Ref no.	Bibliographic citation	Study type	Ev lev	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding	General comments
4	Malignant mesothelioma in south east England: clinicopathological experience of 272 cases. Yates et al. Thorax 1997;52:507-512	Case study	+	272	mean age 65.2 years,	n/a	n/a					***General comments:*** one of the largest and earliest studies with robust exposure and histopathological data. Male preponderence. Right sided predominance 1.6:1. Incidence according to cell type 1/3 epithelioid, 1/3 sarcomatoid and 1/3 mixed. Epithelioid better survival than sarcomatoid. Occupations: shibuilding and repair, boiler, pipe and heating, carpenters, electricians, construction and demolition, insulation work and laggers. Possible non-occupational expsoures: relative of occupationally exposed worker, cut asbestos board for home refit, lived near an asbestos factory. No exposure: office and school, houswork and domestic cleaning, mail sorting and delivery, factory and craft work. Clinical features: chest pain and breathlessness. other symptoms: lassitude, weight loss, night sweats, pneumothorax and chest wall mass. Incidental finding with no symptoms (longer survival). Mean latency 40 years for pleural mesothelioma and 46 years for peritoneal. 38% presented with pleural effusion.
5	Case control study of pleural mesothelioma in workers with social security in	case control	-	119 cases, 353 controls	Mexico cohort							*General comments: greatest risk of MPM were for patients working in the manufacture of other non-metallic products such as occupations involving the manufacture of products with asbestos (water tanks, asbestos sheets, brakes and clutches) 15.6% construction workers and builders. In general 81% of people with MM had asbestos exposure recorded.*
7	Environmental exposure to asbestos and risk of pleural mesothelioma:review and meta-analysis. Bourdes et al. Eurpoean Journal of epidemiology 2000;16:411-417	meta-analysis	+	8 studies on pleural mesothelioma								*General comments: strong relationship between pleural mesothelioma and high environmental exposure to asbestos, whether the source of exposure is domestic or neighbourhood. Higher risk from expsoure to amphiboles than chrysotile. The exposure circumstances investigated in this study are high level expsoure, not common situations such as schools and general urban environment.*
9	A clinical, radiographic and laboratory evaluation of prognostic factors in 363 patients with MPM. Tanrikulu et al. Respiration 2010;80:480-487	case study	-	363	60% men, 40% women. Mean age 50.6.	Environemtal asbestos and Erionite exposure in Turkey						*General comments: not directly applicable to the UK population as mainly environmental exposure abestos/erionite. Retrosepctive review of patients between 1989 to 2010 only patients registered for follow up at their centre ?patient selection bias. Most frequent symptoms dyspnoea (82.1%), chest pain 68%, weight loss 58.9%*
10	Diffuse malignant mesothelioma of pleura. Diagnosis and survival in 92 cases. Adams et al. Cancer 1986;58:1551	retrospective case study	-	92	77% men and 23% women. Mean age for women 60, men 59. One unit in (mayo clinic) patients diagnosed between 1950 - 1980							*General comments: Asbestos exposure documented in 23%; commonest clinical features - 69% pain (mainly non-pleuritic, 59% breathlessness, 33% fever, sweats and chills, cough 27% weight loss 24%; clinical examination findings at presentation were 79% pleural effusion clinically, lymphadenopathy 14%, no abnormal clinical findings 11%, clubbing 6%. The stage at diagnosis was late - and hence difficult to draw conclusions if going for earlier diagnosis*

10	Diffuse malignant mesothelioma of pleura. Diagnosis and survival in 92 cases. Adams et al. Cancer journal 1986; 58 (7):1540-1551	Non-comparative (case series)	-	92	Patients with histologically confirmed MPM. 71/92 male, mean age of males 59 years (range 28-77). Documented asbestos exposure in 24/92	Chest radiograph	Nil - case series	Not specified	Radiographic features	42/92 patients had available chest radiographs. Features identified in patients with MPM - nodular pleural thickening (18/42); irregular thickening of the fissure (12/42); localized mass (6/42); loss of volume of hemithorax (6/42). Nonspecific features - blunted costophrenic angle (25/42);	Not stated	*General comments: Old retrospective case series reviewing only chest radiographs. Based on available data - sensitivity for nodular pleural thickening 43%; irregular thickening of fissure 29%; localized mass 14%; loss of volume of hemithorax 14%. Authors comment features such as the presence of trapped lung or unilateral involvement of hemithorax more likely to be as a result of MPM rather than metastatic lung carcinoma but have performed no direct comparisons in this study.*
13	Role of CT in assessing pleural malignancy prior to thoracoscopy. Hallifax et al. Thorax 2015;70:192-3	Non-comparative (case series)	-	370	Retrospective review of 370 patients undergoing LA thoracoscopy for suspected pleural malignancy. Mean age 72.3 (SD 12.9) years. 202/370 had malignant pleural disease - 110/202 MPM, 92/202 metastatic pleural disease, 167/370 benign pleural disease	CT	Nil	2 years for patients with chronic inflammation and fibrosis on biopsy (n=149) - 9/149 subsequently diagnosed with malignancy - 8/9 MPM. 1/9 metastatic lung adenocarcinoma	Histological diagnosis	For pleural malignancy - sensitivity 68.2%, specificity 78%, PPV 80.4%, NPV 64.9%	Not stated	*A well conducted study. Prospective. Appropriate number of patients for a screening study but no cancer patients in the control group. Length of follow up could be longer - probably not long enough to capture MPM. Cut off slightly higher than what is used clinically*

14	Salonen CT of Pleural lesions with special reference to the mediaatinal pleura. Acta Radiologica Diagnosis 1986;27:527-531	case series DIAGNOSIS	+	84	34 PM, 16 mets with extrapleural malignancy, 34 benign - all biopsy proven		CXR VS CT					*General comments: CT superior to CXR demonstratibf chest wall,, mediastinal and diaphragmatic infiltration significantly better. CXR very poor for detection of cases where mediastinal pleural involvement only (27 false negatives vs 2 for CT). However, old technology and bias introduced in favour of CT by delay times between CXR and CT*
15	Seely MPM: CT and correlation with histology EJT 2009;70:485-491	Case series DIAGNOSIS	"+"	92	MPM - 72 epi; 15 sarcomatous; 5 mixed							*General comments: Loss of volume statististically more common in non-epitheliod than epitheioid. No other variables allowed distinction of histological subtypes. Malignant features (brackets show prevalence in published literature): Pleural thickening 100% (50-90%), meidastinal pleural thickening 95% (66-93%; pleural effusions 87% (72-100%); Interlobar fissure nodularity 72% (29-86%); >1cm 53% (55-59)*
16	Computed tomography findings in 66 patients with malignant pleural mesothelioma due to environmental exposure to asbestos. Okten F, Koksal D, Onal M, Ozcan A, Simsek C, Erturk H. Clinical imaging 30 (2006) 177-180	Case series	-	66	all confirmed MPM patients, Male 68%, Avg age 56.8, all environmental exposure of asbestos	CT	pleural Bx (Ct guided/closed/ LAT/VATS)	not documented	Laterality, effusion, pleural thickening, interlobar fissure involvement, medostinal pleural thickening, diaphragmatic pleural involvement, lung parenchyma involvement	pleural effusion 80% of the cases. Thickening 77.2%interl obar fissure involvement 28.8% of the cases	not declared	*General comments: retrospective review of confirmed MPM and their CT features. Unable to draw any conclusions as no controls from same expsoure. Commonest CT features reported here are 1. pleural effusion, pleural thickening, volume contraction, involvement of mediastinal pleura and interlobar fissure. staging not documented.*

17	Evaluation of pleural disease using MR and CT. With special reference to malignant pleural mesothelioma. Knuuttila et al. Acta radiologica 42 (2001) 502 - 507	Case series	-	34	29 men, 5 women. Median age 62 years. 27 malignant, 7 benign. 18 MPM	enhanced MR and CT	MR against CT with gold standard histology	Not documented for benigns	what features on CT and MR suggest malignancy. For tunour growth along interlobar fissures and fonal thickening MR better (non significant) N1 and N2 node detection both CT and MR not very accurate. For N3 nodes both equally good. MR is better for transdiaphragmatic tumour growth detection	no stats.	not declared	*General comments: small case series. No stats. No follow up mentioned for benign patients. Discusses best MR techniques for detection of different pleural pathologies.*
18	Computed tomography features in malignant pleural mesothelioma and other commonly seen pleural diseases. Metintas et al. Eurpoean Journal of Radiology 41 (2002) 1-9	Case series	+	215	no patient characteristics documented.	CT	no comparison. All malignant patients had biopsy.	12 months for asbestos related non-malignant disease	CT features differentiating malignant from benign: pleural rind, pleural nodularity, pleural thickening >1cm and mediastinal pleural involvement are all highly specific. When 1 or more of these features seen highly likely pleural malignancy.	Invasion of mediastinal structures, pericardium, chest wall, diaphragm and nodular involvement of fissure each can directly sugegst a malignant pleual disease	Not declared	

20	CT in differential diagnosis of diffuse pleural disease. Leung et	Retrospective Case series	-	74	53 male, 21 female. Mean age 63. All patients with diffuse	CT	No comparison. Most patients had	Not documented	CT features most suggestive of malignant	Overall sensitivity 72% specificity	Not declared	*General comments: Out of date paper. Mentions majority of mesothelioma is not related to asbestos exposure. Follow-up duration for non malignants not clearly documented.*
21	CT in differential diagnosis of benign and malignant pleural disease. Yilmaz et al. Monaldi Arch chest disease 2005; 63: 1, 17-22	Case series	-	146	95 male, 51 female. Avg age 50.5 years. 146 patients with pleural disease who had a CT before treatment	CT	histo/cytological confirmation	not documented	pleural nodularity, pleural rind, pleural thickening > 1cm, bilateral involvement, involvement of mediastinal and viscereal pleura, mediastinal/hilar enlargement etc	CT findings most sugegstive of MPM were pleural thickening> 1cm, pleural plaque, involvement of the interlobar fissure (p=0.05) for metastatic pleural disease mediastinal/hilar LN enlargement, parenchymal involvement were significant	not declared	***General Comments:*** Retrosepctive case series, therefore biased. Pleural rind formation and thickening > 1cm are highly sensitive for maligntn pleural disease. MPM from MPD can be differentiated by features like pleural plaques, thickening > 1cm, invokvement of interlobar fissures. MPD is more likely with parenchymal involvement and hilar/mediastinal lymphadenopathy

23	The role of FDG PET-CT in differential diagnosis of pleural pathologies. Elboga et al. Revista Espanola de medicina nuclear e imagen Molecular. 2012;31(4):187-91	Non-comparative (case series)	-	50	Retrospective review of 50 patients who had PET-CT for suspected pleural malignancy. Mean age 57 years (24-79). 37/50 MPM - 34/37 epithelioid, 3/37 biphasic. 13/50 benign (chronic inflammation, granulomatous inflammation, firbous tissue, myofibrosis tissue)	PET-CT	Nil	Not specified	Histological diagnosis	Pleural effusion/nodularity in 26/50, 13/50 calcified pleural plaque/thickening, 11/50 pleural effusion. Increased FDG uptake in pleura in 39/50 (34/39 MPM, 5/39 benign - 3 chronic granulomatous inflammation, 2 pleural plaque). No increased uptake (SUV <2.5) in 11/50 (3/11 MPM, 8/11 benign). No increased	Not stated	*General comments: No metatstic malignant pleural disease included in study. Technical factors - patients fasted for at least 4h prior to scanning, 296-555MBq FDG 60mins prior to scanning. Scan duration 25mins, delayed imaging at 120mins.*
24	Porcel et al. Accuracy of FDG-PET for differentiating benign from malignant effusions. Chest 2015;17(2):502-512	meta-analysisDIAGNOSIS	"++"	14 studies comprising 407 patients with malignant disease and 232 with benign conditions	156 malignant pleural mesotheliomas; use of index test was to discrimante between benignand malignant disease	PET-CT						*General comments: (1) visual/qualitative asessment pooled (11 studies) sens 91% and spec 67% (2) SUV based studies (7) pooled sens 82% and spec 74% (3) Pooled sensitivty significantly higher with visual than semiquantitative but this seems to be an effect of PET alone systems (4) when only hybrid techniques used there is no signficant diffenrece between sens and spec (5) 38.5% of TB effusions and 43% of parapneumonic effusions show avid uptake*

25	Metabolic imaging of malignant pleural mesothelioma with fluorodeoxyglucose positron emission tomography. Benard et al. Chest 1998; 114 (3) 713-722	Cross-sectional study	+	28	Consecutive patients with suspected MPM. 24/28 had malignant pleural disease. 22/28 histologically confirmed MPM.	PET-CT	Nil	Not specified	Histological diagnosis and disease stage	22/24 with malignant pleural disease had elevated uptake in pleura in comparison to mediastinum (20/22 MPM and 2/2 with adenoCA) and one false positive (bilateral inflammatory pleuritis). SUVmax >2.0 used as a cut off to distinguish between benign and malignant pleural diseas (sensitivity 91%, specificity	Not stated	*General comments: PET-CT results (increased uptake in comparison to mediastinum (subjective assessment) and SUVmax) compared to final diagnosis obtained at surgical biopsy/lymph node sampling. Subjective assessment - sensitivity 92%, specificity 75%, overall accuracy 89% for malignant pleural disease, SUVmax >2.0 - sensitivity 91%, specificity 100%, overall accuracy 92% for malignant pleural disease (SUVmax significantly higher in malignancy, no difference between histological subtypes). PET-CT findings did not differentiate the 2 patients with adenocarcinoma from MPM. 2 false negatives - one epithelioid, one biphasic MPM. Staging - sensitivity 83%, specificity 75% in the 10 patients who had surgical staging completed. Technical factors - PENN PET 240H; UGM Medical Systems, axial field view of 12.8cm, transaxial field of view of 51.2cm, spatial resolution of 5.5mm in all 3 planes. Patients fasted for at least 4h pre-scan. 4.25MBq/kg FDG then patients scanned in the supine position 60-90 mins later. Imaging bed moved 6.4cm axially between scans to provide a total of 5-7 overlapping frames. Postinjection transmission scans obtained using either a rotating ^{68}Ge (positron emitter) rod or a ^{137}Cs (single photon emitter) point source.*

26	Clinical implications of 18F-fluorodeoxyglucose positron emission tomography/computed tomography at delayed phase for diagnosis and prognosis of malignant pleural mesothelioma. Abe et al. Oncology reports 2012; 27 (2): 333-338	Non-comparative (case series)	-	90	Patients with a clinical diagnosis or suspected MPM. MPM patients - 27/31 male, mean age 67 (range 47-79), 20/31 asbestos exposed	18F-FDG-PET/CT	Nil - case series	NA	Histological diagnosis and survival	31/90 patients with suspected MPM had this confirmed pathologically (30 histologically, 1 cytologically). SUVmax >2.0 in delayed phase in 31/31 with MPM and in early phase 30/31. 7 false positives in both groups. Early phase -sensitivity 97%, specificity 88%. Late phase-sensitivity 100%,	Not stated	*General comments: Retrospective review of PET-CT scans performed at the PET centre. 31/90 diagnosed with MPM. 12/31 had PET/CT after diagnosis, 19/31 had PET/CT pre-diagnosis. Authors do not report on diagnosis in the 59 patients who did not have MPM or if PET/CT reporter was blinded to pathology results or not. Technique - ^{18} F-FDG PET/CT scans acquired with a Biograph Duo (Siemens), 3.7 Mbq/kg ^{18} F-FDG, 1cm diameter ROI to determine highest uptake area, SUV = decay corrected tissue activity/injected dose. Early phase = 60 mins and delayed phase = 120 min post injection. Patients fasted 6h before procedure.*
27	Ylidrim PETCT in asbestos related pathology 2009;4(12):1480-1484	case series DIAGNOSIS	+	31	asbestos related patholgies - MPM 17 (11 epithelioid, 3 biphaseic, 2 sarcomatoid, 1 undetermined), DPT 5; BAPE 9.	PET-CT	Histology or follow-up					*General comments: TB and metastatic pleural disease excluded. Sensitivity 88.2%, spec 92.9% and overall accuarcy 90.3%. SUV max in malignancy = 6.5+/-3.4, in benign 0.8+/-0.6. 2 malignant cases showed no uptake - 1 epithelioid and 1 sarcomatoid. High negative predictive value (100%) with an SUV threshold of 2.2 - howeverpredictive value of a test depends on prevalence of abnormality in patients being tested so careful follow-up adivsed if clinical suspicion is high.*
28	Treglia et al, Diagnostic Accuracy of FDG-PET and PET/CT, Academic Radiology 2014;21	Study type meta-analysis and systematic review DIAGNOSIS	Ev lev ++	Number of patients 16 studies in systematic review and 11 studies in meta-analysis	Patient characteristics patients with pleural thickening of uncertain cause (patients with known malignancy were excluded)	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding	*General comments: 1 - All 16 studies (PET and PET/CT) showed that the test was usedul and superior comparedw ith diagnostic accuracy of CT alone (2) statistically significant difference in SUV of benign vs malignant but overlap is noted (3)Role of dual time-point imaging is still controversial but malignant disease may have higher increase in SUV on delayed than benign - unclear whether this significantly alters differential (4)False -negatives arise from small malignant lesions or those with low proliferative index (e.g. some epithelioid meso may not be FDG avid); false-positives are maily inflammatory (5) Pooled sens (95%), spec (82%), accuracy (90%), positive predictive value (90%) and negative predictive (91%) values. (6) F-FDG-PET cannot distinguish between different histologies in cases of pleural malignancies (7) Likely to be helpful in cases where standard imaging cannot clearly establish whether a pleural lesion is malignant (8)Tissue always required for final diagnosis (9)Use may reduce need for interventional sampling given very high sensitivity (10) role to guide biopsy uncertain (11)SUV should not be used alone to differentiate benign from malignant (interstudy comparison not possible given variablilityin SUV resulting from technical factors between scanners)*

