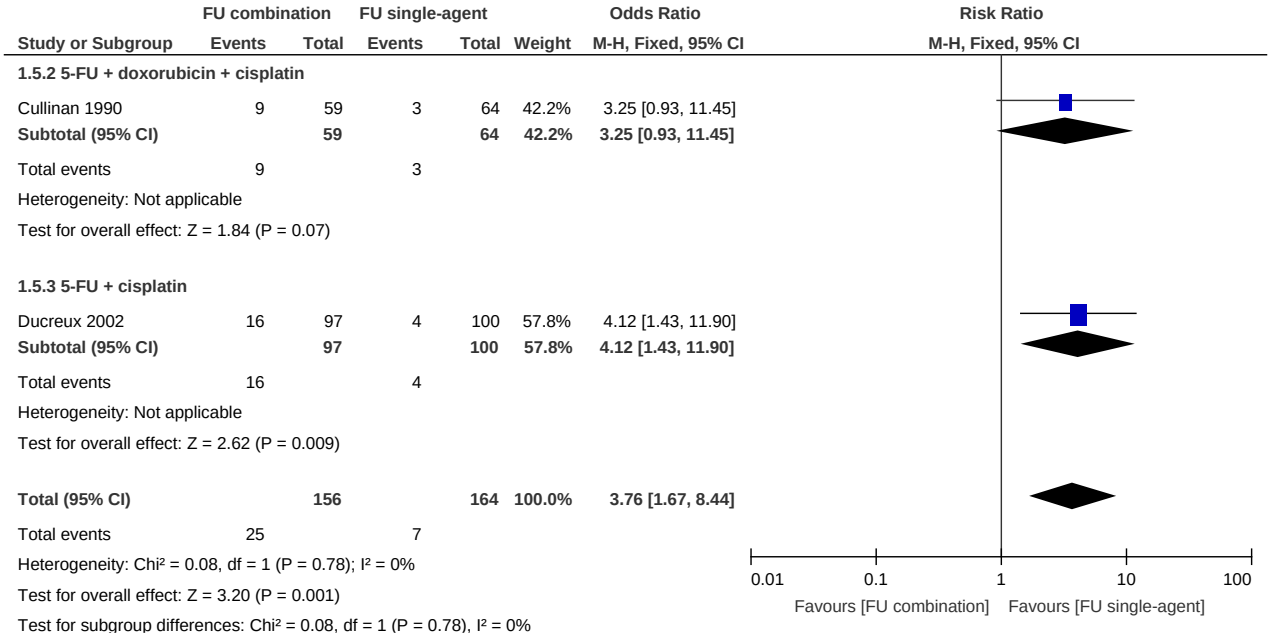


Figure 484: Grade 3/4 toxicities: Diarrhoea

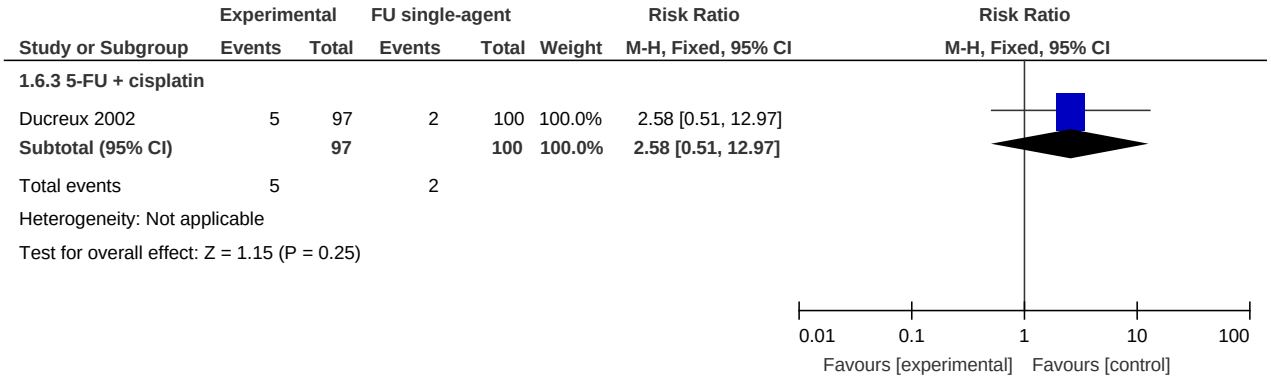


Figure 485: Grade 3/4 toxicities: Leucopoenia

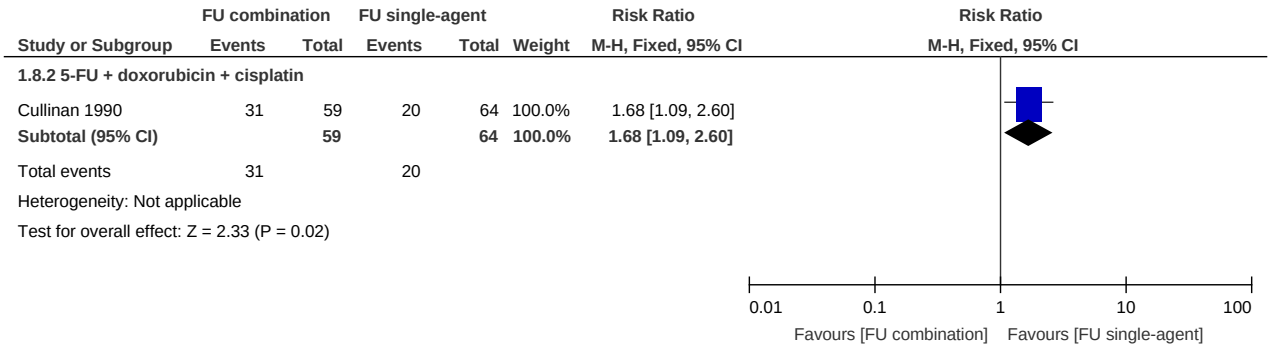
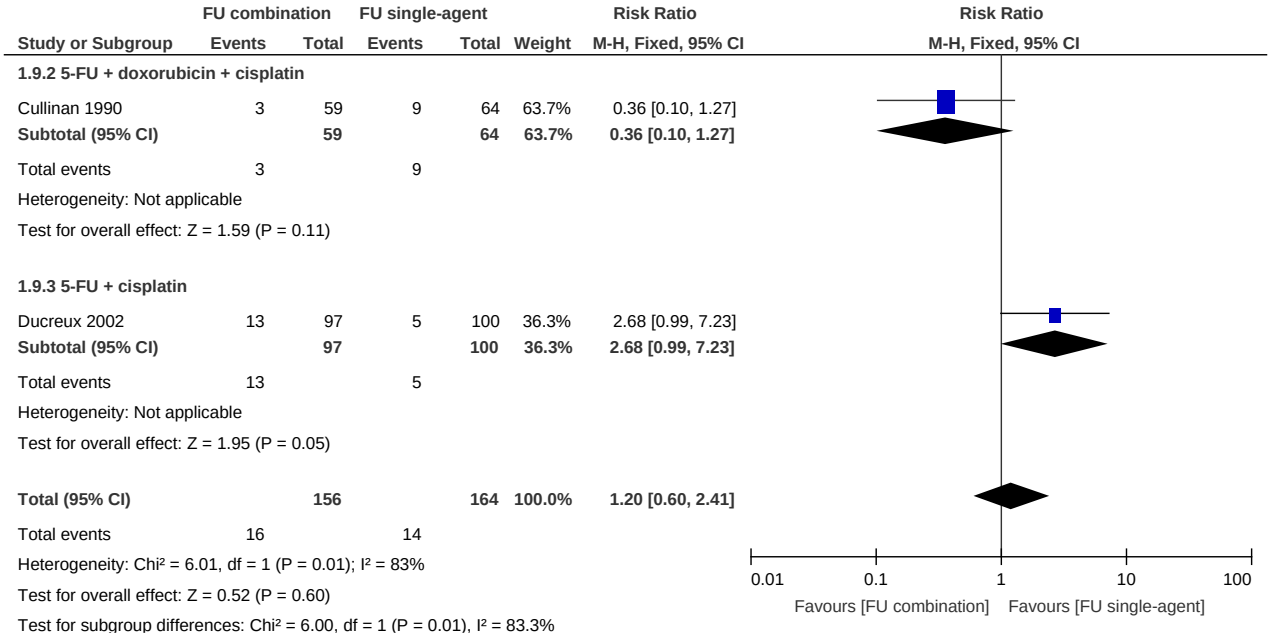


Figure 486: Grade 3/4 toxicities: Stomatitis



H.17.5.2 In adults with locally advanced metastatic pancreatic cancer

Figure 487: Overall response rate (CR + PR)

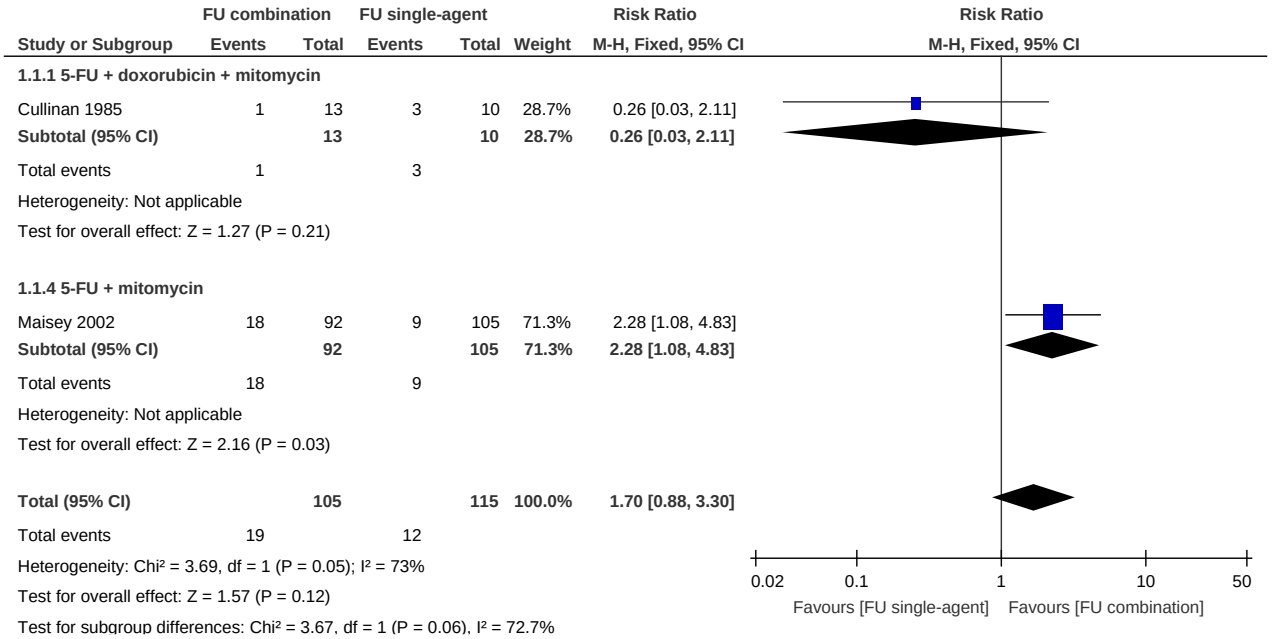


Figure 488: Progression-free survival

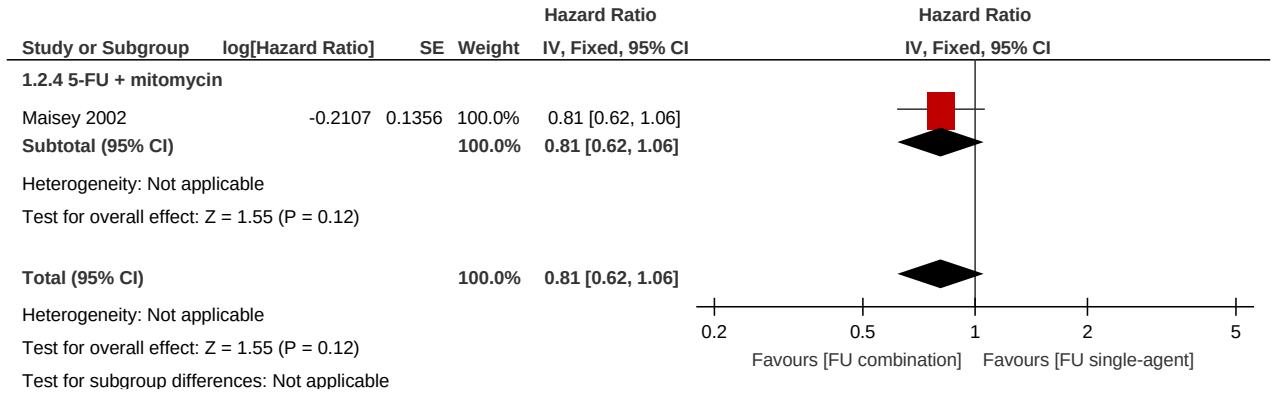


Figure 489: Overall Survival

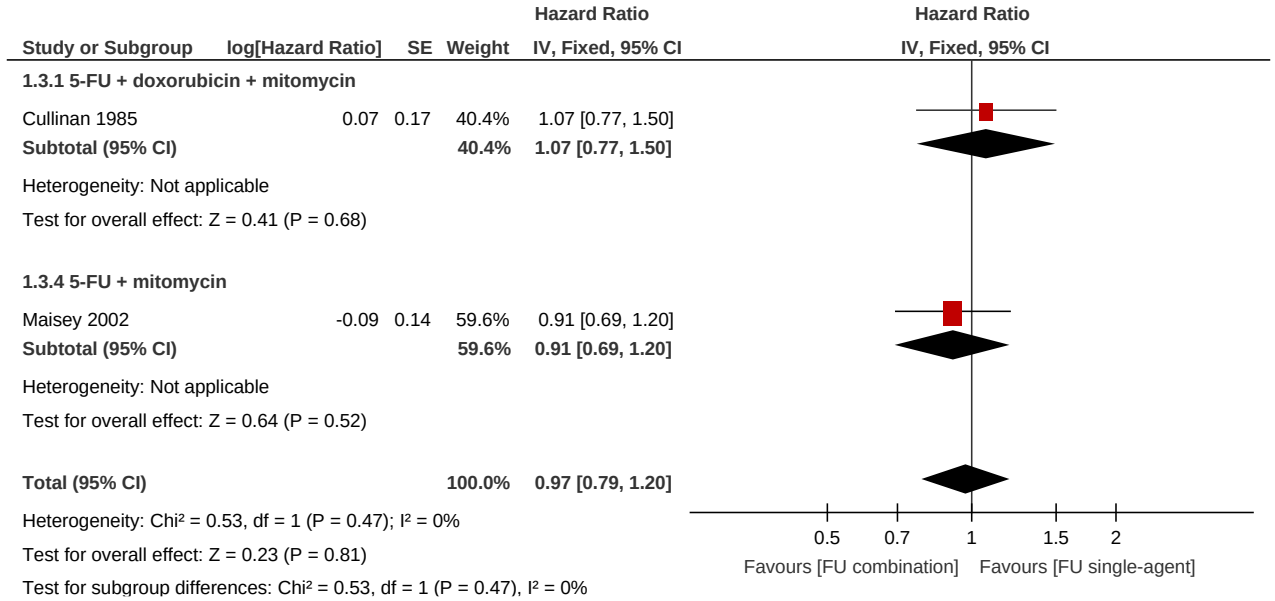


Figure 490: Grade 3/4 toxicities: Diarrhoea

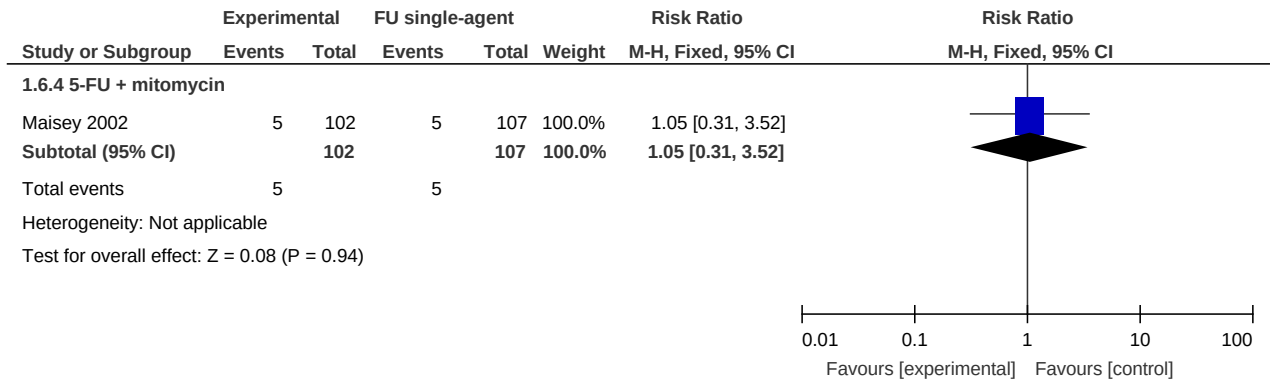


Figure 491: Grade 3/4 toxicities: Neutropenia

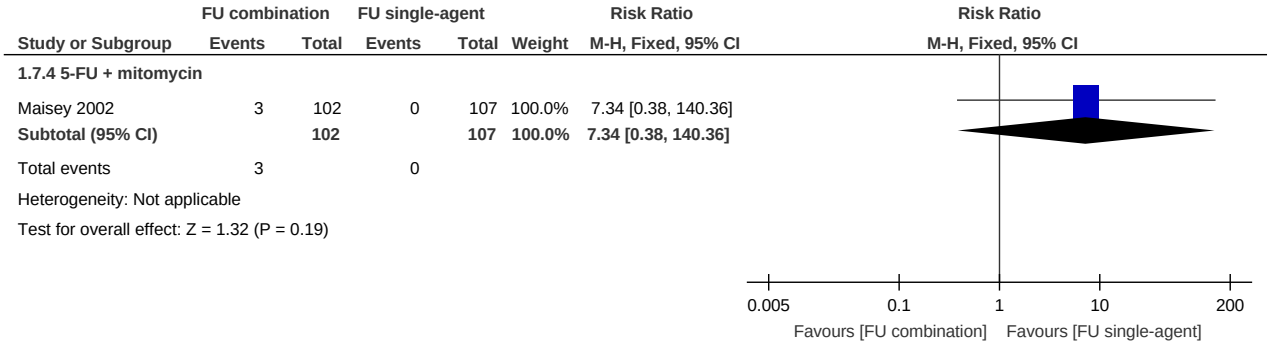
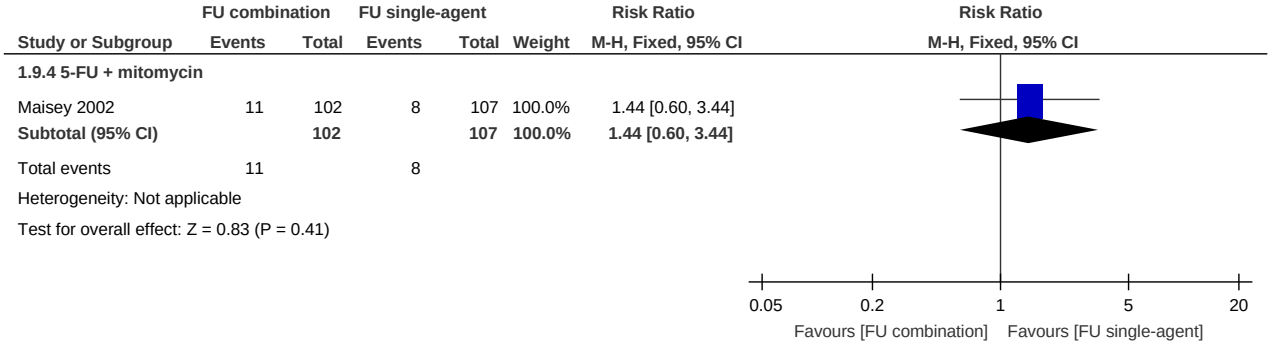


Figure 492: Grade 3/4 toxicities: Stomatitis



H.17.6 Combination 5-FU (FSM) versus other chemotherapy regimens in adults with locally advanced or metastatic pancreatic cancer

Figure 493: Overall response rate (CR + PR)