29	Malignant pleural disease: Diagnosis by using diffusion-weighted and dynamic contrast-enhanced MR imaging - Initial experience. Coolen et al. Radiology 2012;263(3):884-892	Cross-sectional study	++	31	Consecutive patients with suspected MPD between Nov 2009-May 2010. Mean age 60.4 years (13.8); 24/31 male. 14/31 had MPD, 12/14 had MPM. 10/12 epithelioid, 1 biphasic, 1 sarcomatoid	DWI-MRI and DCE-MRI	PET-CT	Not specified	Histological diagnosis	ADC at DWI-MRI in patients with MPD significantly lower than that in patients with BPD. ADC cut-off of 1.52 x $10^{-3}mm^2/s$ resulted in sensitivity 71.4%, specificity 100%, PPV 100%, NPV 81%, overall accuracy 87.1%. Misclassification in ADC range 1.52 - 2.00 x $10^{-3}mm^2/s$. DWI-MRI had superior specificity over PET-CT - 100%	Not stated	*General comments: PET-CT - 9/17 benign cases misclassified as malignant and 2/17 as indeterminate. All 4 cases of talc pleurodesis misclassified as malignant on PET-CT. Technical factors - PET/CT - integrated PET/CT scanner (Biograph, Siemens) - IV 370MBq of FDG 50 mins prior to imaging, images obtained in the transverse plane. DWI-MRI - 3T MRI (Philips) 16-channel coil, precontrast T2-weighted and DW sequences followed by DCE-MRI imaging acquisition during and after injection of 15mL (NB not weight based) of Dotarem contrast agent at 2ml/sec. T1-weighted sequences acquired post contrast. T2-weighted single-shot turbo spin-echo acquisitions had the following parameters- 25 transverse sections, FOV 375 x 302mm, section thickness 8mm, matrix 288 x 187 (voxels 1.3 x 1.6 x 8.0mm), TR 828msec, TE 70msec, intersection gap 1mm, sensitivity encoding with a parallel imaging factor of 2, spectral selection attenuated inversion recovery fat suppression with an inversion time of 180msec, imaging time 20.7 secs during breathhold. DWI - spin echo echo planar imaging sequence - 38 transverse sections, FOV 420 x 323mm, section thickness 5mm, matrix 104 x 80 (voxel 4 x 4 x 5mm), TR 6481msec, TE 60msec, intersection gap 0.7mm, echo planar imaging factor 43, sensitivity encoding parallel imaging factor of 2, short tau inversion recovery fat suppression with an inversion time of 260msec and 2 signals acquired for imaging time 12m19s during free breathing. Diffusion sensitization was performed with b values of 0, 50, 100, 500, 750 and 1000 sec/mm ^{2}. DCE-MRI - 3D T1-weighted fast field-echo sequence- 48 transverse sections, FOV 330x274mm, section thickness 4.4mm and matrix 236x106 (voxel - 1.4x2.6x4.4mm), TR 4.5msec, TE 2.3msec, sensitivity encoding parallel imaging factor 2 and one signal acquired - imaging time 9.7secs per volume during free breathing - sequence repeated 20 times - contrast administered after 4 acquisitions. Post-contrast T1-weighted images acquired in transverse, coronal and sagittal directions with a 3D T1-weighted fast field-echo sequence - 150 sections, FOV 375 x 357mm, section thickness 2mm, matrix 252 x 237 (voxel 1.5x1.5x2.0mm), TR 2.9msec, TE 1.39msec, sensitivity encoding parallel imaging factor of 2.5, one signal acquired for an imaging time of 19.6s during breathhold. No inter-observer or intra-observer variability reported. MRI performed 24 hours before biopsy.*

30	Magnetic resonance appearance of asbestos-related benign and malignant pleural diseases. Boraschi et al. Scandinavian jour of work, environment and health 1999; 25(1): 18-23.	Non-comparative (case series)	++	30	Consecutive patients with suspected MPM. 26/30 male, mean age 58years (SD 11.5). All were asbestos exposed. 11/30 MPM, 19 benign pleural plaques	MRI	Nil - case series	3 years	Histological/Clinical diagnosis after follow-up	SI of pleura on T1 and T2 weighted images compared to chest wall muscle and subjective assessment of morphological features. Inhomogeneous hyperintensity on proton-density T2-weighted images and contrast-enhanced T1-weighted images identified in MPM patients. Morphological features	Not stated	*General comments: 0.5T performed in 26/30 and 1.5T in 4/30 - in clinical practice probably MRI scans will be 1.5 - 3T scanners. Signal intensity and morphology findings compared with histological diagnosis in 11/11 malignant patients and 1/19 benign patients and clinical/radiological follow-up in 18/19 patients. Pleural plaques not typically "suspected MPM" in the absence of other features, e.g. pleural effusion or clinical features to suggest malignancy – eligibility criteria poorly described. Technical factors - 0.5T scanners - MR max plus and Contour, GE Medical systems; 1.5T - Signa, GE Medical systems; conventional spin-echo sequence, cardiac-gated T1 weighted images - TR 450-600ms, TE 20-30ms; cardiac-gated proton density and T2-weighted images - TR 1800-2200MS, TE- 40-120ms. Slice thickness 10mm, matrix 224x160, FOV 38-48cm, imaged in axial plane and "sometimes in an orthogonal plane". Contrast - 0.1mmol/kg Magnevist contrast. Timing of images post contrast administration not reported.*
31	Role of respiratory-triggered diffusion-weighted MRI in the assessment of pleural disease. Revelli et al. British Journal of Radiology 2016	Non-comparative (case series)	-	56	Retrospective review of 56 patients with suspected pleural malignancy. Mean age 69.4 (SD 8.3) years. 12/56 benign (8/12 chronic pleuritis, 4 atypical mesothelial hyperplasia), 44/56 MPM (31/44 epithelioid, 4/44 biphasic, 9/44 sarcomatoid)	DWI-MRI	Nil	Not specified	Histological diagnosis	Benign disease - mean ADC value 1.84 +/- 0.37 x $10^{-3,}$ Epithelioid MPM - 0.96 +/- 0.19 x 10^{-3}, Biphasic MPM - 0.76 +/- 0.33 x 10^{-3}, Sarcomatoid MPM - 0.67 +/- 0.2 x 10^{-3}	Not stated	*General comments: Retrospective review of 56 patients with suspected PM who underwent DWI-MRI 23.8 (SD 19.7) days prior to thoracoscopic biopsy. Average ADC value in benign pleural disease significantly higher than MPM and ADC value significantly higher in epithelioid MPM vs. sarcomatoid MPM. Optimal ADC value cut-off of 1.5 x 10-3 provided sensitivity 100%, specificity 91.67%, accuracy 98.21%, PPV 97.78%, NPV 100% for differentiating MPM from benign pleural disease. Other pleural malignancy not included. Technical factors- 1.5T MRI, respiratory triggered axial DWI*

32	Diffusion-weighted MRI of malignant pleural mesothelioma: preliminary assessment of apparent diffusion coefficient in histologic subtypes. Gill et al. AJR 2010;195(2):W125-30	Cross-sectional study	+	62	62 patients with suspected MPM. 57/62 MPM, 2/62 pleural plaques, 1/62 nonspecific chronic inflammation, 1/62 metastatic pleural tumour, 1/62 malignant lymphoma. 50/57 MPM patients had ADC calculated - 35/50 epithelioid, 10/50 biphasic, 5/50 sarcomatoid	DWI-MRI	Nil	Not specified	Histological diagnosis at EPP/pleurectomypleural biopsy/pleural cytology	ADC at DWI-MRI in patients with epithelioid MPM significantly higher than ADC of biphasic and sarcomatoid subtypes (1.31 (0.15), 1.01 (0.11), 0.99 (0.07) respectively). Differentiating epithelioid vs sarcomatoid subtypes using ADC threshold of 1.1 - sensitivity 60%, specificity 94%, accuracy	Not stated	*General comments: Technical factors - 3T (Siemens), initial coronal and transverse T2-HASTE scans (TR 1200, TE 101, section thickness 5mm, interslice gap 1.5mm, FOV 400 x 400, matrix 320 x 224, iPAT factor 2) and 3D T1-weighted VIBEs (TR 3.34, TE 1.26, section thickness 4mm, interslice gap 0mm, FOV 400x400, matrix 320 x 256, iPAT factor 2. Axial DW images acquired with fat suppression during free breathing - single short spin-echo EPI sequence (TR 4000, TE 84, section thickness 8mm, interslice gap 1.5mm, FOV 400x400, matrix 160 x 96, b values - 250, 500, 750s/mm ^{2} for 3 orthogonal diffusion directions) with autocalibrating partially parallel acquisition (GRAPPA) technique. ADC values calculated using - ADC= -ln(S1/S0)/Bi where S0 and S1 are echo signal amplitudes with diffusion gradient strength set to 0 and G, mT/m and bi is the attenuation factor (250-750 s/mm ^{2})*

33	Malignant Pleural Mesothelioma: Visual Assessment by Using Pleural Pointillism at Diffusion-weighted MR Imaging. Coolen et al. Radiology 2014;274(2):576-584.	Cross-sectional study	++	100	109 consecutive patients with suspected MPM, 9 excluded. 100 patients - mean age 61.4 years (range 18-87), 75/100 men. 67/100 had MPD - 57 MPM (46 epithelioid, 6 sarcomatoid, 3 biphasic, 2 desmoplastic pleural disease), 10 metastatic pleural malignancy	DWI-MRI and contrast-enhanced CT	Nil	Not specified	Histology	Pleural thickening >1mm - sensitivity 81%, specificity 73%, PPV 86%, NPV 65%, accuracy 78%. Circumferential pleural thickening resulting in shrinking lung - sensitivity 60%, specificity 79%, PPV 85%, NPV 84%, accuracy 88%. Pleural pointillism - sensitivity 92.5%, specificity 79%, PPV 90%, NPV 84%,	Not stated	*General comments: Well conducted study comparing the presence of mediastinal pleural thickening, shrinking lung due to circumferential pleural thickening at contrast-enhanced CT and pleural pointillism at DWI-MRI with histological diagnosis. Interobserver agreement 0.71, 0.48 and 0.53 for mediastinal pleural thickening, lung shrinkage and pleural pointillism respectively. Pleural pointillism describes the presence of multiple hyperintense spots at high b value DWI. Technical factors - CT - Somatom Sensation 64 or 16 or Volume Zoom (Siemens), IV 1.5ml/kg iobitridol at a rate of 2.5ml/sec, 120kVp, 120-250mAs (automatic dose modulation), pitch of 1.2mm, collimation 0.75-1.5mm from which 3mm thick axial and coronal images (in plane resolution 0.7x0.7mm) were reconstructed. MRI - 3T (Philips), 16channel coil, non-enhanced T2-weighted single shot turbo spin echo, TR 828msec, TE 70msec, FOV 302x375mm, matrix 187 x 288, fat suppression by means of spectral selection attenuated inversion recovery or SPAIR. DWI-MRI - spin echo echo planar imaging sequence, TR 6481, TE 60, 38 transverse sections, FOV 420x323mm, section thickness 5mm, matrix 104x80 (voxel 4x4x5mm), intersection gap 0.7mm, echo-planar imaging factor 43, sensitivity encoding parallel imaging factor 2, short tau inversion recovery fat suppression with an inversion time of 260msec, 2 signals acquired. Imaging time 12 minutes, 19 seconds during free breathing. Diffusion b values 0, 50, 100, 500, 750 and 1000 sec/mm ^{2}.*
34	Dynamic contrast-enhanced MRI of malignant pleural mesothelioma - a feasibility study of noninvasive assessment, therapeutic follow-up, and possible predictor of improved outcome. **Giesel et al**. Chest 2006; 129:1570-1576	Case series	-	19	17 male, 2 female. Mean age 62.5 years. Stage II and IV disease. Histologically confirmed cases of MPM	MRI	no comparison	n/d	kep, kel, Amp	non-responders had high kep values. Normal and tumour tissue differentiation significant when using Amp and kel. Other measures although maybe clinically significant not statistically significabnt		*General comments: Pilot study. Small numbers. Pharmacokinetic measures are not easily reproducible, not clear re:software used to calculate these measures.*

35	Utility of integrated PET-CT for selection of operable MPM. Wilcox et al. Clinical lung cancer. 2009; 10 (4): 244-248	case study		35	29 men, 6 women. Median age 63 years.	Pet-CT	CT and Surgeical staging	variable. EPP 14 months. Non-surgical candidates 4 month median follow up	Imig Staging	No stats in the paper. 37% patients upstaged on their TNM stage after PET-CT. But 29% of PET group were upstaged at surgery. Therefore PET-CT not v good for assessing loco-regional disease. BUT good for assessing nodal disease and mets.	not declared	*General comments: retrospective study. Highly biased. Overall results suggest PET-CT good to assess nodal disease and mets but not for T staging.*
36	Plathow CT vs PET vs PET/CT vs MR for staging	Diagnostic STAGING	"++"	54	Epithelioid mesothelioma		CT vs PETvsPET/CTvs MRI against gold standard of surgical histopathology and mediastinoscopy of node		comparative sensitivity, specficity and accuracy at staging grade 1-3 meso by IMIG staging	Small	Nil	*General comments: PET/CT outperformed CT, PET and MRI in staging of grade 1-3. Accuracy of CT in stage 2 and 3 0.77 and 0.75. Underestimated stage 3 because of lymph node categorisation. MRI better for identification of chest wall and mediastinal fat invasion so accuracy 0.8 and 0.9 for stage 2 and 3. but MRI limited to thorax so could not detect distal nodal mets and also understaged some with mediastinal fat invasion. PET/CT accuracy 1 for all stages.*
37	Stewart D et al. Pre-op CEMRI. Eur J CT surgery, 2003(24) 1019-1024	Case series STAGING	"-"	49 (out of starting 76) patients with EPP and full nodal staging; If CEMRI showed irresectable i.e. stage 4 then no op, so these patients did not have histology	non-sarcomatoid MPM, patients with inoperable disease on CT had been exclduded.	T1+-Gd, and T2 MRI	Histopathology from EPP and pleurectomy/decortication		IMIG staging; sensit and spec for T3 and below, T2 and below			***General comments:*** Case series with major flaws. Stage 2 vs stage 3 discrimination poor, only 2 stage 4 cases (both correctly staged) but too few to make a firm statement. This lack of T4 tumours makes statements on the ability to distinguish T3 and T4 very difficult to interpret. Authors acknowledge limitations of CEMRI for assessment of pericardial involvment.

39	Staging of MPM: comparison of CT and MRI. Heelan et al. AJR 1999; 172: 039-1047	Diagnostic accuracy. Propsective case series	++	65	54 male, 11 female. Mean age 62. All biopsy proven MPM	CT against MRI	thoracic surgery staging at time of surgery	not documented	Tumour stage as per TNM staging system was evaluated with using CT and MRI and compared against the gold standard - thoracic surgery. ROC curves for each stage and criteria within stages	Both CT and MRI are low in accuracy for staging. For certain TNM criteria such as invasion of diahpragm and invasion endothoracic fascia/single chest wall focus of involvement MRI better than CT	Not declared	*General comments: Good paper overall. One of the first papers to evaluate the TNM staging with current imaging modalities. Well conducted study. Main limitations are inability to include early disease and advanced disease as unable to confirm with gold standard, as patients are unlikely to have surgery if advanced disease. Patients rarely present at T1a stage therefore couldn't involve them.*
40	18-F FDG PET/CT in suspected recurrences of epithelial M{M in asbestos fibers exposed patients (comparison to standard diagnostic follow up). Niccoli-Asabellaet al Clinical imaging 37 (2013) 1098-1103	Diagnostic accuracy	+	57	37 men, 20 woemn. Average age 66 years. Patient with Epithelioid meso already treated with chemo or surgery with a suspicion of recurrence.	PET-CT	CT	12 months	SUV max but exact figure not clear	PET has a high sensitivity, specificity and NPV compared to CT, when identifying local recurrence, lymph nodes and metsastases. But none of the patients underwent surgery for definite confirmation therefore areas missed are unknown.	not declared	*General comments: only epithelioid patients. Modality of treatments were variable with chemotherapy, surgery and radiotherapy. No correlation to initil disease stage. Unable to biopsy all lesions therefore unclear of tru positives or not. Difficult to know false negatives without closer macroscopic/microscopic examination*

41	The clinical importance of MRI versus CT in MPM. Knuuttila et al. Lung cancer 22 (1998) 215-225	case series	-	14	13 male, 1 female. Mean age 58 years. All pateints definite biopsy proven MPM.	MRI against CT	Staged by LAT/Thoracotomy	not documented	staging criteria - invasion through the diaphragm, nodal assessment,	No stats at all. Sample too small	no declared	*General comments: poor study. Very small numbers. Not clear how patients were staged. In conclusion MRI is better at assessing invasion of/through diaphragm. Assessment of interlobar fissure involvementand destruction of bony structures. Both CT and MRI are bad at assessing nodal stage.*
42	MPM: Value of CT and MRI in predicting resectability. Patz et al AJR 159;961-966 November 1992	case series	-	41	30 male, 11 female. Only 24 went on to have surgery as others unresectable. Mean age 54 years. Biopsy proven MPM	CT and MRI	with EPP	not applicable	Is the imaging staging confirmed at surgery	Both MR and CT has a high sensitivity at chest wall, diahpragm and mediastinum for resctability but specificity low. Unable to compare the 2 imaging modalities against each other as numbers small.	not declared	*General comments: well structured study but highly biased (selective population) and small numbers. One of the earliest studies tocompare CT vs Mri for staging. Overall MRI is better to assess diaphragmatic invasion and chest wall infiltration. Both CT and MRI poor at assessing mediastinal disease. No mention of nodal stage*

43	Integrated computed tomography-positron emission tomography in patients with potentially resectable malignant pleural mesothelioma: Staging implications. Erasmus et al. Journal of Thoracic and cardiovascular surgery 2005;129(6)1364-70.	Non-comparative (case series)	+	29	33 patients with biopsy proven MPM under review for EPP/RT. 4 excluded (medical comorbidity). 29/33 scanned. Mean age 63yrs (range 44-77), 26/29 men	PET-CT	Nil	Not specified	Surgical staging - laparoscopy, at EPP	T staging - FDG uptake increased in all primary tumours, no significant diff between subtypes. T stage pathologically confirmed in 24/29 patients - PET-CT accurately staged in 15/24 (63%), overstaged in 2/24 (8%), understaged in 7/24 (29%). N staging - N stage pathologically confirmed in 17/24 -	Not stated	*General comments: T staging - sensitivity 67%, specificity 93%, PPV 86%, NPV 82%, accuracy 83%. N staging (N2 disease) - sensitivity 38%, specificity 78%, PPV 60%, NPV 58%, accuracy 59%. M staging poorly reported. Importantly, not all patients had their staging confirmed pathologically. Technical factors- integrated PET-CT scanner (Discovery ST-8; GE medical systems), images acquired during shallow breathing in 2D mode for 3 minutes per bef position, 60-90 minutes after IV administration of 555-740 MBq of FDG. Non-contrast enhanced CT images acquired in helical mode (speed, 13.5mm/rotation) during suspended mid-expiration at a 3.75mm slice thickness, 140kVp and 120mA.*
44	Imaging before and after multimodal treatment for malignant pleural mesothelioma. Fiore et al. Radiologica medica 2006;111(3):355-364.	Non-comparative (case series)	-	28	Retrospective review of 28 patients with MPM	CT, PET, PET-CT, MRI	Nil	15-18 months	Nil		Not stated	*General comments: Retrospective case series of 28 patients with MPM who had been treated with either RT, chemoRT or chemoRT and surgery. Methods very poorly described. CT features described non-specific to MPM. Staging descriptors - one hemithorax involved 75%, both hemithoraces 20%, mediastinal LN involvement 20%, chest wall invasion 5%, subdiaphragmatic involvement 20%. No descroption of histological confirmation of staging.*

45	Positron emission tomography defines metastatic disease but not locoregional disease in patients with malignant pleural mesothelioma. Flores et al. Journal of thoracic and cardiovascular surgery 2003;126(1):11-15	Non-comparative (Case series)	+	63	63 patients with biopsy proven MPM, 60/63 pre-op, 3/63 during follow up post EPP or P/D. 52/63 men, median age 66years (range 35-82), 44 epithelioid, 16 biphasic, 3 sarcomatoid	PET-CT	Nil	Not specified	Pathological stage post surgery	No differences in SUV values between histological subtypes. T staging - accurate for T0-T3 in 29/32 and for T4 in 4/21 patients - sensitivity for identifying T4 disease 19%, specificity 91%, PPV 57%, NPV 63%. SUV value did not accurately predict T status (AUC 53%). N staging - accurate for N0/N1 in 19/22 and	Not stated	*General comments: Retrospective review of PET-CT scans performed in patients with biopsy performed MPM preior to surgery or during follow up post op. Population studied currently would only really be found in clinical trial (e.g. MARS2) rather than current practice. Technical factors- patients fasted for 6 hours, 10mCi of FDG "at least", emission scans performed a "minimum" of 45 minutes post FDG injection.*