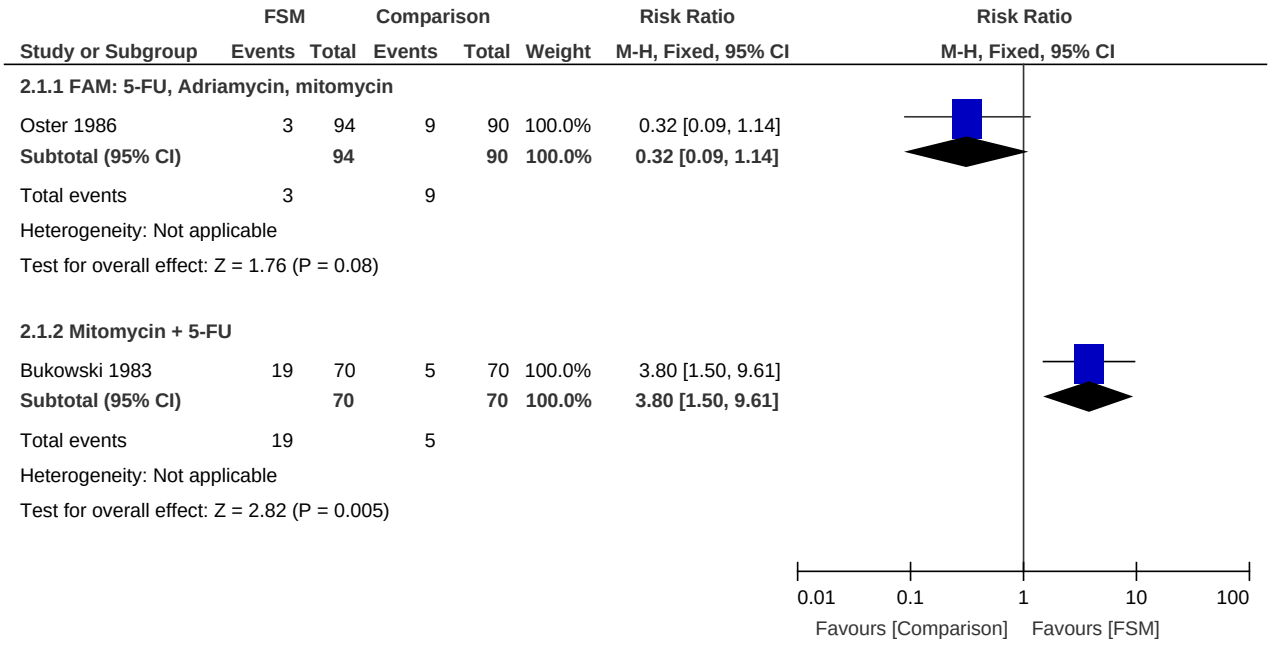


Figure 494: Grade 3/4 toxicities: Diarrhoea

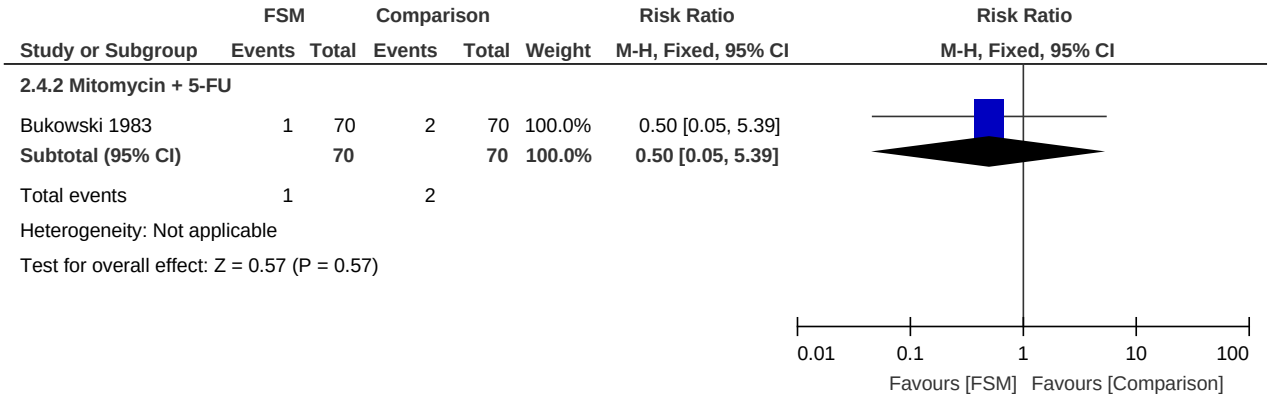


Figure 495: Grade 3/4 toxicities: Nausea/vomiting

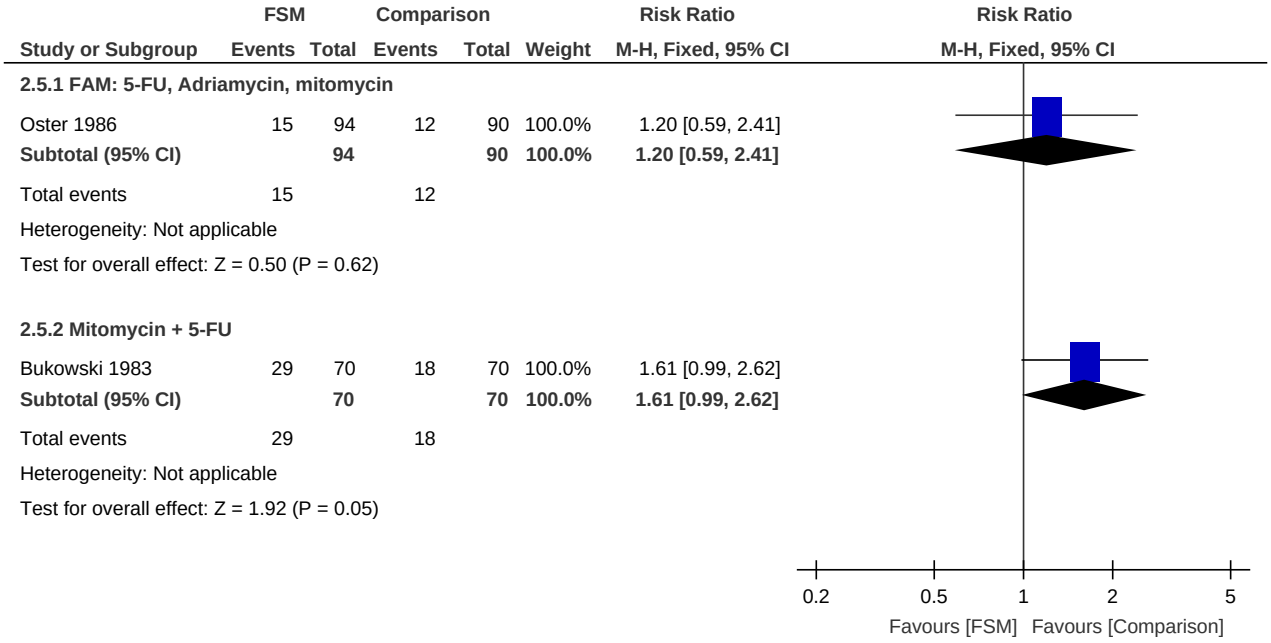


Figure 496: Grade 3/4 toxicities: Leucopoenia

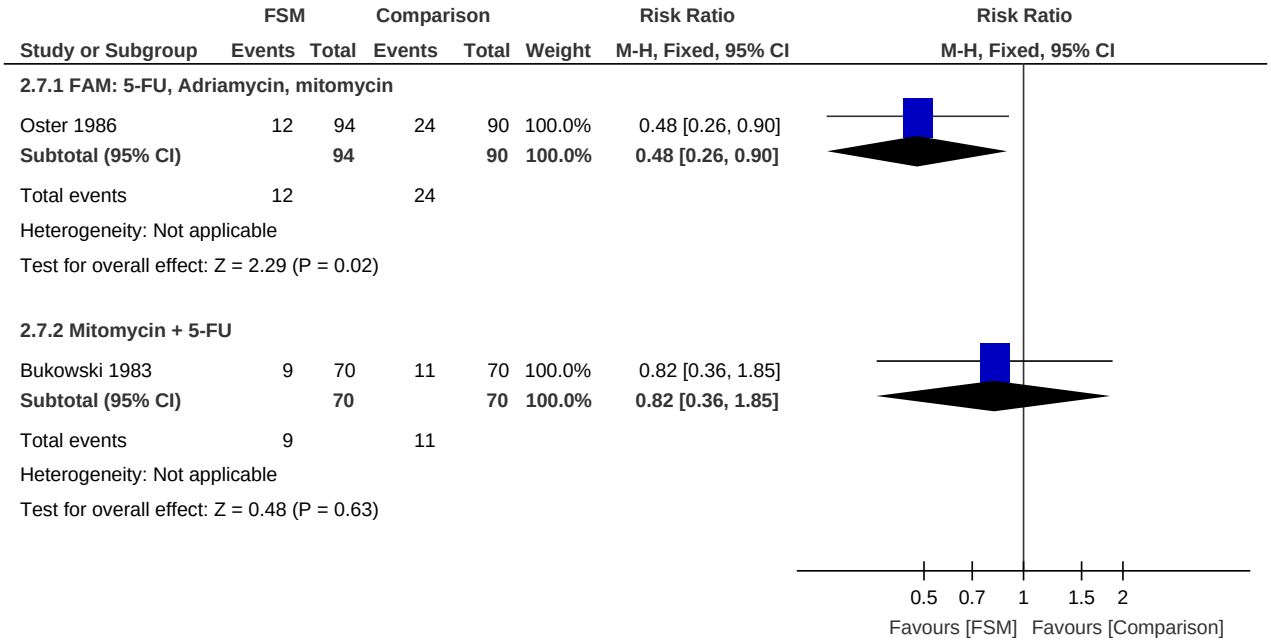


Figure 497: Grade 3/4 toxicities: Thrombocytopenia

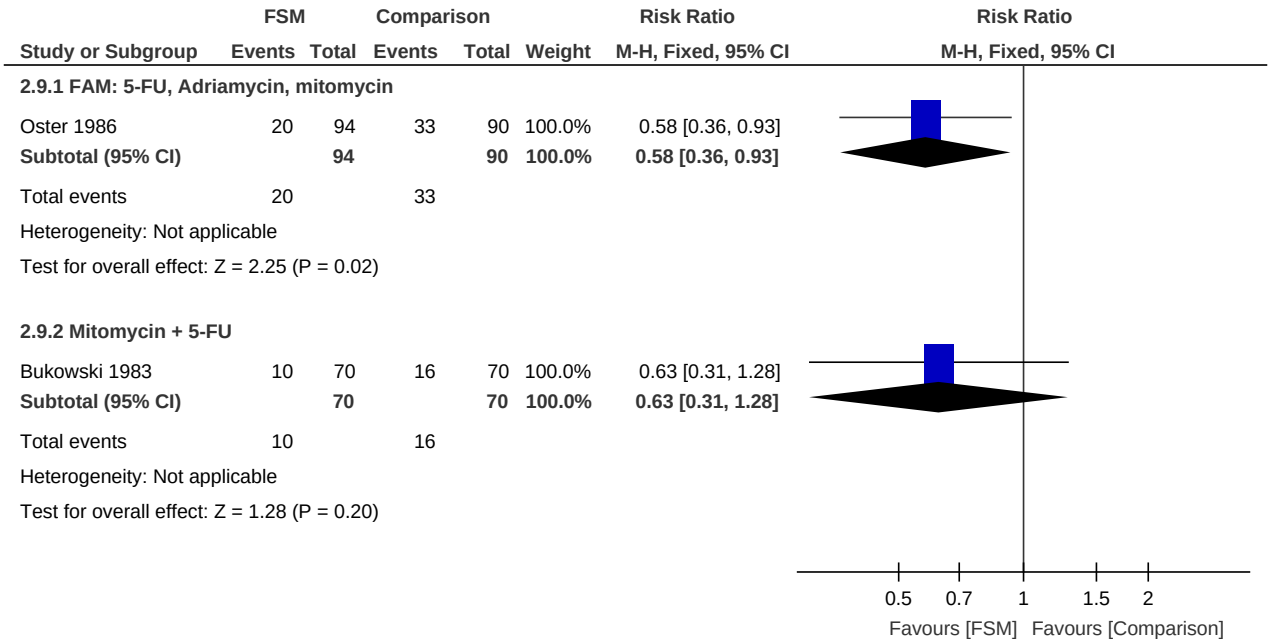
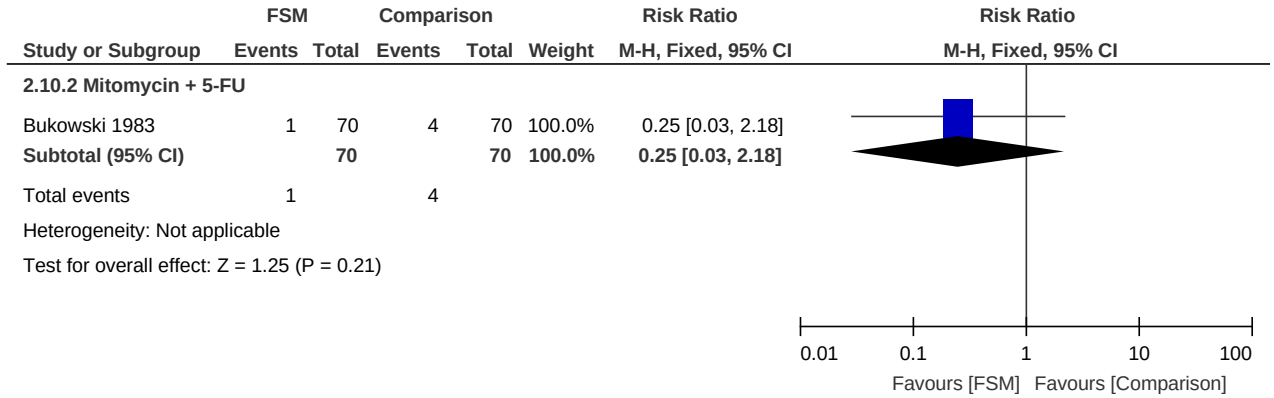


Figure 498: Drug-related deaths



H.17.7 Intra-arterial chemotherapy versus systemic chemotherapy in adults with locally advanced and metastatic pancreatic cancer

Figure 499: Overall response rate (CR + PR)