46	Use of Computed Tomography and Positron Emission Tomography/Computed Tomography for Staging of Local Extent in Patients With Malignant Pleural Mesothelioma. Frauenfelder et al. J computer assist Tomography. 2015;39:160-165.	Cross-sectional study	+	62	Retrospective review of 62 patients with MPM who had induction chemo then EPP. Median age 61years (range 38-72), 53/62 male. Epithelioid 39/62, sarcomatoid 1/62, biphasic 22/62	CT, PET-CT	Nil	Not specified	Pathological stage post EPP	Images interpreted by 3 blinded independent observers. CT for T4 disease - sensitivity 40%, specificity 95%, PPV 66%, NPV 87%, accuracy 84%. CT for N2/N3 disease - sensitivity 70%, specificity 97%, PPV 85%, NPV 88%, accuracy 87%. CT IMIG IV classification - sensitivity 50%, specificity 89%, PPV	Not stated	*General comments: Population described would currently only be typically found in clinical trial (e.g. MARS2) rather than routine clinical practice. Retrospective review therefore only 26/62 received PET-CT which may bias the direct comparative outcomes of CT vs PET-CT. CT performed median of 16 days (0-28) prior to EPP, PET-CT performed median 17 days (1-41) prior to EPP - upper range is probably too high a gap (in clinical practice would be max 28 days between scanning and surgery if using the scan to exclude metastatic/inoperable disease). Technical factors- CT - venous phase CT 100seconds post IV contrast on either a 64-section or 256-section scanner (Siemens). Images reconstructed using a sharp-edged tissue convolutin kernel (B60f) and a medium-smooth soft tissue convolution kernel (B30f) at a slice thickness of 2mm and increment of 1.7mm. PET-CT - low dose CT - 140kV, 40mAs, 0.5s/tube rotation, slice thickness 4.25mm. PET performed with either 180s or 120s emission time per cradle position with 7-slice overlap (matrix 128 x 128), total PET acquisition time 14-21mins. "No contrast media was given during the PET/CT procedure" - no mention of dose/rate of FDG and fasting conditions of patient.*

47	Prognostic value of 18F-FDG standard uptake value by integrated PET/CT in the staging of malignant pleural mesothelioma. Genestreti et al. Techonology in cancer research and treatment. 2012;11(2):163-167	Non-comparative (Case series)	-	27	Retrospective case series of 27 patients with histologically confirmed PET-CT. 21/27 male, epithelioid 23/27, biphasic 4/27. Talc pleurodesis in 13/27	PET-CT	Nil	Not specified	Nil	No correlation with SUVmean or max values with histological subtype. SUVmax values lower in Brigham stage 1/2 disease in comparison to stage 3/4 disease (3.8 (range 2.3-7.6) vs 6.22 (range 3.99-14.74), p=0.018).	Not stated	*General comments: Small retrospective case series, staging does not appear to have been confirmed pathologically - all patients had biopsy confirmed MPM from needle biopsy, thoracoscopy or pleuroscopy. Brigham rather than IMIG staging used. Technical factors - patients fasted 6h before scanning, 5.18MBq FDG/kg, scanning 50-60 mins post FDG administration. Non-enhanced scan during shallow breathing - 80mA, 120kV. PET - 3 min per bed position, 3D acquisition*
48	Diagnostic accuracy of sequential co-registered PET+MR in comparison to PET/CT in local thoracic staging of malignant pleural mesothelioma. Martini et al. Lung Cancer 2016;94	case series. Prospective	-	34 but only 26 with histopatholgical data	median age 66 (40-74) 2 female, 33 males	PET+MR	PET/CT vs histopatholgy	not documented	PET/MR correctly differentiating between T and N stages. Read by 2 independent readers	T stage more likely to be rated higher at low T stages (1-2) by MR compared to PET/CT and vuce versa. N staging was more likely to be rated lower by PET+MR compared to pet/ct.		*Does not add more information to the current evidence base. MR is better at delineating soft tissue invasion with or without PET. Radiologists felt more confident reading PET+MR than PET/CT but this may be due to the same reason as before, re:soft tissue invasion. This srudy shows PET+MR is comparable to PET/CT but in clinicalm practice routine use of MR maybe more diffiult.*

49	Positron Emission Tomography/Computed Tomography for the Pleural Staging of Malignant Pleural Mesothelioma: How Accurate Is It? Pinelli V et al. Respiration 2015;89:558-64	Non-comparative (case series)	-	32	Retrospective review of 32 patients with histologically confirmed MPM - 29/32 epithelioid, 2/32 biphasic, 1/32 sarcomatoid. IMIG Stage I in 3/32, II in 6/32, III in 15/32, IV in 8/32	PET-CT	Thoracoscopic staging	Not specified		Median SUVmax 6.1 - patients with SUVmax <6.1 - median survival 34.07months vs. SUVmax >=6.1 - median survival 12.50 months. Visceral pleural involvement on thoracoscopy -median SUVmax 9.60 +/- 4.07 versus no visceral pleural involvement on thoracoscopy SUVmax 5.20 +/- 3.35 (p	Not stated	*General comment: Patients with pleurodesis excluded. Technical factors- Discovery ST tomograph (CT multislice, 80mA, 140kV), IV 5.5MBq/kg of 18F-FDG, fasted for 6hours. SUVmax measured from a ROI drawn on the hottest voxel of the tumour burden seen on the attenuation-corrected transaxial slice. Very small study, does not add much to the existing literature on PET. Higher the SUV more aggressive the tumour is. 6.1 cut off is somewhat in the middle of previously reported cut offs, but appears to work for this group of patients. Non-epithelioid group is very small.*
50	Zahid et el,What is the best way to diagnose and stage MPM? . ICVTS 12(2011)-254-259	Systematic review DIAGNOSIS AND STAGING	++	14 Studies	Hypothetical clinical situation: Best diagnostic modality in a patient with pleural thickening		FDG-PET vs CT vs MRI vs blind biopsy vs CT biopsy vs Thoracoscopic biopsy			14 papers (selected from 61 - search dates 1950-2010)	Nil	*General comments: PET-CT is superior to MRI and CT in terms of specificity and sensitivity of disease detection and staging of malignant mesothelioma. Surgical pleural biopsy provides the most accurate definitive diagnosis*
51	Sharif et al. Does PET offer prognostic information in MPM? ICVTS 2011;12:806-811	Meta-analysis	"++"									*General comments: Data in relation to staging is essentiallythe same as for the paper by Zahid - same group of authors. This does not add further.*

51	Does positron emission tomography offer prognostic information in malignant pleural mesothelioma? Sharif S et al 2011. Int CV and TS;12:806-11	Literature review	"-"								Excluded - PET and imaging overlap	
61	Fibulin-3 levels in MPM are associated with prognosis but not diagnosis. Kirschner et al. Brit J of Cancer (2015) 113, 963-969	retrospective cse series. 2 cohorts	+	plasma: total MPM 84, non-MPM 56. Pleural fluid MPM 30, non-MPM 60	well matched between the groups including between the 2 cohorts. > 70% epithelioid. Control group group should have ideally been benign effusions rather than pre-CABG patients	FBLN-3 in plasma and pleural fluid	clinico pathological diagnosis of MPM	~ 28 months	sensitivity, specificity, accuracy	Different cut offs used for diagnosis. mean levels Sydney cohort 16.1, Vienna 11.51. Original levels used by Pass not replicated.		*Limitations: ROC curves showed an accuracy of 63.2 for sydney cohort and 56.2% for the Vienna cohort. At a cut off of 29 (used by Pass) sydney cohort sens 13.5%, spec 96.9% and for Vienna cohort 12.7% and 87.5% respectively. Low accuracy for pf FBLN-3 too. Low levels of FBLN-3 at diagnosis was significantly associated with a prolonged survival (at the cut offs used by Pass et al).*

76	Circulating Activin A is a novel prognostic biomarker in MPM - A multi-institutional study. Hoda M et al. European journal of cancer 63 (2016) 64-73	retrospective case series. Looking at prognostic value of Circulating activin A	_	4 cohorts. Total MPM 129, controls 45	mixed group of patients in the 4 cohorts. Some levels are at baseline and some during treatment. Only small number during treatment	plasma activin A levels in MPM patients	clinico radiolgical information	12 months median FUP	Correlation between plasma Activin A and MPM, stage of MPM, tumour bulk and correlation with treatment response	Plasma Activin A levels are elevated in those with MPM compared to controls, median 562 vs 361 ($p<0.0001$) but high in patients with pleuritis/fibrosis. Also high in njon-epithelioid grouyp but numbers small only 19 patients. L:evels correlate significantly if patinet aged < 66 and has epithelioid (Rx response correlation only with		*General comments: This is a good first study showing interesting data for plasma Activin A levels in MPM. However the study is small (129) and the control group is too small and not varied enough to draw any firm conclusions from. Interestingly the levels are significanhtly elevated in pleuritis/fibrosis group therefore the raised levels could be due to a more generalised pleural pathology rather than just MPM and likely to be a high in other cancers too. Propsective validation studies are needed before this can be adopted for routine use.*

77	SMRP in an asbestos exposed population. The dust diseases Board cohort study. Park et al. AJRCCM 178: pp832-837, 2008	Prospective cohort study	++	538	98.3% male mean age 66.9	SMRP levels in asbestos exposed individuals	healthy asbestos exposed/silicosis/asbestosis/DPT/Asbestosis+DPT/PP	1 year	SMRP level of 2.5 nM taken as cut off	only 15 +ve from the 538. 1 lung cancer. No MPM.significant difference in the mean SMRP levels between healthy exposed individuals and asbestos related disorders. Still the levels remained below the cut off 2.5		
78	Is SMRP an upfront predictive marker ofMPM? A prospective study on Italian workers exposed to asbestos. Filiberti et al. Oncology 2014;86:33-43	case series. Prospective	++	Total 1774 = healthy 1227, asbestos related benign disease 152, asbestosis alone 24, 182 other benign disease, 118 had other cancers	average age 62.2			median 47.1 months		median SMRP for all 0.45 at first visit. 59 had SMRP higher than 1.5 with no tumour some asbestos related others chronic renal failure.		*very heavy exposure 29 years on average. 3 cases of MPM epithelioid diagnosed during this period but all had low first visit SMRP. Patients with asbestos related pleuro parenchymal disease had an elevated SMRP compared to healthy individuals but still lower than the 1.5 cut off. levels were elevated with other cancers such as lung, pancreas, ovary and endometrium. limitations younger population. SMRP cannot be used as a screening tool of early MPM not reliable enough*
79	serum biomarkers in patients with mesothelioma and pleural plauqes and healthy subjects exposed to naturally occurring asbestos. Bayram et al. Lung (2014) 192:197-203	case series	+	MM = 24, PP = 277; Healthy exposed = 123, control - 120		osteopontin and SMRP levels in serum	none	n/d	sensitivity, specificity	mesothelin cut off 1.63, sen 58%, spec 83%. Osteopontin 17.27 cut off sens 75%, spec 86%		*Largest study investigating patients with environmental asbestos exposure rather than occupational. Both mesothelin and oseteopontin higher in patients with MM> the combination increases the sesitivity but reduced the specificity slightly. With multiple regression analysis both biomarkers are indepednantly associated with age and smoking pack-years*

80	Performance of biomarkers SMRP, CA125, and CYFRA 21-1 as potential tumor markers for malignant mesothelioma and lung cancer in a cohort of workers formerly exposed to asbestos. Gube et al, Arch of Toxicology, 85:185. 2011	Retrospective serum analysis of a prospectively collected survey of asbestos exposed patient cohort.	+	626 patients enrolled from 1993-97	Mean age 63 years, 92% male, healthy workers with asbestos exposure. As of 2007, a total of 20 mesothelioma cases observed and 12 lung cancers.	Serum concentrations SMRP, CA125, and CYFRA21-1 measured in archived serum samples (2005 and 2006). Samples taken annually in cohort. ? Which sample used - I assume the baseline, enrolment sample but not clear	To final diagnosis	10-12 years in the cohort follow up study.	Diagnostic sensitivity	Non-significant difference in SMRP level in those with LC, meso and normals. CYFRA increased in LC compared to meso and normals - p=0.0062. No temporal relationship between annual levels and diagnosis seen with any biomarker. SMPR sens 10%, spec 91.8%, Ca125 5% and 95.9%, CYFRA 25%	German Social Accident Insurance.	*General comments: Poor sensitivity and high specificity of these 3 markers for the development of MM in asbestos exposed indiviuals. Not likely to be of clinical utility.*

81	Serum Levels of Soluble Mesothelin-Related Peptides in Malignant and Nonmalignant Asbestos-Related Pleural Disease: Relation with Past Asbestos Exposure. Rodriguez Portal et al, Cancer Epid Biomarkers Prev 18:646. 2009	Case series	+	48 normal, 177 asbestos exposed with no pleural disease, 36 MPM, 101 asbestos with benign pleural disease		SMRP serum	Diagnosis	Variable	Diagnostic prediction / sensitivity	Higher SMRP level in MPM patients, no difference in asbestos exposed with and without pleural disease. SMRP higher in those exposed to asbestos than not. For diagnosis of MPM, AUC 0.75 (95% confidence interval 0.68-0.83). At 0.55 nmol/L sensitivity and specificity of 72% and 72%.	Not stated	*General comments: Moderate performance of SMRP - no cancer controls. Possible marker of asbestos exposure and MPM versus asbestos exposed and healthy.*

82	Symptoms and patient-reported well-being: do they predict survival in malignant pleural mesothelioma? A prognostic factor analysis of EORTC-NCIC 08983: randomized phase III study of cisplatin with or without raltitrexed in patients with malignant pleural mesothelioma. Bottomley A et al 2007. J Clinical oncology;25:5770-6	Retrospective case series	"+"	250 patients with histologically confirmed, unresectable MPM, PS<3, no prior chemotherapy, entered into an RCT of cisplatin +/- raltitrexed. Patients had to have adequate hepatic, renal and bone marrow function	RCT recruits.80% male, median age 58, WHO PS 0,1,2 in 25%,62% and 13% respectively. 229 had valid HRQOL assessment.	EORTC QLQ C30 and LC13 used. Scales used for analysis: global QOL, dyspnea, physical functioning,cognitive functioning, appetite loss,N&V, pain, cough, dysphagia. EORTC prognostic index (PI) also included:stage, time since diagnosis, histology, WCC. Also studied platelet count, Hb difference	Survival	Not quantified but "8 times after the completion of treatment"	Prognostic abiity of markers	229 patients had HRQOL measurement. No difference in baseline characteristics and survival between patients with and without valid baseline HRQOL. All scales and biomedical variables except cough prognostic on univariate analysis. On multivariate analysis with bootstrapping (5,000 generated	Supported in part by grants 5U10CA11488-30 through 5U10CA11488-34 from the national cancer institute. Astra Zeneca supplied the raltitrexed and an educational grant for data management and study conduct.The work was also supported in part by the EORTC charitable trust. Author COI: Consultant or advisory role, Christian Manegold, Eli Lilly, Mark Vincent, Astra Zeneca,	*General comments: Very well conducted study in an homogeneous group of patients. Results may not be generalisable to patients with PS>2.*

83	Prognostic factors in patients with pleural mesothelioma: the European Organization for Research and Treatment of Cancer experience. Curran D et al 1998. J Clin Oncology;16:145-52	Retrospective case series	"+"	204 patients with MPM entered into 5 consecutive chemo RCTs.	Eligible for chemo trial. Proven, likely or possible mesothlioma on biopsy. ECOG PS <=2,age <=75, WCC >=3.5, PLT >= 100, biirubin <= 25,. 204 patients, 181 male (89%)	Studied variables age, gender, ECOG PS, time interval since diagnosis, WCC, PLT count, Hb, stage (Butchart), prior treatment, ALP and LDH serum, histologic subtype, certainty of diagnosis. Hb level expressed as difference from 16 g/dL in males and 14 g/dL in females. ALP and LDH considered normal if < 1.25x ULN. Continuous variables categorised into two groups with median as cut point.	OS	No specified but 181 patients died during F/U	Prognostic abiity of markers, derivation of a prognostic score	Univariate: ECOG PS 1-2 vs 0 (RR 1.7, 95% CI 1.2-2.4, p= 0.001); WCC >= 8.3 (RR .9, 95% CI 1.4-2.7, p<0.001); Hb difference >= 1 g/dL (RR.6, 95% CI 1.1-2.2, p=0.006); Probable/possible diagnosis vs definite (RR 1.8 95% CI.3-2.6, p=0.001); Sarcomatoid vs epithelioid or mixed histology (RR 2.7, 95% CI 1.4-5.0, p=0.002) all signficantly	Supported by the Parthenon Trust, UK. No CoI declaration	*General comments:Well-conducted study with good data completeness and relatively homogeneous patient group. Unfortunately none of the chemotherapy regimens was effective so it is possible that some were more harmful than others. Score has subsequently been validated in other patient groups. No patients in this study had PS>2, so not applicable to patients with poorer PS.*

84	Statistical validation of the EORTC prognostic model for malignant pleural mesothelioma based on three consecutive phase II trials. Fennell D et al 2005. J Clin Oncology;23:184-9	Retrospective case series	"+"	145 patients with MPM taking part in phase 2 trials of chemotherapy at a single centre.	M:F 125:20. Median age 60. Taken from trials of vinorelbine/Oxaliplatin (VO, n=26), irinotecan/cisplatin/mitomycin (IPM, n=49), and vinorelbine alone (VIN, n=70). Histologically proven MPM in 142 patients. All patients had PS = 0-2, stage 1-2 = 25%, stage 3-4 = 75%. Epithelioid n=92, sarcomatoid n=17, mixed n=33). 134 patients had an assessable EPS.	EORTC prognostic score (EPS) calculated for all patients (a conditional sum of 5 constants, each included in the score if and only if the condition relating to that constant is met). EPS= 0.55(if WBC > 8.3 x 10e9/L) + 0.6 (if PS = 1 or 2) +0.52 (if histology=probable meso) + 0.67 (if histology = sarcomatoid) + 0.6 (if male). EPS > 1.27 implies high-risk subgroup, EPS < 1.27 low-risk.	Overall survival	Not stated but only 1 patient was still alive at analysis	Prognostic ability of EPS	There was a survival from diagnosis difference between the low-risk and high-risk cohorts demonstrated for the pooled data from all three trials (10.4 mo high risk, 95% 9.0 to 11.8 mo, 18.6 mo low-risk, 95%CI 14.0 to 23.1, LR 25.3, P<0.01), and for the data from the two larger trials (VIN trial, high-risk 9.9 mo 95% CI 8.5 to 11.3 mo,	Funding sources not described. "The authors indicated no potential conflicts of interest"	*General comments: Validation of EORTC prognostic score on a retrospective basis using a different patient group from the derivation set for the score. Patients well characterised as clinical trial participants. Well conducted study. Limitations: Subjects were largely of advanced stage but good PS, all the subjects were given chemotherapy . It is not clear the extent to which results are generalisable to poorer PS patients or patients treated with surgery or supportive care alone.*

85	Existing models, but not neutrophil-to-lymphocyte ratio, are prognostic in malignant mesothelioma. Meniawy T et al 2013. British Journal of Cancer;109:1813-20	Retrospective case series	"+"	Consecutive newly presenting patients with MPM between 1 January 2005 and 31 Dec 2010 to a single Hospital in Western Australia. Selection criteria included an available NLR within 90 days of diagnosis, pathologically confirmed MPM, absence of haematological malignancy and duration of FU >90 days from diagnosis. 369 patients screened, 95 ineligible by selection criteria.	274 patients included. 169 (62%) treated with chemotherapy, including 10 who had trimodality therapy(TMT); 103 patients BSC alone, 2 patients had EPP but no TMT. Median age 69 (40-93), 86.5% male.42% epithelioid, 13% biphasic, 12% sarcomatoid and 33% "others". AJCC stage 1-2 50%, 3-4 43%. PS 0-1 85%, 2-3 12%, missing 3%. EORTC PS = low risk 49.3%, high risk 50.7%, CALGB prognostic group 1-2 20.4%, 3-4 47.8 %, 5-6 29.2%, Missing 2.6%. Overall survival 13.3 mo median.	Outcome prediction study	Overall survival	Median follow-up for patients who were alive was 45.5 months (range 29.0–88.3 months)	Prognostic abiity of markers	Univariate analysis: Shorter OS associated with: age>=65, NE histology, stage 3-4, PS 2-3, weight loss, chest pain, Hb difference >=10g/L, and platelet count > 400. Both EORTC and CALGB models prognostic with HR of 1.62 (1.26-2.08, p<0.001) and 1.65 (1.36-1.99, p<0.001) respectively. Baseline NLR >= 5 was not		*General comments: Histology surprising - 33% "others". Carefully examines the predictive value of NLR at various cutoffs and as a continuous variable and no significant difference in survival found. Independent but not prospective validation of both EORTC and CALGB scores*