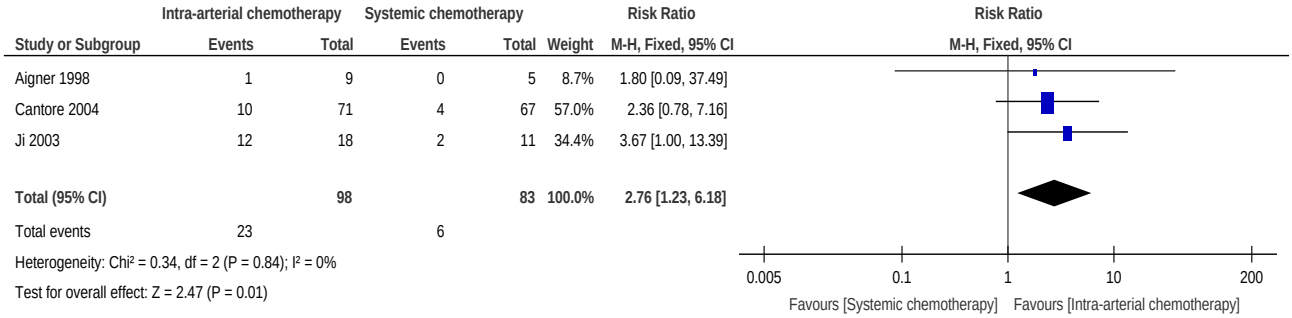


Figure 500: Overall survival

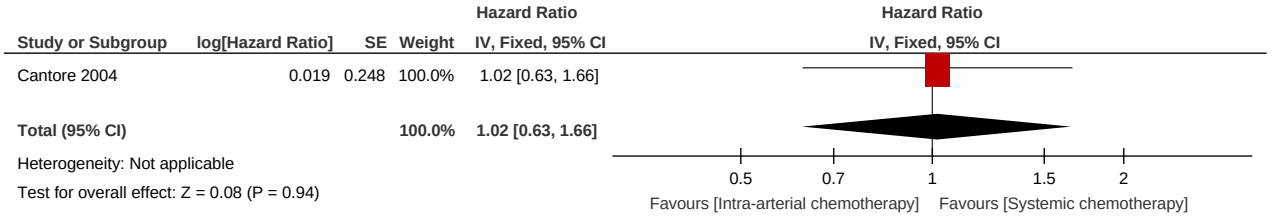
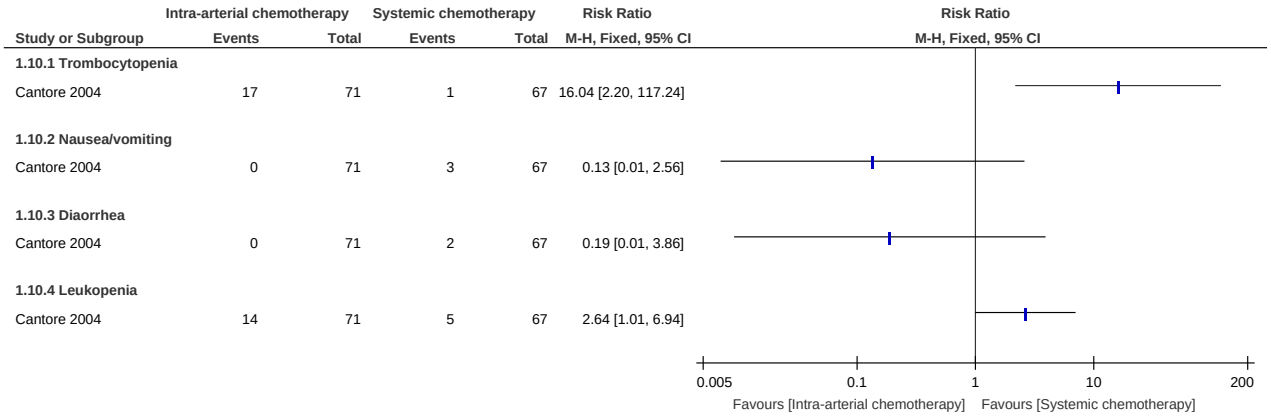
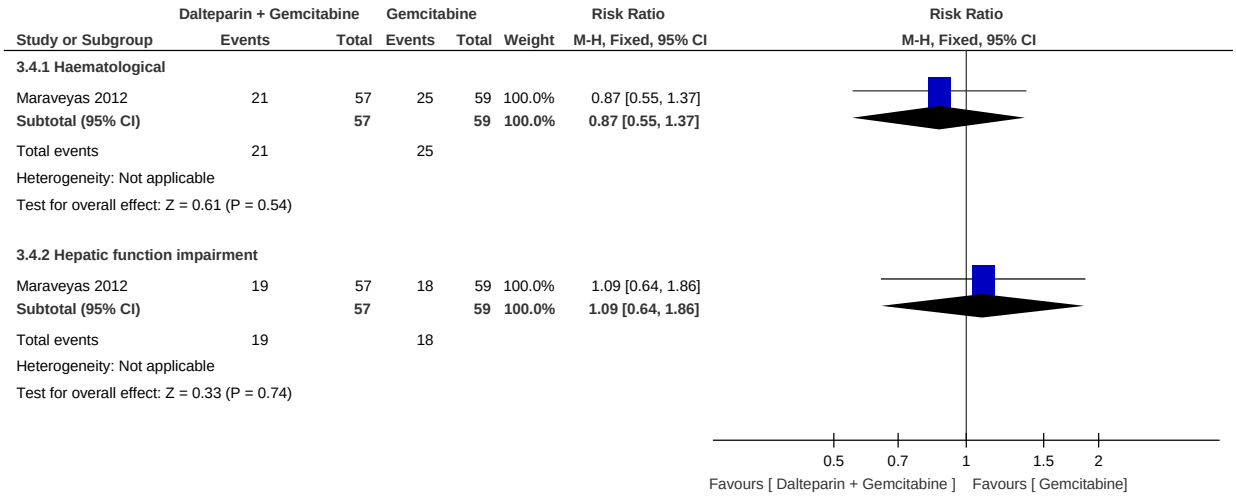


Figure 501: Grade 3/4 toxicities



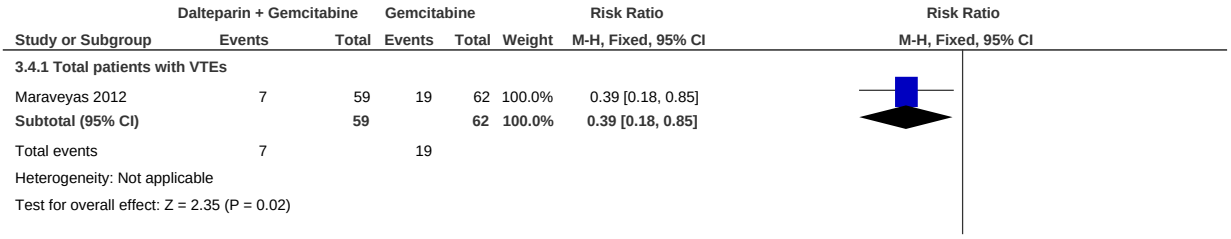
H.17.81 Chemotherapy versus chemotherapy and prophylactic anticoagulant

2 Figure 502: Adverse effects: Grade 3/4 toxicities



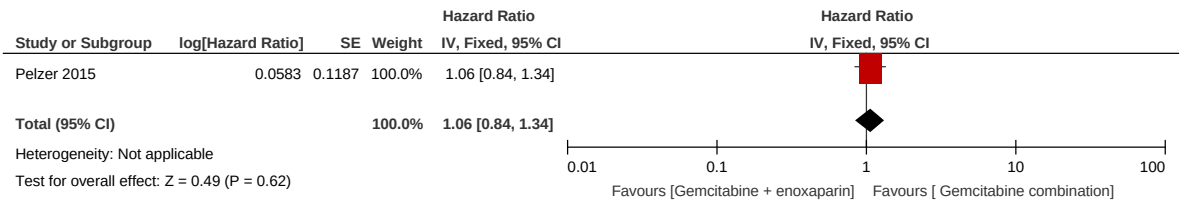
3

4 Figure 503: Adverse effects: vascular thromboembolism events (VTEs)



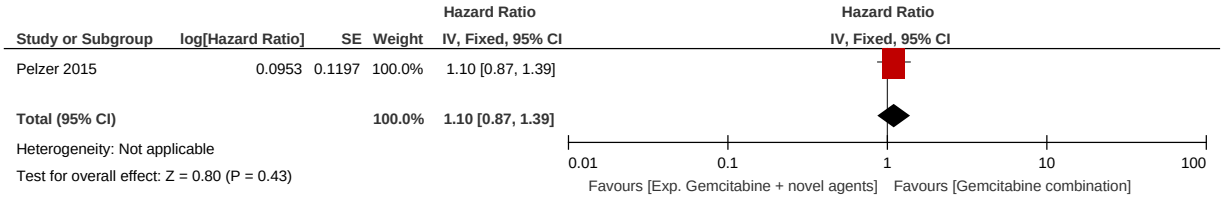
5

6 Figure 504: Combination gemcitabine vs gemcitabine + enoxaparin – Progression-free 7 survival



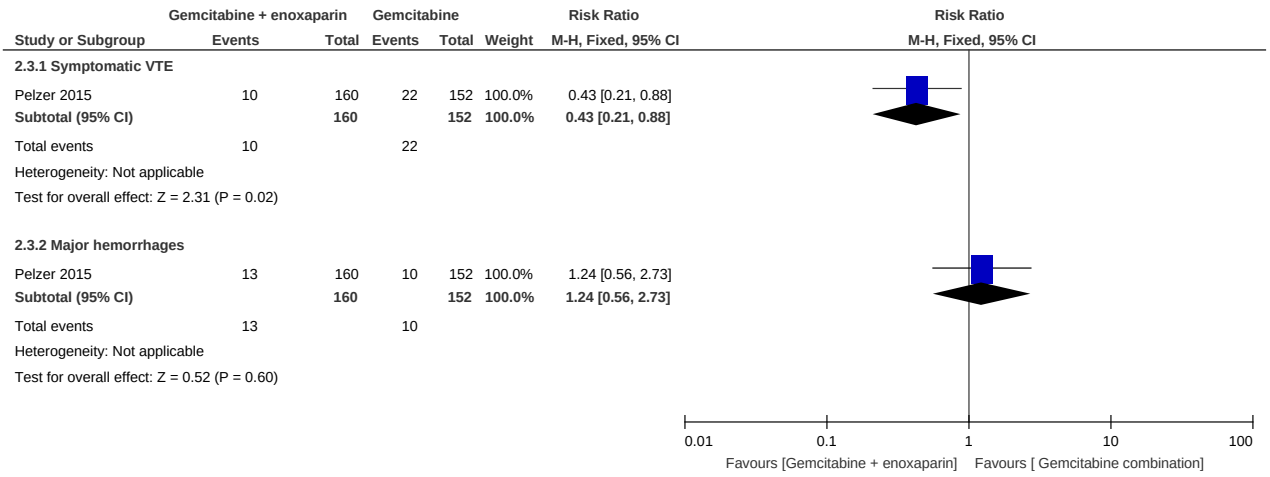
8

9 Figure 505: Combination gemcitabine vs gemcitabine + enoxaparin – Overall Survival



10

Figure 506: Combination gemcitabine vs gemcitabine + enoxaparin – Adverse effects: vascular thromboembolism (VTE)



H.17.94 Second-line chemotherapy versus best supportive care

Figure 507: Progression-free survival

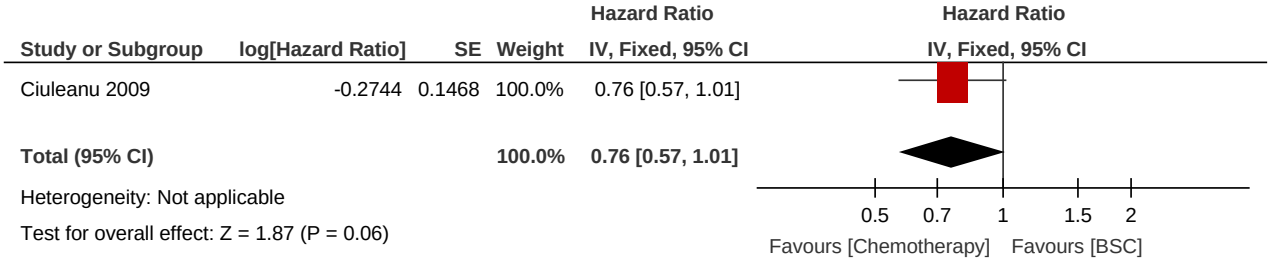


Figure 508: Overall survival

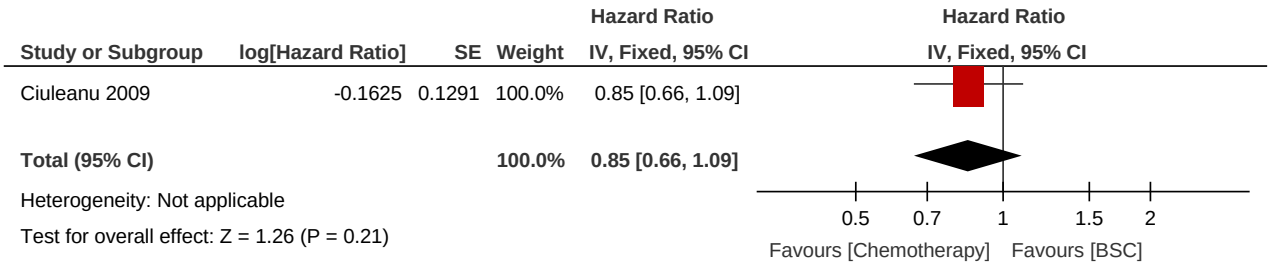
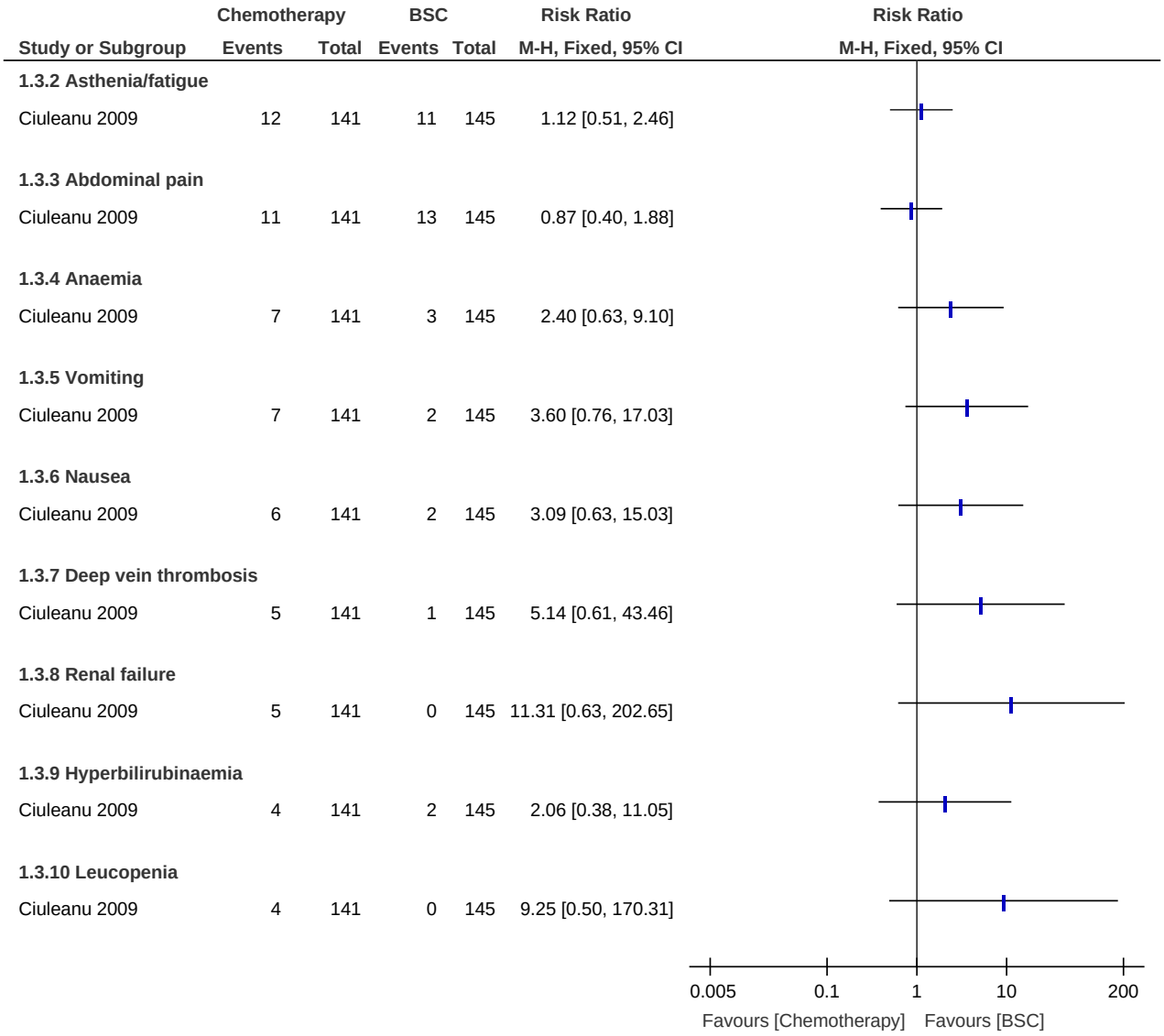


Figure 509: Grade 3/4/5 adverse effects



H.17.10 Second-line chemotherapy versus other chemotherapy

H.17.10.1 LV5FU2-CDDP then Gemcitabine *versus* Gemcitabine then LV5FU2-CDDP in adults with metastatic pancreatic cancer

Figure 510:– Overall response rate (CR + PR)

Figure 511: Progression Free Survival

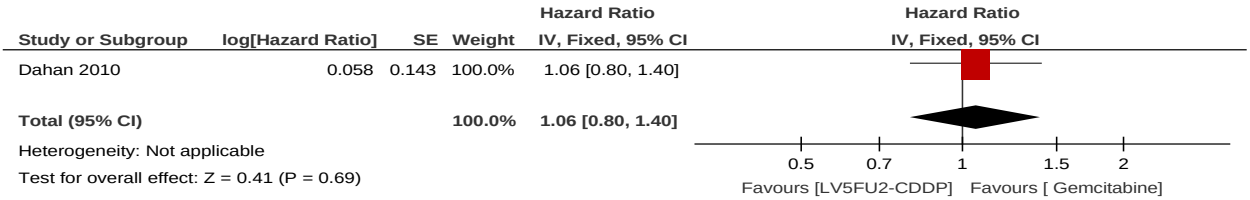


Figure 512: Overall Survival

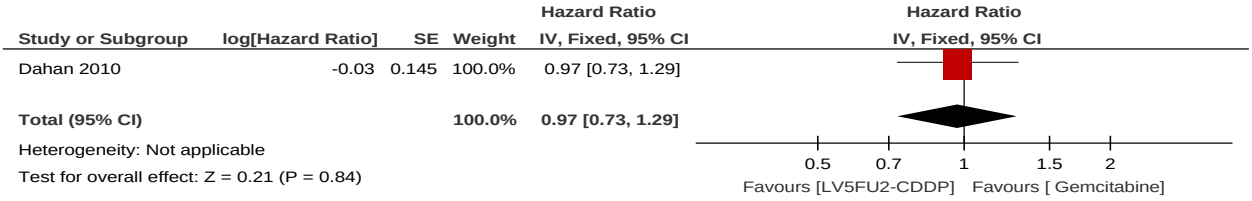


Figure 513: Grade 3/4 toxicities: Nausea/vomiting

H.17.10.2 Irinotecan + raltitrexed *versus* raltitrexed in adults with metastatic pancreatic cancer