86	Prognostic factors for malignant mesothelioma in 142 patients: validation of CALGB and EORTC prognostic scoring systems. Edwards JG et al 2000. Thorax;55:731-735	Retrospective case series	"+"	142 patients derived retrospectively from a list of patients with a pathology specimen diagnosis mesothelioma. Case records and images reviewed. Data sought to compile EPS and CALGB prognostic groups.	142 patients, 91% male. Survival data available for 138. Median age 64. Median OS 5.9 mo. PS 0 n=56, PS 1 n=73. Epithelioid 65, mixed/sarcomatoid 55. Stage not stated. EPS low risk 49, high risk 75. CALGB groups: 1=22, 2=2, 3=55, 4=5, 5=30, 6=9.	Outcome prediction study	Overall survival	Not stated	Prognostic ability of EPS and CALGB	Univariate: male sex, age, wt loss, chest pain, PS>0, WBC>8.3, Plt count >400, Hb<14, NE histology, EPS low risk, CALGB group>1 all associated with worse overall survival. Forward, stepwise multivariabel Cox proportional hazards model, in those cases with complete data (n=101), results quoted HR, 95%CI, p value: male		

87	Factors predictive of survival among 337 patients with mesothelioma treated between 1984 and 1994 by the Cancer and Leukemia Group B. Herndon J et al 1998. Chest;113:723-31	Patients entered into seven phase 2 treatment trials conducted by Cancer and Leukemia Group B (CALGB)	"+"	337 patients entered into 7 phase 2 chemotherapy trials for mesothelioma between 1984 and 1994. All patients had histolgically confirmed MM, PS 0-2, no prior chemotherapy, expected survival > 2 months, > 2 weeks since surgery and > 4 weeks since radiotherapy, adequate renal, hepatic and haematoligical function, no prior MI or arrythmia in preceding 6 months, no other serious medical or psychological problems. 347 screened patients, 10 inelegible leaving 337 eligible with	337 patients entered into 7 phase 2 chemotherapy trials for mesothelioma between 1984 and 1994. All patients had histolgically confirmed MM, PS 0-2, no prior chemotherapy, expected survival > 2 months, > 2 weeks since surgery and > 4 weeks since radiotherapy, adequate renal, hepatic and haematoligical function, no prior MI or arrythmia in preceding 6 months, no other serious medical or psychological problems. 347 screened patients, 10 inelegible leaving 337 eligible with	Outcome prediction (risk group) study examining pretreatment characteristics and relation to survival. Information permitting a stage to be calculated but one investigator used radiological reports and recorded data to classify disease as local vs regional/distant. Regional/distant classification used for metastatic disease or extension into local organs or transdiaphragmatically.	Overall survival	Follow up until death or September 1995 for patients still alive.	Prognostic ability of variables and of derived score	Univariate comparisons using log-rank test: Poor PS (p<0.001), presence of chest pain (p<0.001), presence of dyspnoea (p=0.033), platelet count >400 (p<0.001), weight loss (p=0.004), serum LDH>500 IU/L (p<0.001) and pleural involvement (p=0.003) are associated with worse prognosis. Multivariable analysis used to derive six risk groups	No information provided on funding or CoI	*General comments: A well conducted study examining prognostic variables in patients entered into clinical trials, meaning that data quality likely to be higher than for other retrospective studies. Patients skewed towards better performance status and fewer co-morbidities because of trial entry criteria. Results likely to be applicable in the UK. Derivation of risk groups is cumbersome and non-intuitive but amenable to computerisation.*

88	Predicting survival in malignant pleural effusion: development and validation of the LENT prognostic score. Clive AO et al 2014. Thorax;69:1098-1110	Prospectively collected, retrospectively analysed case series, multicentre, international.	"++"	789 Patients with malignant pleural effusion referred to a chest physician. MPM = 170 (21.5%)	Patients from 3 databases (UK cohort 1, Australian cohort, Dutch cohort) who had malignant pleural effusion and had been followed up for at least 12 mo or till death. Median age by cohort 60-74,	Age, ECOG PS, Cell type, albumin, eGFR, serum BNP, NLR, mGPS (1 point each for CRP>10, albumin <35), PLR, CRP, PFL VEGF, effusion size on CXR, PFL LDH, PFL pH and glucose. Used to develop a prognostic score based on multivariate analysis.	OS	Minimum 12 mo or till death	Prognostic ability of LENT prognostic score	data from all three cohorts used to derive effect upon survival of cell type. Mesothelioma not subdivided into epithelioid and non-epithelioid cell types. LENT prognostic score developed based on results of univariate and multivariate analysis of UK cohort 1 (221 patients) and validated in separate UK cohort 2		*General comments: Very well conducted study with prospective data collection, but only 21.5% of patients had mesothelioma. No sub-type of meso histology described. Only patients with pleural effusion included therefore excludes patients with meso and pleural thickening alone*

89	A novel clinical prediction model for prognosis in malignant pleural mesothelioma using decision tree analysis. Brims F et al 2016. J Thorac Oncol;11(4):573-82	Part-retrospective, part-prospect observational study	"++"	Derivation cohort: 274 retrospectively identified, and 208 prospectively collected patients with pathologically confirmed MPM. Validation cohort 174 prospectively collected patients with histologically proven MPM	Derivation cohort from single Australian cancer centre. Patients with pathologically confirmed MPM. Centre frequently bases diagnosis on cytology alone though means of diagnosis not reported. Median age 69, 86.3% PS 0-1, 86.9% male. Epithelioid 42.5%, biphasic 12%, sarcomatoid 11.4%, histology not defined 34.0%. Symptoms: Weight loss 47.5%, SOB 80.9%, chest pain 58.5%. 61.4% treated with at least 1 cycle chemotherapy. Validation cohort: symptoms (except weight loss),	Outcome prediction study using Classification and Regression Tree (CART) analysis	Overall survival (?from when - ask NM)	Until death or until 31 August 2014	Survival at 18 months	Variables collected: age, sex, date of diagnosis, date of death, histology, symptoms (SOB, pain, weight loss - defined as any wt loss considered significant by physician or MDT), ECOG PS; blood markers: Hb, WCC, platelet count, Na, K, HCO3, creatinine, bilirubin, albumin, ALT; and pleural fluid variables LDH, pH, protein,	Partially funded by National Health and Medical Research Council Centre for Research Excellence Grant 1001020.	Study examining the effect of interaction between individual predictors which may be more reliable than multiple linear regression.

90	Treatment and survival analyses of malignant mesothelioma in Japan. Gemba K et al 2013. Acta Oncologica;52:803-8	Retrospective population-level study of all cases of recorded mesothelioma	"+"	6030 deaths recorded as due to MM, relatives gave consent in 2069 (34%). Data obtained for 1111 cases of whom 929 thought to have mesothelioma (confirmed histologically in 709).	M:F 753:176 (81%:19%). Median age 67 (range 16-94). Pleural origin in 85.5%. Performance status not recorded.	Age, sex, IMIG stage, histological subtype examined as prognostic factors	Overall survival	All patients had died	Prognostic abiity of markers	Age < 70, IMIG stage 1-3 and epithelioid subtype identified as associated with better prognosis in univariable log-rank test. These factors plus female sex also associated with longer survival on multivariable Cox regression. Effect size (in each case the beta value with 95% CI in brackets): Gender 1.55 (1.20-2.01,	is mainly due to the research founda- tion from the Ministry of Health, Labour and Welfare of Japan, 200500129A, 200635021A, 200733015A, 200733015B, 200836010A, 200938007A, and 201032004B. It is a part of the research and develop- ment and dissemination projects related to the 13 fields of occupational injuries and illnesses of the Japan Labour, Health and Welfare	*General comments: A large, retrospective, population-level study. The relevance to a UK population is difficult to assess. Age, sex, histology and staging all confirmed as important prognostic variables.*

91	Malignant pleural mesothelioma: a population-based study of survival. Milano M 2010. Jthoracic Oncol;5:1841-8	Retrospective case series	"+"	Retrospective study of patients registered in a population level registry between 1973 and 2006. Only actively followed patients included (excluded autopsy and death certificate only cases)	9701 patients included, median age 72 (17-103), 81% male, 92% white. Decade of diagnosis: 1970s 6%, 1980s 16%, 1990s 30%, 2000s 48%. Histology: Epithelioid 21%, "fibrous subtypes" 8%, biphasic 4%, mesothelioma NOS 66%. Tumour grade recorded in 10% paeients. Stage "localised" 12%, "regional" 18%, "distant" 57%, unknown 13%. Surgery performed in 22% radiotherapy in 15%. No information on chemotherapy.	Outcome prediction study	Overall survival		Prognostic abiity of markers	Univariate: older age, male sex, higher grade disease, NE histology, higher stage all significantly associated with poorer survival (as was absence of surgery or radiotherapy treatment, not relevant to baseline prognostication) Multivariate (Cox: analysed in 4 groups because of significant missing data on histology	No information provided on funding or CoI	*General comments: A very large retrospective study, an order of magnitute greater than any others available, but with very high proportion of missing data on tumour pathology. Results consistent with the body of evidence from other studies.*

92	Women with malignant pleural mesothelioma have a threefold better survival rate than men. Taioli E et al 2014. Annals Thoracic Surgery;98:1020-4	Retrospective case series	"+"	Population-based retrospectively collected case series using SEER database from 1973-2009. Cases with no pathologically proven MPM, postmortem diagnosis only, age below 18 years or without survival time in the database were excluded. 14,228 cases of MPM included.	14,228 cases, 22% female, 91.7% white. 58.8% had distant disease on staging. Median survival 8.2 mo for men and 9.6 mo for women.	Outcome prediction study	Overall survival	90.7% patients had died by reporting date.	Prognostic abiity of markers	Univariate analysis: Age, race, stage and sex all significantly associated with survival, with better survival for younger age, female sex, localised stage and white race. Sex HR for women 0.78 (95%CI 0.75-0.82, p<0.0001). After stratifiying for age and stage at diagnosis, difference in survival by sex persisted.	"This work was partly supported by CDC grant 5R01TS00009 9-05 and the Norman Mass Foundation to R.M.F." No CoI declared.	*General comments: A very large population-based study confirming the importance of age, stage, sex and in this study race as prognostic factors.*

93	Efficacy and cost of video-assisted thoracoscopic partial pleurectomy versus talc pleurodesis in patients with malignant pleural mesothelioma (MesoVATS): an open-label, randomised, controlled trial. Rintoul et al, Lancet 2014; 384: 1118–27	RCT	-	196, of whom 175 had mesothelioma	Young age, mean 69 years, higher EORTC risk status in pleurodesis group (53% versus 44%)	VATS	Talc slurry and then poudrage as well half way through trial	12 months	Primary = survival. For this key question, outcome was secondary and assessed as "presence or absence of apparent pleural effusion as assessed by reporting radiologist on chest radiograph". No mention of requirement for further pleural procedures.	68 patients of 88 evaluable for pleurodesis in the talc arm, 69 patients of 87 evaluable in the VATs arm. TALC: Pleural effusion reported to have "resolved" in 25/68 (37%) at 1 month, 37/62 (60%) at 3 months, 31/54 (57%) at 6 months and 27/35 (77%) at 12 months. VATS: Equivalent results are	BUPA foundation	*General comments: Not possible to conclude from this study any meaningful comparison for VATs and talc slurry pleurodesis in terms of pleurodesis success – outcome incorrect, very high failure rate in slurry group (around 60% at 1 month).*

93	Rintoul, R. C. R., A. J.:Edwards, J. G.:Waller, D. A.:Coonar, A. S.:Bennett, M.:Lovato, E.:Hughes, V.:Fox-Rushby, J. A.:Sharples, L. D.:Meso, Vats Collaborators, Efficacy and cost of video-assisted thoracoscopic partial pleurectomy versus talc pleurodesis in patients with malignant pleural mesothelioma (MesoVATS): an open-label, randomised, controlled trial, Lancet; 2014;384(9948); 1118-27	RCT	1+	196/175 confirmed MPM, 88 talc, 87 VAT PP.	196 patients recruited (power estimated to be 90 in each arm, 98 recruited to each arm). 120 (61%) had confirmed MPM at diagnosis and 76 (39%) suspected. 11 patients, 11% of VAT PP and 10 patients, 10% of Talc were subsequently found to have other pathology leaving 87 patients in VAT PP and 88 in Talc group eligible.	VAT PP/ Talc Pleurodesis	Talc Pleurodesis vs VAT PP	12 months	Primary Outcome: Survival 1 year after randomisation. Secondary Outcomes: QoL, presence of pleural effusion, lung finction, exercise tolerancecomplications, cost to health service.	within 12 months of randomization 42 (48%) of 87 in VAT PP group had died compared with 38 (43%) of 88 in the Talc group.14 (16%) patients in the VAT PP group and 15 (17%) in the Talc group either withdrew or did not attend the final appointment, leaving 34/87 (39%) in VAT PP and 37/88 (42%) in Talc group	BUPA Foundation	*General comments: 8 years and 3 months, 196 patients/ 175 with confirmed MPM, 88 Talc pleurodesis, 87 VAT PP. Overall Survival same, surgical complications more common after VAT PP, median LOS longer at VAT PP.*

95	Pleurodesis outcome in malignant pleural mesothelioma. Fysh et al, Thorax 68:594. 2013	Retrospective case series	+/-	390 MPM patients	Total of 87 patients underwent talc (86 talc, 1 bleo), 78 surgical pleurodesis (64 VATs, 3 pleuroscopy, 11 thoracotomy). All had poudrage and 12 had pleurectomy (? Which)	Talc via slurry or surgical pleurodesis	Nil	Not specified	Pleurodesis success - success = no further fluid, partial - further fluid but no intervention, failure = further intervention	From registry, 494 patients with MPM, 478 proven MPM, 390 had evaluable data. Overall 42% of patients underwent pleurodesis. Slurry Pleurodesis: Complete success in 29.7%, partial success in 38.8% and failure in 31.5% of patients. Surgical group: 28.2% success, 39.7% partial, 32.1% failure. No	Nil	*General comments: Case series, selection bias will operate between surgical and slurry groups, but no evidence of differential effect of surgical versus bedside pleurodesis. 42% of patients underwent pleurodesis, and overall failure rate (around 30%) is comparable to that seen in malignant pleural effusion in general for MPM.*

98	Pleurectomy for mesothelioma. Brancatisano et al, Medical Journal of Australia 154:455. 1991	Case series	-	50	All MPM - 45 thoracotomoy and pleurectomy, 3 pleurodesis alone, 2 biopsy only. Pulmonary decort required in 28 patients. Advanced or "non-resectable" disease was excluded. Seven patients had prior failed talc (not clear which).	"Pleurectomy" - although different operations, around half had lung decortication and 5 did not undergo pleurectomy (10%)	Nil - case series	24 months with 6 monthly CXR	No clear primary outcome - but survival and fluid re-accumulation (by CXR) was presented	2% operative mortality, 16% major morbidity. Median survival 16 months (3-54 month range) BUT excluded the operative death for this analysis. Pleural fluid recurrence in 1 patient (not stated when), therefore pleural fluid control in 1/49 (excluding dead patient) = 98% success.	Nil stated	*General comments: Non-comparative case series. Good length of follow up but highly selected cases not representative of general mesothelioma population, radiological outcome only used and timecourse not clear. Suggests pleurectomy highly effective in highly selected population, associated with significant morbidity.*

103	Treasure, T. L.-L., L.:Waller, D.:Bliss, J. M.:Tan, C.:Entwisle, J.:Snee, M.:O'Brien, M.:Thomas, G.:Senan, S.:O'Byrne, K.:Kilburn, L. S.:Spicer, J.:Landau, D.:Edwards, J.:Coombes, G.:Darlison, L.:Peto, J.:Mars trialists,Extra-pleural pneumonectomy versus no extra-pleural pneumonectomy for patients with malignant pleural mesothelioma: clinical outcomes of the Mesothelioma and Radical Surgery (MARS) randomised feasibility study. Lancet Oncology;	RCT feasibility	1-	257/112/50, 24 randomized to EPP, 26 to no EPP	MPM patients fit for EPP	EPP	EPP vs no EPP	median 24.7 months	feasibility of randomly assigning 50 patients in 1 year,proportion of patients completing 3modality therapy, perioperative mortality, QoL, survival, Disease Free Survival	50/112 registered/ 257 screened patients were randomised in 3 years, 24 to EPP and 26 to no EPP. Median time between registration and randomization 3.6 months. Median follow up 24.7 months. 62 (55.4%) patients did not proceed to randomization because of disease progression (n=33), inoperabilit	CRUK, June Hancock Mesothelioma Research Fund, Guy's and st Thomas' NHS Foundation Trust	*General comments: Although there is little doubt doubt that EPP is associated with increased morbidity and mortality and a huge impact on QoL I have difficulty adopting the conclusions of MARS: on ly 16 patients had EPP, the number of non completed operations and perioperative deaths is a surrogate marker of variability in experience between centers. Perioperative mortality of 15.8% is strongly supportive of this argument.Furthermore, not all complications of RT were reported (I am personally aware of at least 2 patients with BPF following EPP and RT in MARS with one of them dying approximately 12 months from the operation as a result of the BPF)and the confounding factor of RT (5 patients suffered complications) is not addressed in the study.The trial was a feasibility trial and was not powered to identify potential differences. Even at the feasibility scope, it took 3 years instead of 1 to recruit 50 patients. There was variab ility in chemotherapy regiments*

103	Treasure-Extra-pleural pneumonectomy versus no extra-pleural pneumonectomy for patients with malignant pleural mesothelioma: clinical outcomes of the Mesothelioma and Radical Surgery (MARS) randomised feasibility study-Lancet oncol 2011	RCT	+ +	50	patients randomised after 3 cycles of chemo.pathologically confirmed mesothelioma and no evidence on preoperative CT staging of unresectable disease or distant metastases, fi t enough to undergo preoperative chemotherapy followed by pneumonectomy (according to British Thoracic Society criteria for lung cancer surgery) and the planned postoperative radiotherapy.	EPP followed by RT vs no EPP	no EPP	median follow-up of 24·7 months (21·6–32·2).	The main endpoints were feasibility of randomly assigning 50 patients in 1 year (results detailed in another report), proportion randomised who received treatment, proportion eligible (registered) who proceeded to randomisation, perioperative mortality, and quality of life.	EPP was completed satisfactorily in 16 of 24 patients assigned to EPP; in fi ve patients EPP was not started and in three patients it was abandoned. Two patients in the EPP group died within 30 days and a further patient died without leaving hospital. The hazard ratio [HR] for overallsurvival between	cancer research UK	*General comments: RCT but does not provide evidence re role of RT, Eight of the 16 patients who completed EPP received radical radiotherapy, fi ve of whom had complications. Severe (grade 3 or 4) acute radical radiotherapy sideeff ects were rare: two patients had grade 3 fatigue and one had grade 3 pain. Severe late side-eff ects were fatigue (n=1, grade 3), pneumonitis or dyspnoea (n=2, grade 3), and ascites (n=1, grade 3). One patient developed paraplegia 42 days after completion of radiotherapy; this patient had MRI and clinical features of herpes myelitis (grade 4).*

104	Mollberg, N. M. V., Y.:Kindler, H. L.:Warnes, C.:Salgia, R.:Husain, A. N.:Vigneswaran, W. T., Quality of life after radical pleurectomy decortication for malignant pleural mesothelioma, Annals of Thoracic Surgery, 2012; 94(4); 1086-92	Before-After Study/ interrupted time series	3	28	patients with MPM that had EPD, PS0 and 1, 21 male, 7 female, 69.9+/- 10.2 years(median 66, range 54-89). All paptients had diaphragmatic resection, 21/28 had pericardial resection. 20 patients (71%) received Cis/ Carbo Pem adjuvant chemo.	EPD	before- after surgery, PS0 vs PS1	6 months till death or 12 months postoperatively	QoL	16/28 at baseline (57.1%) were PS0 and 12 (42.9%) PS1. Cronbach's alpha coefficient for the QLQ-C30 multi item scales was>0.7 for all symptom and function domains except for physical function (0.47). 1 (6.3%) PS0 and 5 (41.7%) PS1 patients developed disease progression between 5-6 and 8-9 months; in	none	***General comments:*** QoL study. 2 years, 28 patients, prospective study. Patients completed the EORTC QLQ-C30 at baseline and at 1, 5-6 and 8-9 months after the operation. All patients had CTTA on month 1 nad every 3 months thereafter and QoL questionnaires were completed till death or 12/12 after surgery. The QLQ-C30 measure comprises 5 functional scales (physical, role, emotional, cognitive, and social), 3 symptom scales (fatigue, nausea and vomiting, and pain), 6 single-item scales (dyspnea, sleep disturbance, appetite loss, constipation, diarrhea, and financial impact), and the overall health and global QoL scale. The internal consistency of the multi-item scales was assessed using Cronbach's alpha coefficient (highest possible score for consistency 1, lower 0, >0.7 considered desirable).The assumption was that PS1 would score worse than PS0 at baseline.

106	Burkholder D, Hadi D, Kunnavakkam R, Kindler H, Todd K, Celauro AD, Vigneswaran WT. Effects of extended pleurectomy and decortication on quality of life and pulmonary function in patients with malignant pleural mesothelioma. Ann Thorac Surg. 2015 May;99(5):1775-80. doi: 10.1016/j.athoracsur.2015.01.058. Epub 2015 Mar 29.	Before-After Study/ interrupted time series	3	36	36 patients undergoing eP/D	eP/D	Measurement of EORTC QLQ-C30 and PFT's preoperatively and at 1, 4-5, 7-8, 10-11, 13-14 months	14 months	EORTC QLQ-C30 and PFTs	After EPD, PS 0 patients had no change in global health or function and symptoms scores except for improvement in emotional function: there was had a significant decrease in FEV1, FVC, TLC, FRC, and DLCO values. PS 1/2 patients had no significant change in the PFTs but improveme	not stated	*General comments: possible overlap with Paper 60 (Mollberg NM (2012) - but differing post assessment timepoints, so probably not*

107	Ploenes T, Osei-Agyemang T, Krohn A, Waller CF, Duncker-Rohr V, Elze M, Passlick B.Changes in lung function after surgery for mesothelioma.Asian Cardiovasc Thorac Ann. 2013 Feb;21(1):48-55. doi: 10.1177/0218492312454017	Before-After Study/ interrupted time series	3	48	25 EPP, 23 eP/D	25 EPP, 23 eP/D	pre vs post PFTs		Spriometry	EPP Group: TLC dropped from 4.8L (77.7%) to 3.5L(55.3%) p<0.0006.FVC dropped from 2.8L (77.7%) to 1.8L (47.6) p<0.0002. Other parameters were also significantly reduced after EPP. Pulmonary function was not significantly reduced in the PD group	not stated	

108	Cao, C. Q. Y., T. D.:Bannon, P. G.:McCaughan, B. C., A systematic review of extrapleural pneumonectomy for malignant pleural mesothelioma, Journal of Thoracic Oncology ,2010; 5(10), 1692-703	Systematic Review	3	34 studies, 2462 patients.	Histologically proven MPM treated with EPP. Adjuvant therapy included chemo, RT, PDT, hyper or normo thermic intrapleural chemotherapy.	EPP	no comparison	8.8-31.2 months	Survival, 30day mortalility and morbidity, QoL assessment.	**Median survival** 9.4-27.5 months (some studies report survival from commencement of chemo and not surgery). 1 year 36-83%, 2 years 5-59%, 3 years 0-41%, 5 years 0-24%. **DFS** 7-19 months. When middle 2 quartiles were analysed median survival 12-20 months, 1 year 50-68%, 2	none	*General Comments: Search from 1985 to 2010. Duplicate studies and reviewes excluded, studies published before 1990 and these with <10 patients excluded. 428 references identified,34 studies in final analysis. Significant heterogeneity in patient selection, staging (even use of different staging systems), preoperative invasive mediastinal lymph node staging, completion of 3modality therapy, reporting of survival from time of chemotherapy or diagnopsis and not from time of surgery.*

109	Cao, C. T., D.:Manganas, C.:Matthews, P.:Yan, T. D., Systematic review of trimodality therapy for patients with malignant pleural mesothelioma, Annals of Cardiothoracic Surgery, 2012;1(4):428-437	Systematic Review	3	16 studies, 744 patients had EPP, 612 patients had 3modality tretatment (TMT)	patients with histologically proven MPM treated with EPP and all forms of systemic chemotherapy and radiotherapy	trimodality treatment	no comparison	12.9-69 months	Survival, Disease Free Survival, perioperative mortality, perioperative morbidity, LOS	4 prospective studies with NEOADJUVANT chemo reported Median Survival 16.8--25.5 months on intention to treat analysis with DFS of 10.1-16.3 months . 1 RCT reported median survival of 14.4 months from 24 patients who wer randomized to EPP and DFS of 7.6 months. In studies with ADJUVANT	none	*General Comments: 1 RCT (feasibility testing, MARS), 5 prospective series and 10 retrospective observational studies. Search was run for all studies between 1985 and 2012 and duplicate results wer omited by using the most up to date publication from the relevant centre.Local disease recurrence 4-41%, distant 5-56% overall disease recurrence 27-84%. In the 4 prospective studies the majority of patients ((57-71%) were able to complete 3modality therapy on intention to treat analysis. For the only RCT (MARS) the comments are: median survival reported was 14.4 montsh for 14 patients that underwent EPP. survival outcomes were calculated from ramdomization which was average 3.6 months after registration. Conclusions were speculative, drawn from a feasibility testing study, chmoe was non standardized, as was timing of shemoradiation, numbers were limited and there were significant protocol violations between the 2 arms. mortlaity of 18% wasone of the highest ever reported in recent lioterature. The authors conclude that the evidence for 3modality treatment (with EPP) in the current literature is inconsistent . a number of prospective studies have reported relatively favourable outcomes on intention to teat analysis. One RCT reported unfavourably for EPP but further studies are required before conclusions are drawn for thisprocedure. The meta analysis is limited by potential publication biasand the majority of the data was from teriary centres with specialized interest in MPM hence the results might be non applicable to non specialized institututions.*

110	Cao, C. T., D. H.:Pataky, K. A.:Yan, T. D., Systematic review of pleurectomy in the treatment of malignant pleural mesothelioma, Lung Cancer 2013; 81(3): 319-27	Systematic Review	3	34 studies, 1935 patients: 12 studies with EPD, 8 with P/D, 14 with Partial Pleurectomy.	Patients with MPM that underwent any form of pleurectomy based treatment. Age, gender, histopathology, staging, adjuvant therapy (neoadjuvant or adjuvant chemo, PDT, Immunotherapy, RT) varied greatly between institutions.	Extended P/D (EPD), P/D and Partial Pleurectomy	EPD vs P/D vs Partial Pleurectomy	9-86.7 months	Perioperative mortality, long term survival, perioperative morbidity, DFS, QoL outcomes.	**EPD:** MEDIAN SURVIVAL: 11.5-31.7 months (middle 2 quartiles 15-25), DFS 7.2-16 months,MORTALITY 0-11%, MORBIDITY 20-43%, LOS 7-15 days , **P/D:** MEDIAN SURVIVAL 8.3-26 months (middle 2 quartiles 12-18 months), DFS 6-7.4 months,MORTALITY 0-7.1%, MORBIDITY 13-48%, LOS 7-14days , **Partial**	none	***General comments:*** *search 1985-2012. Aim to assess safety and efficacy of EPD, P/D and Partial Pleurectomy. Abstracts, case reports, conference presentations, editorials and expert opinions were excluded. Review articles were omitted due to potential publication bias and possible duplication of results. Studies that included fewer than fifteen patients or presented data with less than 6 months follow-up were also excluded. 1. Extended P/D: parietal and visceral pleurectomy to remove all gross tumour with resection of the diaphragm and/or pericardium as required. 2. P/D: parietal and visceral pleurectomy to remove all gross tumour without resection of the diaphragm or pericardium. 3. Partial pleurectomy: partial removal of parietal and/or visceral pleura for diagnostic or palliative purposes but leaving gross tumour behind. Survival was calculated from day of surgery in most studies however the dates of Diagnosis (6 studies), date of chemotherapy (1) or study entry (1 study) were used in some reports. For EPD local recurrence occured in 26-57% of patients, distant in 0-24% and both local and distant in 6-43% with limited data for disease recurrence in P/D and Partial Pleurectomy groups.* ***CONCLUSIONS:*** *All 3 pleurectomy techniques have similar* ***mortality*** *rates of less than 8% (1 study reported higher) with the majority reporting <4%. Morbidity is <50% in all the studies. Median overall and Disease Free Survival appeared to be longer in patients who underwent EPD in comparison to P/D or Partial Pleurectomy. These advantages might come at a cost of slightly higher morbidity and LOS. LIMITATIONS OF SR: al lstudies werecase series reports reporting selected patients treated in specialized centres. there was significant heterogeneity in reporting, such as the commencement date for reporting survival. EPP might offer superior clearence when disease involves the fissures. IN CONCLUSION pleurectomy procedured for MPM can be performed safely but vary greatly in terms of surgical technique and clinical intent. EPD might achieve a longeroverall and disease free survival compared to P/D or Partial Pleurectomy but this might be associated with highr morbidity and longer hospitalization.*

111	Cao, C. T., D.:Park, J.:Allan, J.:Pataky, K. A.:Yan, T. D., A systematic review and meta-analysis of surgical treatments for malignant pleural mesothelioma, Lung Cancer, 2014;83(2): 240-5	Systematic Review	3	1145 patients with MPM, 632 EPP and 513 EPD.	MPM patients that underwent EPP or EPD. Adjuvant modalities varied.	EPP, EPD	EPP vs EPD	9-25 months	Mortality, Morbidity, Survival,	All cause **perioperative mortality** significantly lower for EPD compared to EPP: 2.9% vs 6.8%; RR 0.53; 95%CI 0.31-0.91; p=0.02; I2=0%. **Perioperative morbidity** was also significantly lower for EPD: 27.9% vs 62%; RR 0.44, 95% CI 0.30-0.63; p<0.0001, I2=44%. **Survival** was calculated from *Date of Surgery*	none	*General comments: A systematic review of the literature was performed on six electronic databases to identify all relevant data on comparative outcomes of extended P/D and EPP in a multimodality setting. Endpoints included perioperative mortality and morbidity, as well as long-term overall survival . Electronic searches across 6 databases from dates of inception to September 2013. Meta analysis was performed. 7 comparative studies were assessed, all observational studies. An I2 value of greater than 50% was considered substantial heterogeneity.*

133	PALLIATIVE C-J. Lindén- Effect of hemithorax irradiation alone or combined with doxorubicin and cyclophosphamide in 47 pleural mesotheliomas: a nonrandomized phase II study-Eur Respir J, 1996, 9, 2565–2572	single arm, single institution phase II	+	47 (48 eligible)	a histologically proven diagnosis of pleural mesothelioma based on a biopsy of the pleural tumour; 2) a performance index of 70 or more according to the Karnofsky scale [13]; 3) an age of less than 80 yrs for radiotherapy (RT) and an age of less than 70 yrs for combined therapy (RTCT); 4) a calculated postirradiation vital capacity exceeding 1.5 L,after an expected total loss of gas exchange function in the irradiated lung (dynamic spirometry	hemithoracic RT with a total dose of 40 Gy, fractionated as 2 Gy·day-1 for 5 days a week. Patients in good condition 1 month after radiotherapy were offered supplementary chemotherapy consisting of doxorubicin and cyclophosphamide.	none	?	evaluation of pain and PS before and after RT/RR/survival	The median survival following the initiation of RT was 7 months in all patients (n=47), 6 months in the RT group (n=31), and 13 months in the combined RTCT group (n=16). Chest pain, performance status and body weight were not favourably affected by the radiotherapy. Eleven patients had acute radiation pneumoniti	Swedish Heart-Lung Foundation.	*radical Rt alone +/_ chemo; side effects (and tools used to evaluate toxicity) of RT not well described*
135	Allen et al. FATAL PNEUMONITIS ASSOCIATED WITH INTENSITY-MODULATED RADIATION THERAPY FOR MESOTHELIOMA. Int. J. Radiation Oncology Biol. Phys., Vol. 65, No. 3, pp. 640–645, 2006	cohort, retrospective	-	13	patients with resected MPM treated with IMRT after EPP and adjuvant chemotherapy	postop IMRT	none	median follow-up of 16 months (range, 15 to 17 months).	toxicity	6/13 patients developped grade 5 pneumonitis	?	*General comments: variability in type and timing of chemo with RT*

136	Allen- INFLUENCE OF RADIOTHERAPY TECHNIQUE AND DOSE ON PATTERNS OF FAILURE FOR MESOTHELIOMA PATIENTS AFTER EXTRAPLEURAL PNEUMONECTOMY	cohort, retrospective	-	39	MPM, post EPP, all received chemo (before, or during RT)	postop hemithoracic RT	moderate dose RT vs high dose RT	23 months (range, 6–72).	patterns of failure and patient outcomes	local failure rate was 50% (12 of 24) after MDRT and 27% (4 of 15) after HDRT (p = NS).	?	*General comments: RT evolved with time during this study (dose and technique), variability in type and timing of chemo used*
137	bille-Induction chemotherapy, extrapleural pneumonectomy, and adjuvant radiotherapy for malignant pleural mesothelioma: experience of Guy's and St Thomas' hospitals-Gen Thorac Cardiovasc Surg (2012) 60:289–296	cohort, prospective	+	25	Patients with MPM who were eligible for EPP after chemo and RT and multimodality therapy	EPP after completion of neoadjuvant chemo	none	?	outcome after tri-modality therapy	One-year survival was 54.5%; 2-year survival was 18.2%.	?	General comment: evaluation of trimodality, not all patients received RT (81%)
138	Bolukbas-Survival after trimodality therapy for malignant pleural mesothelioma: Radical Pleurectomy, chemotherapy with Cisplatin/Pemetrexed and radiotherapy-Lung Cancer 71 (2011) 75–81	cohort, prospective	+	35	MPM deemeded suitable for trimodality therapy	Radical pleurectomy followed by 4 cycles of chemotherapy with Cisplatin (75mg/m2)/Pemetrexed (500mg/m2) and radiotherapy 4–6 weeks after operation.	none	Median follow-up 21.7 months	out come after trimodality therapy	Overall median survival was 30.0 months. One-, 2-, and 3-year-survival were 69%, 50% and 31%, respectively.	?	Comments: The patients underwent irradiation of the chest wall and wound in the area of the thoracotomy as well as the drainage tube tracts. If gross tumor remained in the mediastinum and/or elsewhere in the thorax irradiation was broadened. Areas of concern received a boost.

139	Flores-Induction chemotherapy, extrapleural pneumonectomy, and postoperative high-dose radiotherapy for locally advanced malignant pleural mesothelioma: a phase II trial-JTO 2006	single-institution, prospective, single-arm trial	+	21	pathologic diagnosis of MPM, clinically staged as T3-4, N0-2, M0 based on CT scan findings. Karnofsky performance status ≥70% and initial laboratory values including white blood cell 3000/mm3, platelet count 100,000/mm3, hemoglobin 8 mg/dl, serum creatinine 1.5, and bilirubin 1.9. postoperative predicted forced expiratory volume in 1 second and single breath diffusing capacity to be at least 35%. Patients not eligible for this protocol included those	Induction therapy four cycles of gemcitabine and cisplatin. Patients without disease progression by computed tomography underwent EPP followed by adjuvant hemithoracic RT (54 Gy).	none	median follow-up 9 months	feasibility and potential efficacy of preoperative chemotherapy with gemcitabine and cisplatin, followed by EPP and adjuvant high-dose hemithoracic EBRT	Eight of nine patients undergoing surgical exploration had EPP. The median survival of all patients was 19 months. Patients who had an EPP had a median survival of 33.5 months. Patients with unresectable tumors had a median survival of 9 months (p 0.01).	?	*General comments: only nine patients undergoing surgical exploration and 8 of them had EPP.*

140	Kristensen-Pulmonary toxicity following IMRT after extrapleural pneumonectomy-for malignant pleural mesothelioma-Radiotherapy and Oncology 92 (2009) 96–99	prospective single cohort	+	26	stage T1–3N0M0 suitable trimodal therapy	induction chemotherapy followed by extrapleural pneumonectomy and IMRT. The entire preoperative pleural surface area was treated to 50 Gy and areas with residual disease or close surgical margins were treated to 60 Gy in 30 fractions. five daily fractions during 1 week to the entire ipsilateral hemithorax with concomitant 5 Gy boost to areas at risk followed by EPP within 1 week of completing neoadjuvant IMRT. +/- Adjuvant chemotherapy	none	not specified in paper	to compare lung dosimetric parameters in patients who did and in patients who did not experience fatal radiation pneumonitis in order to estimate safe lung dose constraints in the trimodal therapy setting	The main toxicities were nausea, vomiting, esophagitis, dyspnea, and thrombocytopenia. One patient died from an intracranial hemorrhage during severe thrombocytopenia. Four patients (15%) experienced grade 5 lung toxicity, i.e. pneumonitis 19–40 days after the completion of radiotherap	?	*General comments: eligibility crietria not well defined*

141	PD Lucchi-Four-Modality Therapy in Malignant Pleural Mesothelioma: - A Phase II Study- J Thorac Oncol. 2007;2: 237–242	prospective, single arm and single centre phase II	+	49	younger than 75 years of age with histologically proven stage II or III MPM diagnosed by thoracoscopy. Additional eligibility criteria included Eastern Cooperative Oncology Group (ECOG) performance status of 2, no history of malignancy or chemo- or radiotherapy, adequate bone marrow reserve (leukocytes 3500/ L, platelets 100,000/ L), and adequate liver (bilirubin 1.5 mg/dL) and renal function (serum creatinine 1.5 mg/dL and creatinine clearance 65 mL/min)	four-modality treatment with intrapleural preoperative interleukin-2 (18 106 UI/day for 3 days), pleurectomy/decortication, intrapleural postoperative epidoxorubicin (25 mg/m2 for 3 days), interleukin-2 (18 106 UI/day for 3 days), adjuvant radiotherapy (30 Gy), systemic chemotherapy (cisplatin 80 mg/m2 day 1, gemcitabine 1250 mg/m2 days 1 and 8 for up to six courses) and long-term subcutaneous interleukin-2 (3 106 UI/day on 3 days per week).	none	median follow-up of	post op mortality rates, survival	There was no postoperative mortality. Postoperative morbidity included bleeding (n 1) and arrhythmias (n 3). After a median follow-up of 59 months (range, 14–81), 13 patients are still alive and the median actuarial survival is 26 months (31 and 21 months for stages II and III, respectively	?	*General comments: RT targets were the surgical scars and eventual residual disease. RT treatment poorly described. Toxicity of tretament inc RT poorly reported*