Figure 514: Overall response rate (CR + PR)

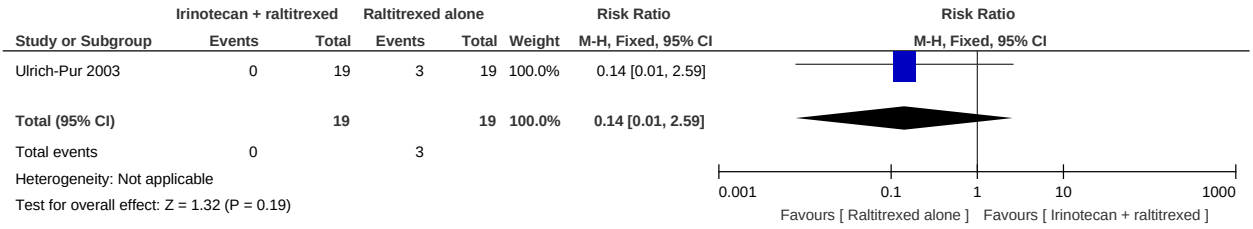
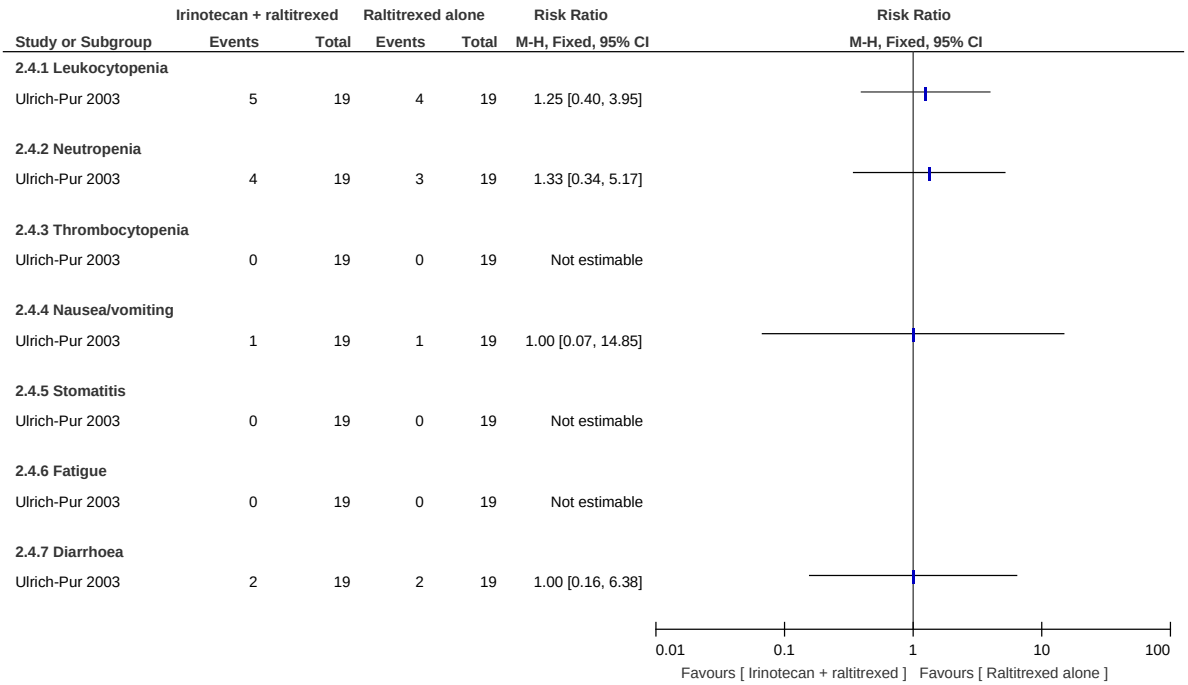


Figure 515: Grade 3/4 toxicities



H.17.10.3 5-FU and Oxaliplatin *versus* bolus 5-FU and bolus FA in adults with locally advanced or metastatic pancreatic cancer

Figure 516: Overall response rate (CR + PR)

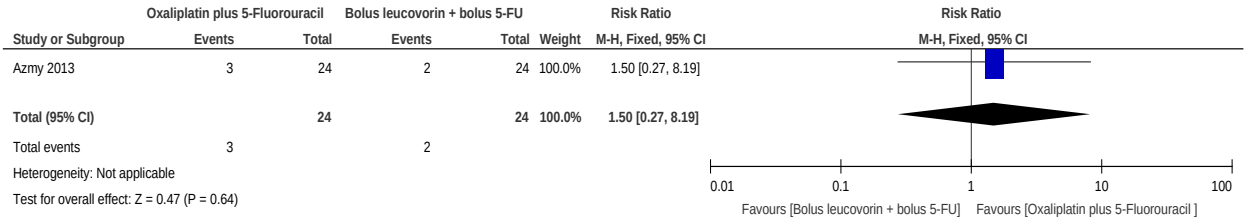
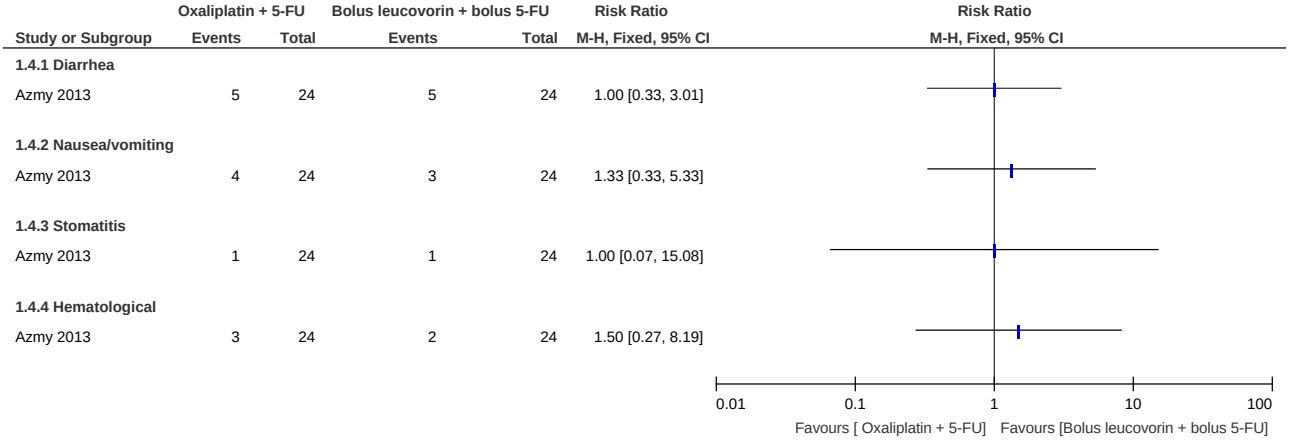


Figure 517: Grade 3/4 toxicities



H.17.10.4 Oxaliplatin + 5-FU *versus* FA + 5-FU in adults with locally advanced and metastatic pancreatic cancer