142	Minatel-Tomotherapy after pleurectomy/decortication or biopsy for malignant pleural mesothelioma allows the delivery of high dose of radiation in patients with intact lung-Journal of Thoracic Oncology 2012	prospective, cohort study	+	28	thirty-five patients were treated with radical P/D or had a pleural biopsy for an MPM, and suitable for adjuvant or definitive radiotherapy (tomotherapy).	The dose prescribed to the planning target volume, defined as the entire hemithorax, including chest-wall incisions and drain sites and excluding the intact lung, was 50 Gy delivered in 25 fractions. All patients underwent fluorodeoxyglucose-positron emission tomography for staging after surgery. Any fluorodeoxyglucose-avid areas or regions of particular concern for residual disease were given a simultaneous boost of radiotherapy to 60 Gy.	none	median follow-up o f 19 months (range, 6–29 months)	toxicity of RT CTCAE v3.0	Five patients (17.8%) experienced severe respiratory symptoms corresponding to grade 2 pneumonitis in three cases, and grade 3 pneumonitis in two cases. No fatal respiratory toxicity was reported. Controlateral lung V5 was strongly correlated with the risk of pneumonitis. Patients who	?	*patients recruited 2009-2011 same authors published a further paper in 2014 with a smaller number of patients on lung term outcome (patients recruited 2009-2010). likely overlap*

143	Minatel-Radical pleurectomy/decortication followed by high dose of radiation therapy for malignant pleural mesothelioma. Final results with long-term follow-up-Lung cancer 2014	prospective, cohort study	+	20	The majority of the patients were male(90%) and had a median age of 68. 90% were epithelioid;8(40%) were stages I–II,and12(60%)were stages III–IV.Nineteen (95%) patients received systemic chemotherapy. All patientscompleted the radiotherapy course having received the planned dose.	P/D followed by high dose radiotherapy.The clinical target volume was defined as the entire hemithorax excluding the intact lung. The dose prescribed was 50 Gy in 25 fractions. Any FDG-avid areas or regions of particular concern for residual disease were given a simultaneous boost to 60 Gy. Chemotherapy was not a component of the study and was administered elsewhere prior to RT, in the majority of the cases.Patients who experienced tumor progression during	none	median follow-up of 27months (range9–45months)	long-term survival	The median OS and PFS were 33 and 29 months,respec-tively. No fatal toxicity was reported.Five Grades 2–3pneumonitiswere documented.	?	*General comments: small cohort, risk of patient selection bias, surgery or chemotherapy related toxicities and deaths were not considered in the analysis*

144	Rice-Dose-dependent pulmonary toxicity after postoperative intensity-modulated radiotherapy for malignant pleural mesothelioma	retrospective, single centre	-	63	Patients considered eligible for EPP had no evidence of extrathoracic disease and no multiple discontinuous areas of chest wall involvement or invasion of mediastinal structures shown on conventional imaging (computed tomography [CT] of the chest and upper abdomen).	extrapleural pneumonectomy and IMRT	none	?	pulmonary-related death (PRD) and non–cancer-related death within 6 months of IMRT.	23 (37%) had died within 6 months of IMRT (10 of recurrent cancer, 6 of pulmonary causes [pneumonia in 4 and pneumonitis in 2], and 7 of other noncancer causes [pulmonary embolus in 2, sepsis after bronchopleural fistula in 1, and cause unknown but without pulmonary symptoms or recurrent disease in 4]).	?	*General comments: yes, although retrospective, it highlights the toxicity of hemithoracic IMRT and provides important info on lung dose constraints. On multivariate analysis, only V20 was predictive of PRD (p 0.017; odds ratio, 1.50; 95% confidence interval, 1.08 –2.08) or non–cancer-related death (p 0.033; odds ratio, 1.21; 95% confidence interval, 1.02–1.45).*

145	Pagan-5-year prospective results of trimodality treatment for malignant pleural mesothelioma-Journal of Cardiovascular Surgery 2006	prospective, cohort study, single centre	+	54	suitable extended pleuropneumonectomy (EPP)	extended pleuropneumonectomy (EPP), to be followed by chemotherapy (paclitaxel+carboplatin) and radiotherapy (50 Gy)	none	1 month-6 yrs	survival and postop mortality	The 30-day or in-hospital operative mortality rate was 4.5% (2 deaths), the major morbidity 36%, and the overall complication rate 50%. At 5 years the projected survival of the 42 surgical survivors submitted to EPP is 19%; median survival is 20 months.	?	*General comments: good quality paper*

146	Rusch-A phase II trial of surgical resection and adjuvant high-dose hemithoracic radiation for malignant pleural mesothelioma-Journal of Thoracic & Cardiovascular Surgery 2001	phase II, single centre	+	88	potentially resectable, biopsy-proven MPM.	All patients were to undergo an EPP unless contraindicated by their preoperative pulmonary function. PD was also performed.For patients undergoing EPP, adjuvant external-beam radiation started 3 to 5 weeks postoperatively. The target volume included the entire hemithorax, the thoracotomy incision, and chest tube incisions. A total of 54 Gy was delivered through anterior and posterior fields in 30 daily fractions of 1.8 Gy by using 6-MV or higher photons.	none	?	to determine the feasibility of EPP combined with high-dose, postoperative external-beam hemithoracic radiation; (2) to determine the feasibility of combining P/D with intraoperative radiation and postoperative external-beam radiation; (3) to determine the patterns of local and distant recurrence after this combined modality treatment; and (4) to estimate overall survival after this combined modality	Seven (7.9%) patients died postoperatively. Adjuvant radiation administered to 57 patients (54 undergoing extrapleural pneumonectomy and 3 undergoing pleurectomy/decortication) at a median dose of 54 Gy was well tolerated (grade 0-2 fatigue, esophagitis), except for one late esophageal fistula. The median survival	?	

147	tonoli-Adjuvant radiotherapy after extrapleural pneumonectomy for mesothelioma. Prospective analysis of a multi-institutional series-Radiother&Oncol 2011	prospective, multicentre cohort study	+	56	mesothelioma patients consecutively treated with post-operative radiotherapy after extrapleural pneumonectomy	3DCRT, IMRT or with helical tomotherapy. dose fractionation used: 45 Gy in 25 of 50 Gy in 25 fractions to the hemi-thoracic space and the ipsilateral mediastinum. In some cases a simultaneous integrated boost was given to the sites of positive margins identified at pathologic examination	none	median follow-up of 20 months (mean 26.2, range 5–74).	overall survival, LRC, DMF, DF, DSS, OS	Three year locoregional control (LRC), distant metastasis free (DMF), disease free (DF), disease specific (DSS) and overall survival (OS) rates are 90%, 66%, 57%, 62%, and 60%, respectively. 2 pts died as a result of RT-related toxicity	?	*General comments: 3 centres, selection bias*

148	Van Schil-Trimodality therapy for malignant pleural mesothelioma: results from an EORTC phase II multicentre trial-Eur J Cancer 2010	single arm multicentre phase II	+	59	Pathologically proven MPM cT3N1M0 or less (UICC TNM)	Induction chemotherapy consisted of three courses of cisplatin 75 mg/m-2 and pemetrexed 500 mg?m-2. Nonprogressing patients underwent extrapleural pneumonectomy followed by postoperative radiotherapy (54 Gy, 30 fractions).	none	?	primary end-point was ''success of treatment'' (defined as a patient who received the full protocol treatment within the defined time-frames, and was still alive 90 days after the end of protocol treatment without progression or evidence of grade 3–4 toxicity) and secondary end-points were toxicity, and overall and progression-free survival.	55 (93%) patients received three cycles of chemotherapy with only mild toxicity. 46 (79%) patients received surgery and 42 (74%) had extrapleural pneumonectomy with a 90-day mortality of 6.5%. Post-operative radiotherapy was completed in 37 (65%) patients. Grade 3–4 toxicity persisted after 90	EORTC	*Comments:Using threedimensional (3D) conformal radiotherapy, a dose of 54 Gy was delivered to the entire hemithorax, thoracotomy incision and sites of chest drains in once-daily fractions of 1.8 Gy. Median radiotherapy dose was 54.0 Gy (range 43.2–54.0 Gy). In 18 patients, a chest wall bolus was given. Median V20 to the contralateral lung was 2.0% (range 0.0–30.4%). Median maximum dose to spinal cord was 43.3 Gy (range 9.5–52.5 Gy). Two patients died after radiotherapy due to pneumonia, one having Aspergillus infection.*

149	Weder-Multicenter trial of neo-adjuvant chemotherapy followed by extrapleural pneumonectomy in malignant pleural mesothelioma-ann oncol 2007	multicentre phase II, single arm	+	61	histologically confirmed diagnosis of MPM, including all subtypes and clinical T1–T3, N0–2, M0 disease considered to be completely resectable as evaluated by a thoracic oncology tumor board including a thoracic surgeon	Neo-adjuvant chemotherapy consisted of three cycles of cisplatin and gemcitabine followed by EPP. Postoperative radiotherapy was considered for all patients	none	median follow-up of 46	patterns of failure Based on the center of the recurrent tumor, treatment failures were categorized as in-field local failures (within the 90% isodose line), marginal failures (between the <90% and 50% isodose lines), and out-of-field failures (outside the 50% isodose line).	the median time to in-field local failure from the end of RT was 10 months. Forty-three in-field local failures (64%) were found with a 1- and 2-year actuarial failure rate of 56% and 74%, respectively. For patients who underwent P/D versus those who received a partialpleurectomy or were deemed		*General comments: radiotherapy* *Radiotherapy was recommended to areas of obvious incomplete resection and to high-risk areas as defined by the surgeon, such as the sinus phrenicocostalis and sites of surgical incisions.The radiotherapy dose recommended was 60 Gy in 2-Gy daily fraction* *5 times per week for residual macroscopic disease and 50 Gy in 2-Gy daily fraction 5 times per week for high-risk areas. If not radically resected, port-site incisions were to be irradiated with a single dose of 1 · 8 Gy.*

150	Stahel RA, Riesterer O, Xyrafas A, Opitz I, Beyeler M, Ochsenbein A, Früh M, Cathomas R, Nackaerts K, Peters S, Mamot C, Zippelius A, Mordasini C, Caspar CB, Eckhardt K, Schmid RA, Aebersold DM, Gautschi O, Nagel W, Töpfer M, Krayenbuehl J, Ribi K, Ciernik Lf, Weder W. Neoadjuvant chemotherapy and extrapleural pneumonectomy of malignant pleural mesothelioma with or without hemithoracic radiotherapy (SAKK 17/04): a randomised,	RCT; phase II	+ +	151 patients receiving neoadjuvant chemotherapy, of whom 113 (75%) had extrapleural pneumonectomy	pathologically confi rmed malignant pleural mesothelioma; resectable TNM stages T1–3 N0–2, M0; WHO performance status 0–1; age 18–70 years.	In part 1, patients were given three cycles of neoadjuvant chemotherapy (cisplatin 75 mg/m² and pemetrexed 500 mg/m² on day 1 given every 3 weeks) and extrapleural pneumonectomy; the primary endpoint was complete macroscopic resection (R0–1). In part 2, participants with complete macroscopic resection were randomly assigned (1:1) to receive high-dose radiotherapy or not. The target volume for radiotherapy encompassed the entire hemithorax, the	adjuvant RT vs no RT	median follow-up of 54·2 months (IQR 32–66)	The primary endpoint of part 1 was the proportion of patients achieving complete macroscopic resection (R0 and R1). The primary endpoint in part 2 was locoregional relapse-free survival, analysed by intention to treat.	113 patients had extrapleural pneumonectomy, with complete macroscopic resection achieved in 96 (64%) of 151 patients. We enrolled 54 patients in part 2; 27 in each group. Median locoregional relapse-free survival from surgery, was 7·6 months (95% CI 4·5–10·7) in the no radiotherapy group and	Swiss Group for Clinical Cancer Research, Swiss State Secretariat for Education, Research and Innovation, Eli Lilly.	
167	Arber A, Spencer L. 'It's all bad news': the first 3 months following a diagnosis of malignant pleural mesothelioma. Psychooncology. 2013 Jul;22(7):1528-33.	Qualititative case series	3	10	8 men and 2 women with MPM from two acute trusts in the South of Englands	N/A	N/A	N/A	N/A	N/A	N/A	Surrey, West Sussex and Hampshire Cancer Network	*General comments: All participants reported high levels of uncertainty and feelings of a lack of control leading to psychosocial distress since receiving their diagnosis. All the participants found it difficult to cope with their diagnosis because of all the negative information and 'bad news' around MPM, and this led to feelings of despair. The study is limited by a small sample size and by the fact that participants who were interviewed during the first 3 months following diagnosis were living in an affluent part of the UK.*

168	Granieri, A. T., S.:Tamburello, A.:Casale, S.:Cont, C.:Guglielmucci, F.:Innamorati, M. Quality of life and personality traits in patients with malignant pleural mesothelioma and their first-degree caregivers. Neuropsychiatric Disease & Treatment. 2013; 9:1193-202.	Qualititative cross-sectional case control	2-	122	27 patients (eight women and 19 men) affected by MPM, with a mean age of 61.41 ± 8.82 years; 55 first-degree relatives (43 women and 12 men), with a mean age of 56.51 ± 13.66 years;and 40 healthy controls (22 women and 18 men), with a mean age of 44.63 ± 13.02 years.	N/A	Quality of life	N/A	World Health Organization Quality of Life–BREF (WHOQOL-BREF) and the Minnesota Multiphasic Personality Inventory-2 Restructured Form (MMPI-2-RF).	Patients with MPM had a greater belief that goals cannot be reached or problems solved, while often claiming that they were more indecisive and inefficacious than the healthy controls. First-degree relatives reported lower opinions of others, a greater belief that goals cannot be reached or problems solved,	Not recorded	*General comments: Terminal patients and patients with major medical comorbidities were excluded. Case ascertainment process likely to have led to selection bias.*
168	Clayson H, Seymour J, Noble B. Mesothelioma from the patient's perspective. Hematol Oncol	Qualititative case series	3	15	13 men and 2 women with MPM. Mean age 69.	N/A	N/A	N/A	N/A	N/A	Royal College of General Practioners	***General comments:*** *Four main themes emerged: coping with symptoms, the burden of medical interventions, finding out about mesothelioma and psychosocial issues. Dyspnoea was the commonest symptom and the unpredictability and often speed of onset caused great distress. All patients acknowledged asbestos as the cause of their disease. Terminal patients were excluded. Case ascertainment process likely to have led to selection bias.*
170	Moore S, Teehan C, Cornwall A, Ball K, Thomas J. 'Hands of Time': the experience of establishing a support group for people affected by mesothelioma. Eur J Cancer Care (Engl). 2008 Nov;17(6):585-92.	Qualitative case series	3	6	4 patients and 2 carers attending a mesothelioma support group in the UK.	N/A	N/A	N/A	N/A	N/A	MacMillan Cancer Support and Ely Lilly	***General comments:*** *Six responses were received from 21 attendees. All of those that responded found the group useful in terms of sharing experiences and gaining information.*

171	Chamming's S, Clin B, Brochard P, Astoul P, Ducamp S, Galateau-Salle F, Ilg AG, Goldberg M, Gramond C, Imbernon E, Rolland P, Pairon JC. Compensation of pleural mesothelioma in France: data from the French National Mesothelioma Surveillance Programme. m J Ind Med. 2013 Feb;56(2):146-54.	Case series	3	2407	MPM patients recorded in the French National Mesothelioma Surveillance Programme 1999 to 2009.	N/A	N/A	N/A	N/A	N/A	National Institute for Health Surveillance (InVS), the Ministry of Labour, and the Ministry of Health.	***General comments:*** *A linked database study which determined that 30% of patients with MPM were not recorded as having claimed occupation disease compensation. Claims were lower in older patients, women and white collar workers.*
172	Cree MW, Lalji M, Jiang B, Carriere KC. Under-Reporting of Compensable Mesothelioma in Alberta. Am J Ind Med. 2009 Jul;52(7):526-33.	Case series	3	568	Histological confirmed mesothelioma cases recorded in the Alberta Cancer Registry between 1980 and 2004. Included 83 with non-pleural mesothelioma.	N/A	N/A	N/A	N/A	N/A	Alberta Cancer Board	***General comments:*** *A linked database study which determined that 42% of patients with MPM were not recorded as having claimed occupation disease compensation.*

173	Kuschner WG, Varma R, Flores R, Agrawal M, Guvenc-Tuncturk S. Missed opportunities to counsel patients with malignant pleural mesothelioma about causation and potential compensation. Am J Med Sci. 2012 Mar;343(3):206-9.	Case series	3	16	MPM diagnosed 1999-2009 at 3 americal veterans affairs hospitals. 15 men. Mean age 72.	N/A	N/A	N/A	N/A	N/A	Not recorded	***General comments:*** *Retrospective case note review. One patient had documented evidence of compensation advice.*
175	48. Observer variability in mesothelioma tumor thickness measurements: Defining minimally measurable lesions. Armato et al. JTO 2014; 9 (8) 1187-1194	Restrospective review of existing database	+	50	90% male, 70% epithelioid, 10% sarcomatoid, equal laterality distribution	CT modified RECIST criteria to measure disease	6 observers measured 170 tumour foci on 50 CT scans with mesothelioma	n/a	Tumour charcterized by various features. Interobserver variability calculated	Avg across the 170 sites 11.61mm with SD 8.19mm. Median 9.68mm.	Raine medical research fouyndation and cancer council Western Australia	*Does not add much to the follow-up question. In this study the emdian tumour thickeness was less than the minimally measurable lesion thickness of 10mm. Significant interobserver variability noted. There fore poses the question how reliable is RECIST when used as measure of tumour response. Primary observer is an oncologist, unsure if the other observers are radiologists or not, which is a weakness in this study.*
176	Modified RECIST criteria for assessment of response in malignant pleural mesothelioma. Byrne MJ et al. Annals of oncology 15; 257-260:2004	retrospective review of prospectively collected data from 2 RCTs	+	73 patients. Tumour measurements from 236 scans.	not given	modified RECIST CT criteria	RECIST criteria	3.4 years	difference between RECIST and mRECIST	no difference in the overall classificatio n of 'response rates' between RECIST and mRECIST. But response class did correlate with survival (15.1 responders, 8.9 non-responders)		*Authors suggest that mRECIST is a better measure of tumour in mesothelioma compared to RECIST but there was no difference in overall response figures.*

177	Early response evaluation in MPM by PET. Ceresoli et al. Journ of clinical oncology 24:4587-4593. 2006	prospective case series	+	22 patients.	Bx proven MPM. Having Pem alone or Pem/Carbo. PET before chemo and after 2 # Median age 63, 77% male	PET-CT	CT	median 15.4 months	metabolic responders compared with partial response, stable disease according to CT findings.	median TTP of MR twice that of non-responders. CT criteria not predictive of TTP		*metabolic responders- 20-25% decrease in FDG up take (SUVmax). Talc patients did not affect the study results-only 2 patients. Small study but good results.*
178	Volumetry: an alternative to assess therapy response for MPM? Frauenfelder et al. ERJ 2011; 38:162-	restrospective case review	+	30 patients. All treated with neo-adjuvant chemo Cis/pem or Cis/Gem followed by EPP	not given	Volumetry	mRECIST	not given	variability between RECIST and volumetry when assessing response to	with volumetry all observers classed patients in the same		*Observers are trainee thoracic surgeon and 2 radiologists. Correlation between the 2 systems are looked at individually but not with overall survival which would be useful. This study proves the high intraclass correlation and interobserver agreement but this is not correlated to survival. The software used here is in house ?commercially available. Each scan can take more 15 minutes when taking into account the manual adjustments required on some scans. How practical is this in real life?*
180	CT, RECIST and MPM. Nowak et al. Lung cancer (2005) 49S1, S37-S40	review article	-	n/a	n/a	n/a						*review article comparing the evolution of radiographic measures for MPM, from WHO criteria to mRECIST and future directions. Nil to add to above studies as discussing the above studies in this paper.*
186	Carella, R. D., G.:D'Errico, A.:Salerno, A.:Egarter-Vigl, E.:Seebacher, C.:Donazzan, G.:Grigioni, W. F. 2001 Immunohistochemical panels for differentiating epithelial malignant mesothelioma from lung adenocarcinoma: A study with logistic regression analysis American Journal of Surgical Pathology 25 1 43-50	Non-comparative (case series)	+	46 MPM, 20 lung adenocarcinoma	MPM - 32/46 male. 32/46 epithelioid, 10 biphasic, 4 desmoplastic	Calretinin, thrombomodulin, CK5/6, High weight CKs, MOC31, Ber-EP4, CEA		NA	Presence or absence of focal or diffuse antibody reaction (absence = <2% positive cells)		Not reported	***General comments:*** Calretinin 40/46 MPM positive, 2/20 Lung CA positive - sensitivity 89%, specificity 90%, Overall accuracy 89%. Cytoplasmic staining only, nuclei remain unstained. Sarcomatoid component of biphasic MPM completely unstained. Thrombomodulin - 29/46 MPM positive, 1/20 Lung CA positive - sensitivity 64%, specificity 95%, overall accuracy 74, predominantly membranous staining. No reactivity in spindle cell component of biphasic MPM. CK5/6 - 40/46 MPM positive, 1/20 lung CA positive - sensitivity 89%, specificity 95%, overall accuracy 91%. Cytoplasmic staining with perinuclear enhancement. High weight cytokeratins - 41/46 MPM positive, 5/20 lung CA positive- sensitvity 91%, specificity 75%, overall accuracy 86%. MOC31 5/46 MPM focally reactive, 18/20 lung CA positive. Ber-EP4 - 4/46 MPM positive, 20/20 lung CA positive. CEA- 2/46 MPM focal staining, 17/20 lung CA. Using logistic regression - combination of calretinin + Ber-EP4 OR CK 5/6 + Ber-EP4 correctly identified 97% of cases. Calretinin + CK5/6 + Ber-EP4 OR CK5/6 + Ber-EP4 + CEA correctly identified 98% of cases.

187	Klebe, S. N., M.:Leigh, J.:Henderson, D. W. 2009 Diagnosis of epithelial mesothelioma using tree-based regression analysis and a minimal panel of antibodies Pathology 41 2 140-148	Non comparative (case series)	+	173 MPM, 27 secondary adenocarcinoma	172 epithelioid MPM	CAM 5.2, CK5/6, calretinin, HBME-1, thrombomodulin, WT-1, EMA, CEA, CD15, B72.3, BG8 and TTF-1		NA	positive staining, equivocal staining (<2% cells stained or if uncertain if true staining or just high background staining) or neagtive staining		Nor reported	***General comments:*** Epithelial marker - CAM5.2 - 100% sensitivity, 0% specificity. MPM markers - calretinin 98.2% sensitivity, 81.5% specificity. CK5.6 - 96.6% sensitivity, 57.9% specificity. EMA - 90.9% sensitivity, 7.7% specificity, HBME-1 - 89.2% sensitivity, 76% specificity. Thrombomodulin - 89.6% sensitivity, 56% specificity. WT-1 - 77.8% sensitivity, 88.9% specificity. Adenocarcioma markers- B72.3 - 98.2% sens, 4.2 spec, BG8 - 83.2 sens, 88.5 spec, CD15 - 68.2 sens, 73.1 spec, CEA - 100% sens, 63% spec, Ber-Ep4 - 82.4% sens, 83.3% spec. TTF-1 - 92.9 sensitivity. 52.9% specificity. Tree-based regression analysis - panel of 3 Abs - calretinin, BG8 and CD15
188	Lucas, D. R. P., H. I.:Madan, S. K.:Adsay, N. V.:Wali, A.:Tabaczka, P.:Lonardo, F. 2003 Sarcomatoid mesothelioma and its histological mimics: A comparative	Non comparative (case series)	-	36 mesothelioma, 24 sarcoma, 10 pulmonary sarcomatoid carcinoma	EPP/local resection specimens. 10/36 biphasic, 10/36 sarcomatoid. 16/36 epithelioid	pancytokeratin, CK5/6, calretinin, WT-1, thombomodulin		NA	Intensity and distribution of immunostainin g		Not reported	***General comments:*** Pancytokeratin- 100% epithelioid MPM, 100% epithelioid component of biphasic MPM, 90% sarcomatoid component of biphasic turmours. 70% of sarcomatoid MPM, 17% sarcoma, 90% sarcomatoid carcinoma. CK5/6 - 100% epithelioid MPM. 40% epithelioid component of biphasic, 10% sarcomatoid component of biphasic, 0% sarcomatoid MPM, 4% sarcoma, 0% sarcomatoid carcinoma. Calretinin, both cytoplasmic and nuclear staining present - 100% epithelioid MPM, 90% epithelioid component of biphasic, 60% sarcomatoid component of biphasic, 70% sarcomatoid MPM- staining less intense and diffuse than eptihelioid, 17% sarcoma, 60% sarcomatoid carcioma. WT-1 (confined to nuclei)- 69% epithelioid MPM, 60% epithelioid component of biphasic, 20% sarcomatoid component of biphasic, 10% sarcomatoid MPM. 4% sarcoma, 0% sarcomatoid carcinoma. Thrombomodulin - 81% epithelioid MPM. 90% epithelioid component of biphasic, 50% sarcomatoid component of biphasic, 70% sarcomatoid MPM (less intense and diffuse than epithelioid). 38% sarcoma. 40% sarcomatoid carcioma
189	Ordonez, N. G. 2013 Mesothelioma with signet-ring cell features: Report of 23 cases Modern Pathology 26 3 370-384	Non comparative (case series)	-	23 epithelioid MPM with signet ring cell features + 7 cases of signet ring cell adenocarcinoma	20/23 male, mean age 60 years, 12/23 asbestos exposed, 16/23 smokers, 21/23 pleural meso, 2/23 peritoneal	Light microscopy, IHC (calretinin, CK5/6, CK7, CK20, WT-1, podoplanin, mesothelin, MOC-31, CEA, TAG72, CD15, TTF1, Napsin A, CDX2. Electron microscopy		mean time to death 15 months (range 3-42 months)			Not reported	***General comments:*** All MPM +ve for calretinin, keratin 5/6, keratin 7, mesothelin. 93% +ve for podoplanin and 91% for WT-1. No MPM reacted for MOC-31, CEA, TAG-72, CD15, TTF-1, Napsin A or CDX2. Lung adeno - 100% positive for keratin 7, CEA, naspin A, 86% for TTF-1 and TAG-72, 71% for CD15 and 14% for mesothlin. All lung adenoca negative for calretinin, keratin 5/6, WT-1, podoplanin and CDX2. Electron microscopy - signet ring like appearance primarily caused by the presence of a single or sometimes multiple intracytoplasmic lumina - as lumen increases in size they progressively displace the nucleus towards the periphery of the cell whereas in signet ring cell adenoacrcinoma of the lung the signet ring morphology was primarily caused by an intracytoplasmic accumulation of a large number of mucin granules of moderate electron density.
190	Brockstedt, U. G., M.:Dobra, K.:Dejmek, A.:Hjerpe, A. An optimized battery of eight antibodies that can distinguish most cases of	Non-comparative (case series)	-	176	119 epithelioid MPM and 57 metastatic adenocarcinoma	Vimentin, MNF116, Calretinin, EMA at cell membrane, Thrombomodulin, HBME-1, CEA, CD15, BerEp4, Sailosyl-TN		na	positivity of staining		Swedish heart and lung fund and the swedish cancer fund	***General comments:*** Vimentin reactivity in epithelial cells - 77/119 (64.7%) MPM, 8/57 (14%) adenocarcinoma. MNF116 reactivity in fibrous cells - 68/119 (57.1%) in MPM, 15/57 (26%) in adenocarcinoma, Calretinin - 110/119 (92.4%) in MPM, 16/57 (28%) adenocarcinoma. EMA reactivity at cell membrane - 94/119 (79%) MPM, 18/57 (32%) in adenocarcinoma. Thrombomodulin - 74/119 (62.2%) in MPM, 13/57 (23%) in adenocarcinoma. HBME-1 - 91/119 (76.5%) MPM, 20/57 (35%) adenocarcinoma. CEA - 2/119 (1.7%) MPM, 37/57 (65%) adenocarcinoma. CD15 - 18/119 (15.1%) MPM, 46/57 (81%) adenocarcinoma. BerEp4 - 19/119 (16%) MPM, 40/57 (70%) adenocarcionma. Sialosyl-TN - 28/119 (23.5%) MPM, 46/57 (81%) adenocarcinoma.

191	Comin, C. E. D., S.:Novelli, L.:Santi, R.:Asirelli, G.:Messerini, L. h-Caldesmon, a useful positive marker in the diagnosis of pleural malignant mesothelioma, epithelioid type	Non-comparative (case series)	-	140	70 epithelioid MPM, 70 lung adenocarcinoma	h-Caldesmon, calretinin, CK5/6, Thrombomodulin, EMA, CEA, TTF-1, Ber-Ep4, B72.3, CD15		NA	Immunoreactivity (positive (strong/moderate/mild) or negative). The % of immunostained cells: 1+ (1 - 25%), 2+ (26 - 50%), 3+ (51 - 75%), 4+ (76 -		Not reported	***General comments:*** Caldesmon Is a cytoskeleton-associated protein present in smooth and non-smooth muscle cells, involved in the regulation of cellular contraction. The high molecular weight isoform (h-Caldesmon) is thought to be restricted to smooth muscle and myoepithelial cells. h-Caldesmon - Epithelioid MPM 68/70 (97%) positive (60/70 4+, cytoplasmic). 0/70 Lung adenocarcinoma positive. Non-neoplastic mesothelial cells also intensely positive. Calretinin - Epithelioid MPM 70/70 positive (58/70 4+, nuclear and cytoplasmic). Lung adenocarcinoma - 3/70 positive (1+). CK5/6 - Epithelioid MPM 68/70 positive (43/70 4+, cytoplasmic). Lung adenocarcinoma - 2/70 positive. Thrombomodulin - MPM 53/70 positive, 11/70 lung adenocarcinoma positive. EMA - 67/70 MPM positive, 70/70 lung adenocarcinoma positive. CEA - 0/70 MPM positive, 64/70 lung adenocarcinoma positive. TTF-1 - 0/70 MPM positive, 54/70 lung adenocarcinoma positive. Ber-Ep4 - 8/70 MPM positive, 68/70 lung adenocarcinoma positive
192	Comin, C. E. N., L.:Boddi, V.:Paglierani, M.:Dini, S. Calretinin, thrombomodulin, CEA and CD15: a useful combination of immunohistochemical markers for differentiating pleural epithelial	Non-comparative (case series)	-	65	42 Epithelioid MPM, 23 lung adenocarcinoma	Calretinin, thrombomodulin, CD44H, HBME-1, CEA and CD15		NA	Immunoreactivity (positive (strong/moderate/mild) or negative). The % of immunostained cells: 1+ (1 - 25%), 2+ (26 - 50%), 3+ (51 - 75%), 4+ (76 - 100%).		Not reported	***General comments:*** Calretinin - 42/42 postivie, both nuclear and cytoplasmic reactivity, 2/23 adenocarcinoma weakly positive - 1 in <10% of cells. Thrombomodulin - 39/42 MPM positive (membranous), 5/23 adenocarcinoma positive. CD44H - 42/42 MPM positive (cell membrane surface), 13/23 lung adenocaricnoma positive. HBME-1 - 41/42 MPM positive (2 membranous, 15 cytoplasmic, 6 both). CEA - 4/42 MPM showed focal and weak reactivity, 22/23 adenocarcinoma showed cytoplasmic staining. CD15 - 2/42 MPM positive, 23/23 adenocarcinoma positive. Overall - Calretinin - 100% sensitivity, 91.3% specificity. Thrombomodulin - 92.9% sensitivity, 78.3% specificity. CD44H- 100% sens, 43.5% spec, HBME-1 - 97.6% sens, 0% specificity. EMA - 97.6% sens, 0% spec.
193	Cury, P. M. B., D. N.:Corrin, B.:Nicholson, A. G.The use of histological and immunohistochemical markers to distinguish pleural malignant mesothelioma and in situ mesothelioma from reactive mesothelial hyperplasia and reactive pleural fibrosis. Journal of Pathology 1999;189(2):251-7	Non-comparative (case series)	-	65	31 MPM - 14 epithelioid, 14 biphasic, 3 sarcomatoid. "In situ component found in addition to invasive tumour in 7 cases. 20 reactive meosthelial hyperplasia, 14 reactive pleural fibrosis	EMA, bcl-2, p53 protein		NA	Nuclear staining with p53, cytoplasmic staining for bcl-2, cell membrane staining for EMA		Not reported	***General comments:*** p53 - 30/31 MPM +ve, higher proportion of tumour cells stained positive in epithelioid areas. 13/20 reactive mesothelial hyperplasia - surface mesothelial cells showed weak focal nuclear positivity for p53. 3/14 reactive pleural fibrosis positive for p53 (focal staining). EMA - 30/31 MPM strong and widespread positivity, staining stronger in epithelioid component. Reactive mesothelial hyperplasia - 5/20 postiive staining for EMA. Reactive pleural fibrosis - 6/14 positive for EMA. BCL-2 - 0/31 MPM positive, reactive mesothelial hyperplasia - 0/20 positive, reactive pleural fibrosis - 0/14 positive.

194	Cury, P. M. B., D. N.:Fisher, C.:Corrin, B.:Nicholson, A. G. Value of the mesothelium-associated antibodies thrombomodulin, CK5/6, calretinin and CD44H in	Non comparative (case series)	-	124	61 epithelioid MPM, 63 metastatic adenocarcinoma - 21 breast, 19 lung, 10 colon, 6 ovart, 4 kidney, 1 epididymis, 1 uterus, 1 pancreas.	Thrombomodulin, CK5/6, calretinin, CD44H		NA	Positive staining - +ve for thrombomodulin and CD44H if any tumour cells showed positive membrane staining. CK5/6 +ve if any		Not reported	***General comments:*** Thrombomodulin - 55/61 (90%) MPM positive, 12/63 (19%) adenocarcinoma +ve. CK5/6 - 39/43 (91%) MPM positive, 9/63 (14%) adenocarcinoma positive. CD44H - 39/43 (91%) MPM positive, 27/60(45%) adenocarcinoma positive. Calretinin - 47/51 (92%) MPM positive, 23/59 (39%) adenocarcinoma positive. All 4 antibodies stained reactive mesothelium.
202	Attanoos, R. L. G., H.:Gibbs, A. R. Mesothelioma-binding antibodies: thrombomodulin, OV632 and HBME-1 and their use in the diagnosis of MPM. Histopathology 1996;29(3);209-15	Non-comparative (case series)	+	75	42/75 Mesothelioma- 27/42 pleural, 15/27 peritoneal. 32/75 lung adenocarcinoma	Thrombomodulin, OV632, HBME-1		NA			Not reported	***General comments:*** Thrombomodulin - +ve in 14/27 (52%) of pleural mesotheliomas - 8/12 (67%) epithelioid, 4/10 (40%) biphasic, 2/5 (40%) sarcomatoid and 8/15 (53%) peritoneal mesothelioma, 2/32 (6%) lung adenocarcinoma. Staining predominantly membranous. OV632 +ve in 23/27 (85%) of pleural mesotheliomas- 12/12 (!00%) epithelioid, 8/10 (80%) biphasic and 3/5 (60%) sarcomatoid, 4/15 (27%) of peritoneal mesothelioma and 20/32 (63%) lung adenocarcinoma. HBME-1 +ve in 16/27 (59%) of pleural mesotheliomas - 7/12 (75%) epithelioid, 7/10 (70%) biphasic and 0/5 sarcomatoid; 10/15 (67%) peritoneal mesothelioma and 23/32 (72%) lung adenocarcinoma. Authors conclude that only thrombomodulin specific enough to be of routine clinical use (however sensitivity 75% for epithelioid MPM and 52% for pleural mesothelioma)
203	Brown, R. W. C., G. M.:Tandon, A. K.:Allred, D. C. Multiple marker immunhistomchemical phenotypes distinguishing malignant pleural mesothelioma from pulmonary adenocarcinoma. Human Pathology 1993;24(4):347-54		+	137	34 MPM - 29/34 Pleural, 5/34 peritoneal and 103 lung adenocarcinomas	7 IHC markers - CEA, B72.3, Leu-M1, polyclonal anti secretory component (SC), CA125, vimentin, thrombomodulin and periodic acid-Schiff-diastase histochemistry for mucin		NA	Degree of staining - estimating the proportion of positive tumour cells on the slide - 0 = none, 1 = <1/1-, 2= 1/10-1/3, 3=1/3 - 2/3, 4= >2/3. All tumours with score >0 were counted as positive		NCI Cancer Center Support	***General comments:*** CEA - 97% adenoCA positive (cytoplasmic, diffusely distributed), 3% MPM positive - negative CEA 97% specific and 97% sensitive for MPM). B72.3 - 90% adenoCA positive (surfact membrane and cytoplasm, heterogeneously distributed), 0% MPM positive. Leu-M1 - 77% adenoCA positive (surface membrane and cytoplasmic), 6% MPM positive (apical and restricted to tubopapillary formations). PAS-distase- 66% adenoCA positive (cytoplasmic, heterogeneously distributed), 9% MPM positive (focal distribution). Secretory component - 62% adenoCA positive (cytoplasmic), 0% MPM positive. CA125 - 15% adenoCA positive, 3% MPM positive. Vimentin - 19% adenoCA positive, 65% MPM positive (highly variable extent and distribution of staining). Thrombomodulin - 58% adenoCA positive, 60% MPM positive (cytoplasmic, membranous and heterogeneously distributed, generally more intense and widely distributed in MPM). Overall best combination of markers - CEA -ve/B72.3 -ve/Leu-M1 -ve = 99% specificity and 91% sensitivity for MPM.