Figure 518: Progression-free survival

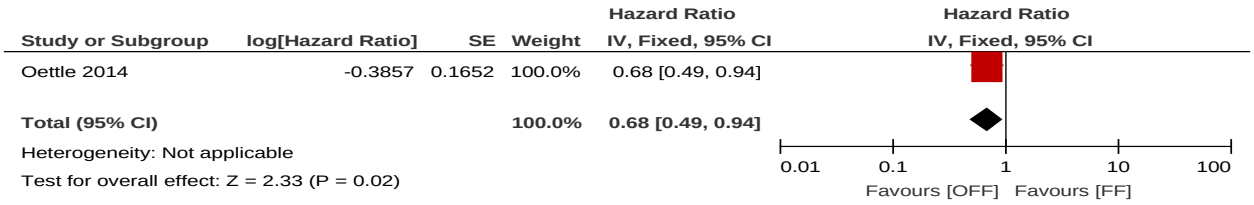


Figure 519: Overall Survival

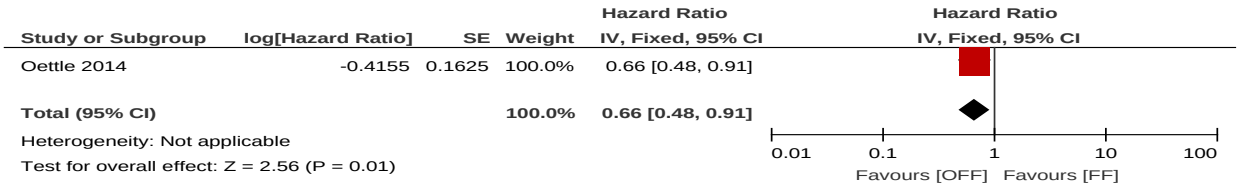
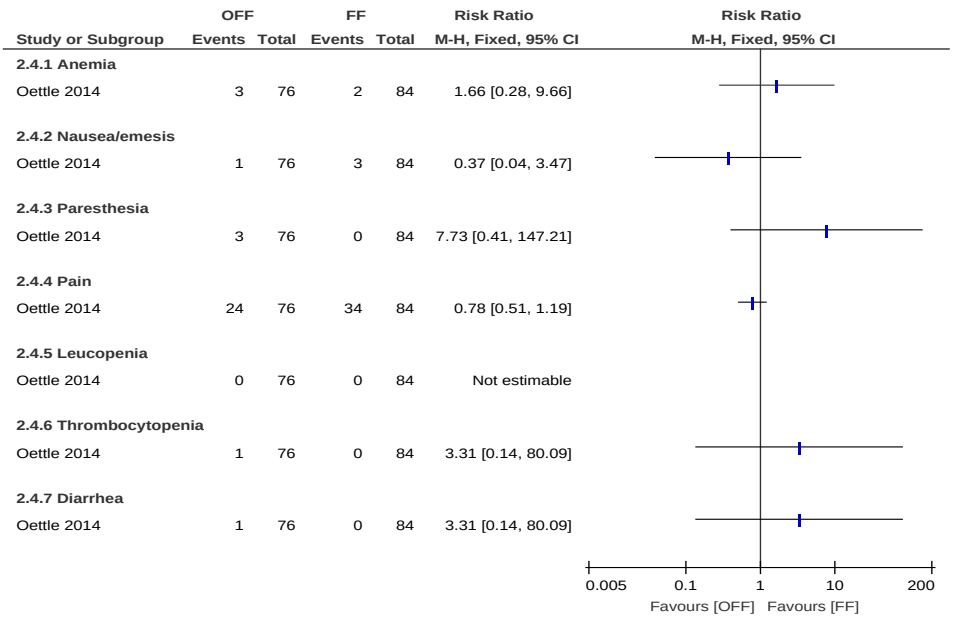


Figure 520: Grade 3/4 toxicities



H.17.10.5 Capecitabine + erlotinib then gemcitabine *versus* gemcitabine and erlotinib then capecitabine in adults with locally advanced or metastatic pancreatic cancer

Figure 521: Overall response rate (CR + PR)

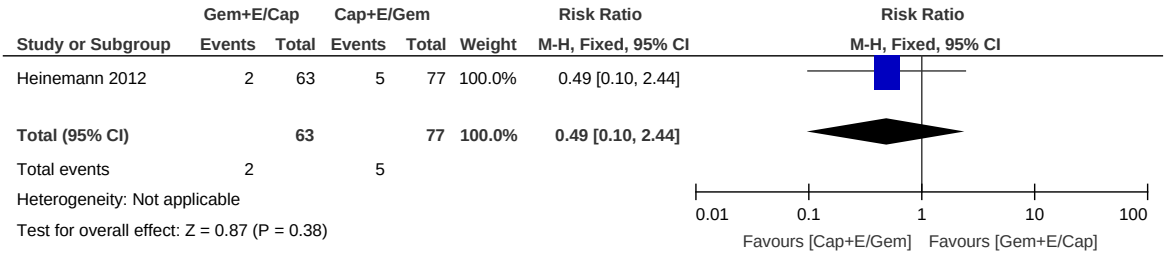


Figure 522: Overall survival

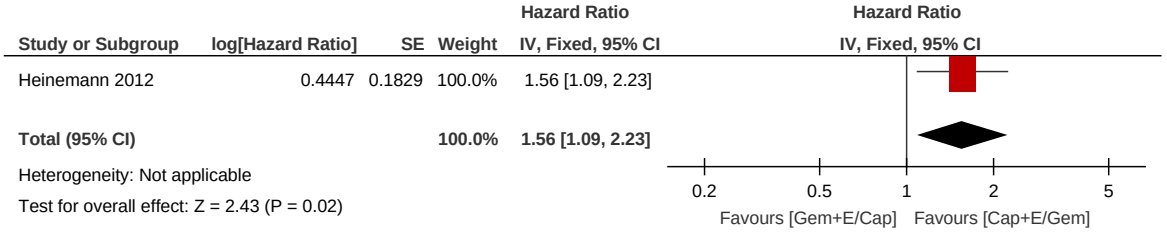
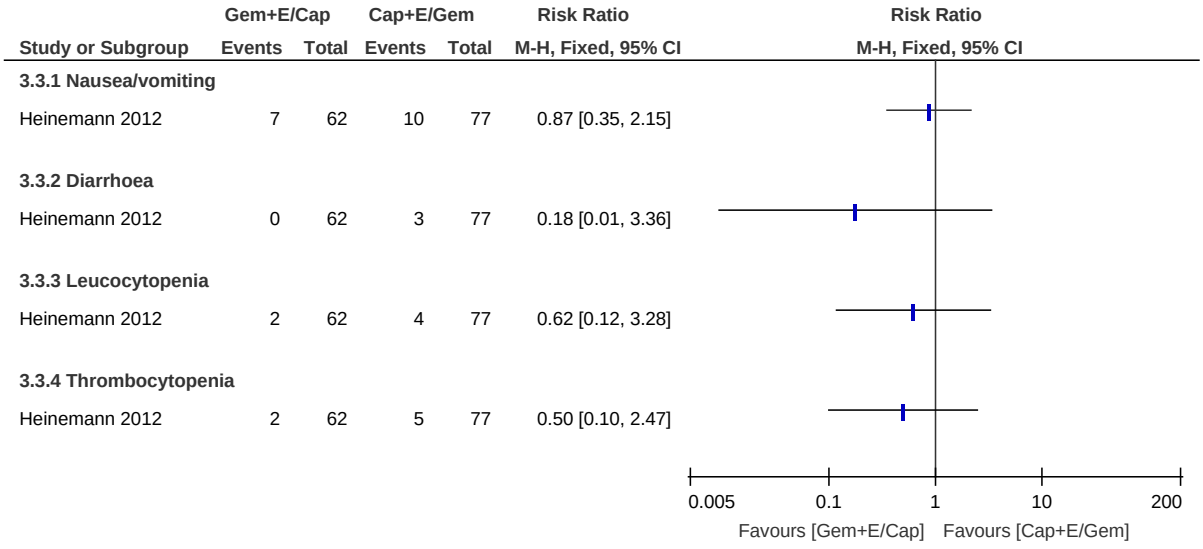


Figure 523: Grade 3/4 toxicities



H.17.10.6 Modified FOLFOX6 (infusion) vs infusional 5-FU and FA in adults with locally advanced or metastatic pancreatic cancer

Figure 524: Overall response rate (CR + PR)

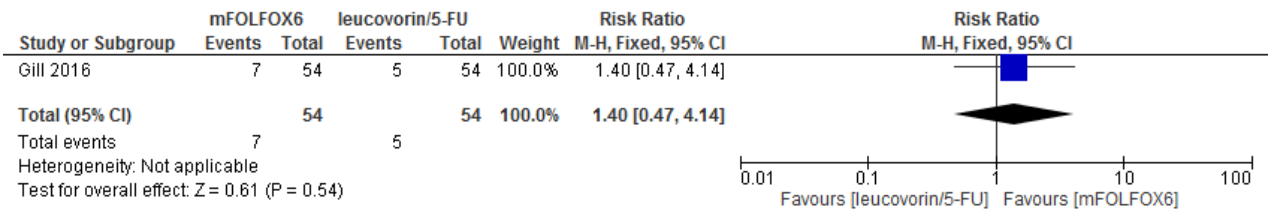


Figure 525: Progression-free survival

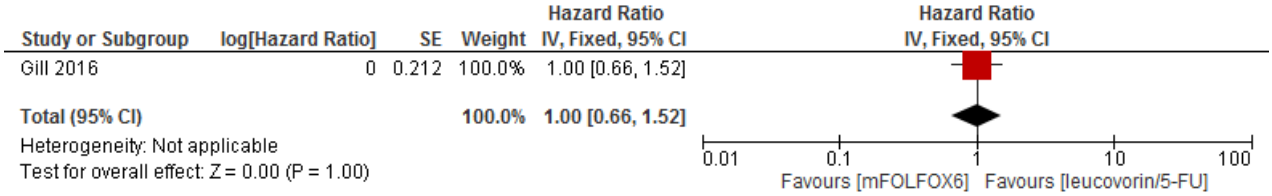


Figure 526: Overall survival

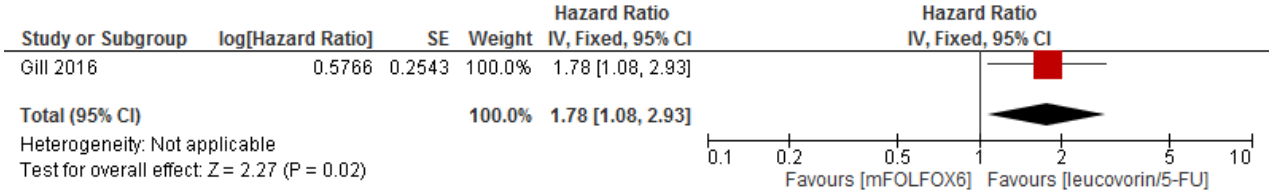


Figure 527: Grade 3/4 toxicities