204	Collins, C. L. O., N. G.:Schaefer, R.:Cook, C. D.:Xie, S. S.:Granger, J.:Hsu, P. L.:Fink, L.:Hsu, S. M. Thrombomodulin expression in MPM and pulmonary adenocarcinoma. Am J Pathology 1992;141(4):827-33	Non-comparative (case series)	-	79 (+ 2 mesothelioma cell lines)	31 MPM - 29 epithelioid, 2 biphasic. 48 lung adenocarcinoma	Thrombomodulin		NA	Expression of thrombomodulin in tissue		NIH grant	***General comments:*** All MPM stained positively with thrombomodulin - cytoplasmic and cell surface staining. Cells of the cultured meso cell lines also stained positively. Thrombomodulin expressed on cell surface of normal endothelial and mesothelial cells + reactive mesothelial cells isolated from pleural effusion also stained positively. 1/48 adenocarcinoma stained positively with thrombomodulin.
205	Dejmek, A.B., U.:Hjerpe, A. Optimization of a battery using nine immunocytochemical variables for distinguishing between epithelial mesothelioma and adenocarcinoma APMIS 1997;105(11)889-94	Non-comparative (case series)	-	153	110 MPM. 43 metastatic adenocarcinoma	Vimentin, Keratin, CAM5.2, EMA, HBME-1, Thrombomodulin, CEA, CD15, BerEp4, Sialosyl-TN		NA	Immunoreactivity (positive if >20% tumour cell population or when foci (>5 cells) with strong reactivity present		Not reported	***General comments:*** Vimentinreactivity in epithelial cells - 60/100 MPM, 1/43 adenocarcinoma. Keratin - 90/110 MPM, 23/43 adenocarcinoma. CAM5.2 - 108/110 MPM, 43/43 adenocarcinoma. Coexpression of vimentin and CAM 5.2 - 59/110 MPM , 1/43 adenocarcinoma. EMA (cell membrane) - 82/110 MPM, 9/43 lung adenocarcinoma, EMA (fibroblasts) - 33/110 MPM, 0 adenocarcinoma, EMA (cytoplasm) - 92/110 MPM, 39/43 adenocarcinoma. Thrombomodulin - 69/110 MPM, 10/43 adenocarcinoma. HBME-1 - 78/110 MPM, 11/43 adenocarcinoma. CEA - 1/110 MPM, 29/43 adenocarcinoma. CD15 - 22/110 MPM, 35/43 adenocarcinoma. BerEp4 - 14/110 MPM, 28/43 adenocarcinoma. Sialyl-TN - 24/110 MPM, 34/43 adenocarcinoma
206	Dejmek, A. H., A. The combination of CEA, EMA, BerEp4 and hyaluronan analysis specifically identifies 79% of all histologically verified mesotheliomas causing an effusion. Diagnostic cytopathology 2005;32(3):160-6	Non-comparative (case series)	-	89 + 107	36 + 21 MPM, 53 + 86 adenocarcinoma	CEA, EMA, mEMA, BerEp4, Vimentin, Thrombomodulin, CA125, Siadlyl-Tn, HBME-1. Hyaluronan		NA	ICC reactivity		Nor reported	***General comments:*** CEA - old cases - 1/32 MPM positive 42/53 adenocarcinoma positive, new cases - 0/18 MPM positive, 51/84 adenocarcinoma positive. EMA - old cases 28/36 MPM positive, 49/52 adenocarcinoma positive, new cases - 12/19 MPM positive, 72/80 adenocarcinoma positive. mEMA - old cases - 21/36 MPM positive, 1/52 adenocarcinoma positive, new cases - 11/19 MPM positive, 0/72 adenocarcinoma positive. BerEp4 - old cases 6/36 MPM positive, 51/53 adenocarcinoma positive. New cases - 3/19 MPM positive, 77/85 adenocarcinoma positive. Vimentin - old cases - 26/33 MPM positive, 25/49 adenocarcinoma positive. New cases - 17/18 MPM positive, 34/70 adenocarcinoma positive. Thrombomodulin - 6/7 MPM positive, 28/59 adenocarcinoma positive. CA125 - 12/13 MPM positive, 46/70 adenocarcinoma positive. Sialyl-TN - 0/7 MPM positive, 47/61 adenocarcinoma positive. HBME-1 - 5/7 MPM positive, 28/58 adenocarcinoma positive. Hyaluronan - hyaluronan level >75mg/l found in 20/57 MPM cases. No adenocarcinomas had values >25mg/l - 36/57 MPM cases had hyaluronan >25mg/l.

207	Fetsch, P. A. A., A.:Hijazi, Y. M. Utility of the antibodies CA19-9, HBME-1, and thrombomodulin in the diagnosis of malignant mesothelioma and adenocarcinoma in cytology. Cancer 1998;84(2):101-8	Non-comparative (case series)	-	87	38 MPM - 28 Epithelioid, 6 biphasic, 1 sarcomatoid. 49 adenocarcinoma - 15 breast, 8 ovary, 5 prostate, 10 lung, 11 GI.	CA19-9, HBME-1, Thrombomodulin		NA	Positive staining		Not reported	***General comments:*** CA19-9 - 1/38 MPM positive, 24/49 ACA positive (3/10 lung). HBME-1 - 34/38 MPM positive - thick membranous staining in 28/34, thin membranous in 6/34. 6/38 MPM also had cytoplasmic HBME-1 staining but always in association with membranous staining. HBME-1 - 28/43 ACA positive (18/28 thick membranous, 10/28 thin membranous, 8/8 lung). Thrombomodulin - 24/36 MPM positive staining both cytoplasmic and membranous, 21/40 ACAs positive again both cytoplasmic and membranous. In general thrombomodulin staining was "less intense" in ACA compared to MPM. Authors conclude that CA19-9 may be useful but thrombomodulin and HBME-1 lack specificity to be of routine clinical utility
211	Clover, J. O., J.:Edwards, C. Anti-cytokeratin 5/6: a positive marker for epithelioid MPM. Histopathology 1997;31(2):140-3	Non-comparative (case series)	-	60	27 metastatic lung adenocarcinoma, 33 MPM - 10/33 sarcomatoid or desmoplastic, 23/33 epithelioid or biphasic.	Cytokeratin 5/6			Positive/Negative staining		Not reported	***General comments:*** 23/23 epithelioid or biphasic - positive CK5/6 immunostaining. Saromatoid area weak or absent. Focal positivity in 1/27 lung adenocarcinoma.
213	Delahaye, M. v. d. H., F.:van der Kwast, T. H. Complementary value of five carcinoma markers for the diagnosis of malignant mesothelioma, adenocarcinoma metastasis, and reactive mesothelium in serous effusions. Diagnostic cytopathology 1997;17(2):115-20	Non-comparative (case series)	-	154	41 MPM, 25 reactive effusions (malignancy with effusion and negative f/u for 2 years), 88 metastatic adenocarcinoma - lung, breast, GI, ovarian.	anti-CEA, MOC-31, Leu-M1, B72.3, Ber-Ep4		Reactive effusions had been F/ U for at least 2 years	Positive staining		Not reported	***General comments:*** CEA - 0/41 MPM positive, 0/25 reactive positive, 48/88 adenocarcinoma (18/24 lung) positive. MOC-31 - 5/41 MPM positive, 0/25 reactive mesothelium positive, 67/88 adenocarcinoma (20/24 lung) positive. Leu-M1- 0/41 MPM positive, 0/25 reactive mesothelium positive, 25/88 adenocarcinoma (13/24) positive. Ber-Ep4 - 1/41 MPM positive, 0/25 reactive mesothelium positive, 69/88 adenocarcinoma (20/24 lung) positive. B72.3 - 1/41 MPM positive, 0/25 reactive mesothelium positive, 68/88 adenocarcinoma (18/24 lung) positive. Conclusion - these markers can help differentiate adenocarcinoma from mesothelioma/reactive mesothelium on cytology but is not helpful in diagnosing mesothelioma or differentiating meso from benign reactive effusions

214	Garcia-Prats, M. D. B., C.:Sotelo, T.:Lopez-Encuentra, A.:Mayordomo, J. I. A comparative evaluation of immunohistochemical markers for the differential diagnosis of malignant pleural tumours. Histopathology 1998;32(5):462-72	Non-comparative (case series)	+	63	40 MPM - 26 epithelioid, 10 sarcomatoid, 4 biphasic. 23 metastatic carcinomas to the pleura (15 lung adenocarcinoma)	CAM5.2, K903, IT20, EMA, CEA, Leu-M1, B72.3, Ber-H2, Ber-Ep4, Vimentin, Desmin		NA	positivity of staining - + for focal staining <30% tumour cells, ++ = 30-60%, +++ >60% tumour cells		Research fund of the health ministry of spain	***General comments:*** CAM5.2 - 39/40 MPM positive, 15/15 lung adenocarcinoma, K903 - 25/40 MPM positive - 19/26 Epithelioid, 3/10 sarcomatoid, 3/4 biphasic; 8/15 lung adenocarcinoma positive. IT20 - 18/40 MPM positive - 15/23 epithelioid, 1/10 sarcomatoid, 2/4 biphasic; 2/15 lung adenocarcinoma positive. EMA - 36/40 MPM positive - 25/26 epithelioid, 8/10 sarcomatoid, 3/4 biphasic; 2/15 lung adenocarcinoma positive. CEA - 1/40 MPM positive (biphasic patient); 10/15 lung adenocarcinoma positive. Leu-M1 - 2/40 MPM positive (1 epithelioid and 1 sarcomatoid); 7/15 lung adenocarcinoma positive. B72.3 - 0/40 MPM positive, 10/15 lung adenocarcinoma positive. Ber-H2 - 16/40 MPM positive, 2/15 lung adenocarcinoma positive. Ber-Ep4- 1/40 MPM positive (biphasic patient); 13/15 lung adenocarcinoma positive. Vimentin - 35/40 MPM positive - 23/26 epithelioid, 8/10 sarcomatoid, 4/4 biphasic; 1/15 lung adenocarcinoma positive. Desmin - 18/40 MPM positive - 12/26 epithelioid, 4/10 sarcomatoid, 2/4 biphasic; 0/15 lung adenocarcinoma positve. With a cut off of one positive cell - Vimentin - sensitivity 87.5%, specificity 95.7% for MPM, Desmin - 45% sensitivity, 100% specificity for MPM. Ber-H2 - sensitivity 42.5%, specificity 87% for MPM. At a cut off of >30% positive cells - Vimentin - sensitivity 55%, specificity 95.7%. Combination of negative Ber-Ep4 and positive vimentin - 85% sensitivity and 100% specificity for MPM.
215	Dejmek, A. H., A. 2000 Reactivity of six antibodies in effusions of mesothelioma, adenocarcinoma and mesotheliosis: Stepwise logistic regression analysis Cytopathology 11	Non comparative (case series)	-	36 MPM, 53 lung adenoCA, 24 reactive effusions	Not specified	CEA, CCAM5.2, EMA, Leu-M1, Vimentin, BerEp4		NA	Positive immunostaining - 'moderate or strong' considered positive. 'weak staining or staining only found in occasiona dispersed cells negative'		Not reported	***General comments:*** CEA - 1/32 MPM +ve, 42/53 lung adenoCA +ve, 0/24 reactive +ve. Vimentin - 26/33 MPM +ve, 25/49 lung adenoCA +ve, 20/24 reactive +ve. CAM5.2 - 33/34 MPM +ve, 50/51 lung adneo +ve, 24/24 reactive +ve. BerEp4 - 6/36 MPM +ve, 51/53 lung adeno +ve, 24/24 reactive +ve. Leu-M1 - 5/35 MPM +ve, 24/47 lung adeno +Ve, 1/24 reactive +ve. EMA (Any staining) - 28/36 MPM +ve, 49/52 lung adeno +ve, 1/24 reactive +ve. EMA (membranous staining) - 21/36 MPM positive, 1/52 lung adeno +ve, 0/24 reactive +ve. Stepwise logistic regression - CEA -ve, BerEp4 -ve and mEMA +ve - sensitivity 47%, specificity 100%.
216	Aerts, J. G. D., M.:van der Kwast, T. H.:Davidson, B.:Hoogsteden, H. C.:van Meerbeeck, J. P. 2006 The high post-test probability of a cytological examination renders further investigations to establish a diagnosis of epithelial	Non comparative (case series)	-	39 patients - 14 epithelioid MPM, 12 adenocarcioma (7/12 lung), 13 benign effusions	Not detailed	Morphology, IHC (Tag 72, BerEp4, anti-CEA, EMA) and electron microscopy	Histology	Not specified	Sensitivity, specificity, likelihood ratio and post-test probability		Not reported	***General comments:*** Prospective study. Method of identification of patients and inclusion/exclusion criteria not specified.Diagnostic performance for MPM - Morphology - sensitivity 86%, specificity 96%, LR 21.5, PTP - 92%. For IHC (MPM if only EMA stained positive and rest negative) - sensitivity 71%, specificity 100%, LR 100, PTP 100%. For electron microscopy (4 /39 not analysed due to technical difficulties) - sensitivity 57%, specificity 96%, LR 21.5, PTP 92%

217	al-Saffar, N. H., P. S., 1990, Vimentin, CEA and keratin in the diagnosis of mesothelioma, adenocarcinoma and reactive pleural lesions, ERJ 1990;3(9):997-1001	Non-comparative (case series)	+	74 speciments- 38 MPM, 19 adenoca, 17 reactive mesothelial proliferation	Meso population - 27/38 surgical biopsies - 17/27 epithelioid, 6/17 fibrous, 4/17 biphasic; 11/38 necropsy specimens - 7/11 epithelioid, 3/11 fibrous, 1/11 biphasic	CEA, Cytokeratin, vimentin		NA	% of staining with marker - negative = 0%, + = 1-20%, ++ 21-50%, +++ = 51-100%		Not reported	***General comments:*** Vimentin +ve in 14/17 epithelioid MPM, 6/6 sarcomatoid MPM, 3/4 biphasic MPM, 0/19 adenocarcionma, 13/17 reactive mesothelial proliferation. CEA +ve in 0/17 epithelioid, 0/6 sarcomatoid, 0/4 biphasic, 19/19 adenocarcinoma, 0/17 reactive mesothelial proliferation. Cytokeratin +ve in 13/17 epithelioid, 2/6 sarcomatoid, 4/4 biphasic, 15/19 adenocarcinoma, 8/17 reactive mesothelial proliferation. Reactivity to vimentin also demonstrated in other tissue constituents including fibroblasts, vascular smooth muscle cells, histocytes, post-capliiary venules and endothelial cells. PM cases not as consistent - ?due to fixation.
219	Bakir, K. K., N. E.:Deniz, H.:Guldur, M. E. TTF-1 and surfactant B as co-adjuvants in the diagnosis of lung adenocarcinoma and pleural mesothelioma. Annals of Diagnostic Pathology 2004;8(6):337-41	Non comparative (case series)	-	45	15/45 MPM - 7 male, 8 female, mean age 54.9 years (subtypes not specified), 30/45 - lung adenocarcinoma - 24 male, 6 female, mean age 57.4 years.	TTF-1 and Surfactant B		NA	Degree of staining - - no reaction, + 0-10%, ++ 11-50%, +++ >50%. Nuclear staining for TTF-1 and cytoplasmic staining for SP-B considered +ve		Not reported	***General comments:*** SP-B - MPM - 2/15 + pale staining, 13/15 negative. Lung adenocarcinoma - 4/30 +++, 2/30 ++, 24/30 negative- no statistically significant difference between MPM and lung adenocarcinoma. TTF-1 - MPM - 15/15 negative. Lung adenocarcinoma - 22/30 +ve staining (14/16 well differentiated).
221	Attanoos RL, Griffin A , Gibbs AR. The use of immunohistochemistry in distinguishing reactive from neoplastic mesothelium. A novel use for desmin and	Non comparative (case series)	+	100	60 epithelioid MPM (22 closed pleural biopsies, 20 open pleural biopsies and 18 PM). 40 reactive mesothelial hyperplasia, atypical mesothelial hyperplasia	Desmin, EMA, p53, Bcl-2, P-glycoprotein, PDGF-R beta		NA	No staining, 1+ = <25% cells positive, 2+ = 26-75%, 3+ = >75% cells positive and intensity of staining - low, moderate or high		Not reported	***General comments:*** Desmin - 6/60 (10%) MPM - all cytoplasmic, 34/40 (85%) reactive. Epithelial Membrane Antigen (EMA) - 48/60 (80%) MPM - membranous staining, 8/40 (20%) reactive. p53 - 27/60 (45%) MPM - nuclear distribution, 0/40 (0%) reactive. Bcl-2 - 0/15 (0%) MPM, 0/15 Reactive. P-glycoprotein - 2/15 (13%) MPM, 0/15 reactive. PDGF-R beta - 15/15 MPM., 6/15 (40%) reactive. Authors conclude that Desmin as a marker of reactive mesothelium and EMA as a marker of neoplastic mesothelium and mutated p53 protein useful.
222	Bateman, A. C. a.-T., R. K.:Newman, T.:Williams, J. H.:Herbert, A. Immunohistochemical phenotype of MPM: predictive value of CA125 and HBME-1 expression. Histopathology 1997,30(1):49-56	Non comparative (case series)	-	31	17 MPM - 8 epithelioid, 9 biphasic and 2 sarcomatoid. 14 adenocarcinoma - 3/14 lung, 4/14 breast, 2/14 large bowel, 2/14 oesophagus, 1/14 kidney, 2/14 unknown primary	HBME-1 and CA125		NA	Positive staining		Not reported	***General comments:*** CA125 - 15/17 MPM positive (membranous staining), 7/14 adenocarcinoma positive. HBME-1 - 17/17 MPM positive (membranous and cytoplasmic), 10/14 adenocarcinoma positive. CA125 and HBME-1 labelling positive in epithelioid component of biphasic tumours only (except 1 case- spindle cell component positive for HBME-1). Authors conclude that CA125 and HBME-1 while sensitive are not sufficiently specific to be useful for differentiation of MPM from adenocarcinoma

224	Cagle, P. T. B., R. W.:Lebovitz, R. M. p53 Immunostaining in the differentation of reactive processes from malignancy in pleural biopsy specimens. Human Pathology 1994;25(5):443-8	Non-comparative (case series)	+	73	40/73 MPM- 20 epithelioid, 11 biphasic, 9 sarcomatoid, 13/73 reactive hyperplasia, 18/73 metastatic adenocarcinoma, 2/73 suspicious but inconclusive of malignancy (later confirmed as malignant on resection) - 12	p53					Not reported	***General comments:*** Mutated p53 protein demonstrate markedly increased stability and therefore not rapidly degraded and accumulate in the nucleus. 47.5% MPM positive for p53 - 78% sarcomatoid positive, 36% biphasic positive, 40% epithelioid positive. 50% metastatic adenocarcinoma +ve p53 in >10% atypical cells. 0% reactive mesothelial hyperplasia positive with p53. Authors conclude that the total number of atypical cells in a biopsy specimen and the proportion of these cells that are immunopositive must be taken into account but p53 may be useful as an adjunct in the diagnosis of malignancy in equivocal pleural biopsy specimens.
225	Husain, A. N. M., M. K.:Gibbs, A.:Hiroshima, K.:Chi, Y.:Boumendjel, R.:Stang, N.:Krausz, T.:Galateau-Salle, F. 2014 How useful is GLUT-1 in differentiating mesothelial hyperplasia and fibrosing pleuritis from epithelioid and sarcomatoid mesotheliomas? An international collaborative study Lung Cancer 83 3 324-328	Non comparative (case series)	+	MPM - 78, Mesothelial hyperplasia - 31, fibrosiing pleuritis - 29	41/78 epithelioid, 29/78 sarcomatoid, 3/78 biphasic, 5/78 desmoplastic	GLUT-1		NA	% cells +ve immunostaining - 0%, 1-25% = 1+, 26-50% = 2+, >51% = 3+ Membranous or cytoplasmic staining		Not reported	***General comments:*** Unstained formalin fixed paraffin-embedded tissue - GLUT-1 +VE in 21/29 (72%) of sarcomatoid MPM, 21/41 (50%) epithelioid MPM, 3/3 (100%) biphasic, 0/5 desmoplastic, 0/29 fibrosing pleuritis and 0/31 mesothelial hyperplasia. Sarcomatoid - 3 cases 1+, 15 cases 2+, 3 cases 3+. With epithelioid MPM - 10 cases 1+, 11 cases 2+. Predilection for peri-necrotic tumour. % of tumour cells stained variable therefore utility of GLUT-1 restricted in limited biopsy material
	Bibliographic citation	Study type	Ev lev	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding	