BMJ Open

Protocol for a prospective observational cohort study collecting data on demographics, symptoms and biomarkers in people with mesothelioma (ASSESS-meso)

Ruairi J H Conway [ID] ,[1,2] Jenny Symonds,[2,3] Deborah Walton,[2,3] Janet Probets,[3] Charles Comins,[4] Louise Stadon,[3] John E Harvey,[2,3] Kevin G Blyth,[5,6] Nick A Maskell,[2,3] Anna C Bibby[2,3]

For numbered affiliations see end of article.

Correspondence to
Dr Ruairi J H Conway;
ruairi.conway@doctors.org.uk

ABSTRACT

Introduction Mesothelioma is a heterogeneous disease that can be challenging to monitor and prognosticate. ASSESS-meso is a multicentre, prospective, longitudinal observational cohort study of patients with mesothelioma. The primary aim is to describe different clinical phenotypes and investigate predictive and prognostic factors, including biomarkers from blood and pleural fluid. The secondary aim is to provide a resource for future trials and substudies.

Methods and analysis We aim to recruit 700 patients with a histological, cytological or clinicopathological diagnosis of mesothelioma, at any anatomical site (pleural, peritoneal, pericardial, etc). Longitudinal data will be collected, including clinical information, radiological investigations, blood tests and patient-reported outcome measures for breathlessness, chest pain and sweats. Preplanned analyses will use Cox proportional hazards method to evaluate factors associated with survival, linear and logistic regression models to investigate associations with symptoms, and analysis of variance modelling to explore changes in symptoms over time.

Ethics and dissemination Ethical approval has been granted by the Research Ethics Committee South West—Central Bristol (17-SW-0019) and Health Research Authority (IRAS ID 220360). A study steering committee has been established and results will be published OpenAccess in peer-reviewed journals.

Trial registration number ISRCTN: 61861764.

INTRODUCTION

Mesothelioma is an aggressive asbestos-associated malignancy of the serosal surface that affects the pleura most commonly (malignant pleural mesothelioma, MPM).[1] Mesothelioma is usually incurable with a median survival of 8–14 months from diagnosis.[2 3] For two decades, cisplatin and pemetrexed doublet was the standard of care for MPM, despite offering a median survival benefit of just 2.8 months, compared with single-agent

---

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ ASSESS-meso is a pragmatic prospective observational cohort study, which allows collection of longitudinal data in a representative cohort of patients with mesothelioma for the first time.

⇒ The high volume of demographic and disease characteristic data, alongside patient-reported outcome measures across multiple domains, will allow us to describe clinical phenotypes and factors associated with poor prognosis.

⇒ Collection and storage of serial biological samples throughout the clinical journey provides an invaluable resource for further exploration into key unanswered research questions around diagnostic and treatment response biomarkers.

⇒ The main limitation is that our study is observational, and therefore, analysis will be primarily descriptive with scope for regression analysis and hazards modelling.

---

cisplatin.[4] Recently, addition of the vascular endothelial growth factor antibody bevacizumab to this regimen has been shown to extend survival to 18.8 months.[5] Surgical resection approaches have failed to demonstrate significant improvement in survival[6–9] and are therefore no longer routinely offered, particularly in the UK setting. Pleurodesis via VATS or talc slurry and poudrage, and indwelling pleural catheters are useful for pleural fluid management.[7 10]

However, the greatest breakthrough in MPM treatment came in early 2021 with the demonstration that combination ipilimumab (CTLA4 antagonist) and nivolumab (PD1 antagonist) enhanced overall survival compared with cisplatin/pemetrexed[11]—a finding that is likely to change the standard of care in the front-line setting. Further

novel therapies are under investigation, including oncolytic viruses, mesothelin-targeted agents and multimodal approaches.[12–14]

The mesothelioma literature consists predominantly of clinical trials, reflecting the impressive efforts that have been channelled into finding effective treatments over the past decade.[4 5 11 15] However, trial populations are often skewed towards patients with better performance status, younger age and fewer comorbidities, limiting generalisability to the wider mesothelioma population.[16] In addition, most clinical trials require patients to have received or be willing to receive chemotherapy, which excludes a proportion of patients.[17] There is a need to collect representative, longitudinal data in people with mesothelioma, to better understand the natural history of the disease and phenotype the highly variable disease pathways and prognosis.

Monitoring mesothelioma is challenging, and the current gold standard of modified RECIST criteria applied to CT images is limited.[18] Modified RECIST suffers from high intraobserver variability, poor correlation with volumetry and frequent mismatch with TNM staging.[19] Alternative approaches to disease monitoring and evaluation of treatment responses are required. A blood or pleural fluid-based biomarker could provide this resource, as well as potentially contributing to characterisation of disease phenotypes and prognostication.

Finally, ASSESS-meso aims to provide a resource for future clinical trials and substudies. Randomised interventional trials will be embedded within ASSESS-meso, based on the Trials within Cohorts (TwiCs) methodology.[20] A highly pragmatic design, TwiCs replicate real-world clinical care, yielding generalisable effectiveness outcomes, with the additional benefit of efficient recruitment and reduced risk of attrition.

METHODS AND ANALYSIS
Study design and aims
ASSESS-meso is a multicentre, prospective, longitudinal observational cohort study of patients with mesothelioma. The primary aim is to describe varying clinical phenotypes, investigate the clinical and biochemical factors associated with survival and response to treatment, and collect serial biological samples in a representative patient cohort. A secondary aim is to provide a resource for future clinical trials (TwiCs) and substudies.

Participants
Patients with a diagnosis of mesothelioma, at any anatomical site, achieved through any investigative method, will be eligible.

To participate, participants must meet all of the following inclusion criteria:
► Histological, cytological, clinicopathological or clinicoradiological diagnosis of mesothelioma, confirmed by local or regional lung cancer or mesothelioma multidisciplinary team (MDT).

► Willing and able to comply with study follow-up assessments.
► Willing and able to provide written informed consent.

A person who meets any of the following criteria will be ineligible:
► Age <18 years old.
► Unable to give written informed consent.
► Declines ongoing hospital follow-up.

Setting and sites
Up to 20 recruiting sites will be selected across the UK. To be eligible, centres need to be at least a secondary care-level institution, caring for at least 10 patients with mesothelioma a year (either via respiratory, oncology, thoracic surgery or other specialties), and have access to discussion at a local or regional MDT. To date, the study is open at 15 hospitals (listed in online supplemental Appendix). Recruitment started on 4 July 2017. Potential study participants will be identified at MDT meetings, pleural clinics, oncology clinics and nurse-led clinics. Potential participants will be screened by a member of the ASSESS-meso team and those who are eligible will be invited to discuss the study at their subsequent clinic appointment.

Enrolment
Eligible participants will be provided with a participant information sheet (PIS) and given the opportunity to discuss the study with a member of the ASSESS-meso research team and ask questions. Patients will have as much time as required to consider participation; there is no time limit between date of diagnosis and study enrolment. If they decide to participate, written informed consent will be obtained. If a patient is enrolled during a telephone or virtual appointment, witnessed verbal consent will be obtained by two members of the research team.

Participants will be asked to provide additional consent for blood and pleural fluid samples to be stored (if available) anonymously. Consent will be sought to allow sharing of pseudoanonymised biological samples with other researchers for future ethically approved research studies. Participants will also be invited to consent to be screened for future trials (TwiCs), to undergo random selection for the same trials and for their data to be used as comparison data in those trials if they are not selected.[20]

Withdrawal
Participants have the right to withdraw consent for their involvement in ASSESS-meso at any point. Withdrawal does not have to be justified and will not affect future or ongoing care. Participants can withdraw consent for all study involvement (in which case all data including biological samples will be destroyed), or from involvement with certain elements of the study (eg, further follow-up visits, the use of their existing recorded clinical data in future analyses, the storage and use of their biological samples).

Table 1 Schedule of investigations and assessments

Investigation	Baseline assessment	Follow-up assessments
Clinical review		
Patient demographics	✓	n/a
Disease characteristics	✓	n/a
Patient comorbidities	✓	n/a
Medication history	✓	✓
Oncological treatment history	✓	✓
Pleural intervention history	✓	✓
Patient-reported outcome measures		
VAS (breathlessness, chest pain, sweats)	✓	✓
Quality of life assessment	✓	✓
Pain (BPI)	✓	✓
Anxiety and depression (HADS)	✓	✓
Biological samples		
Blood	✓	✓
Pleural fluid	✓ (if available)	✓ (if available)
Pleural biopsy retrieval	✓ (if available)	n/a
Blood and pleural fluid for storage	✓ (if available)	✓ (if available)
Imaging		
CXR	✓	✓*
TUS	✓*	✓*
CT scan	✓	✓*
Assessment of eligibility for any current trials	✓	✓

*If clinically indicated.
BPI, brief pain inventory; CXR, chest X-ray; HADS, Hospital Anxiety and Depression Score; n/a, not available; TUS, thoracic ultrasound scan; VAS, Visual Analogue Scale.

Data collection

Electronic case report forms will be used to collect data at the initial baseline assessment and all subsequent follow-up visits. At each visit, assessment will occur across four main domains: clinical evaluation, patient-reported outcome measures (PROMs), biological samples and imaging (table 1). Study follow-up will occur when the participant attends for review as part of standard clinical care, at a minimum of 3 monthly. Data will be collected on a bespoke password-protected online database provided by REDCap (Vanderbilt University; Nashville, USA).

Clinical evaluation

Baseline demographics, comorbidities, performance status and medication history will be recorded for all patients. Disease characteristics will also be collected (histology, stage, mode of diagnosis), as will any oncological treatments received and pleural intervention history. Involvement of specialist teams, including palliative care or specific palliative interventions (eg, cordotomy) will also be recorded.

Patient reported outcome measures

PROMs for quality of life (QoL) and symptom severity (breathlessness, pain, sweats, anxiety and depression) will be completed at each study visit. Validated tools will include the EuroQol 5 Dimensions 5 Level health questionnaire (EQ-5D-5L),[21] the EORTC Quality of Life Questionnaire Core Questionnaire PALliative Cancer (QLQ-C15-PAL),[22] the Brief Pain Inventory,[23 24] and the Hospital Anxiety and Depression Score (HADS).[25]

Symptom scores for breathlessness, chest pain and sweats will be evaluated by using 10 cm Visual Analogue Scale (VAS). VAS is a validated tool for assessing breathlessness and chest pain in malignant pleural disease and is acceptable to patients.[26 27]

Biological samples

Baseline blood tests will include full blood count, urea and electrolytes, liver function tests, C reactive protein, lactate dehydrogenase (LDH), total protein, glucose and serum mesothelin. If appropriate, pleural fluid will be obtained and sent for protein, LDH, glucose, mesothelin and cytology. With consent, the research team will retrieve the biopsy on which the diagnosis of mesothelioma was made and, if there is sufficient tissue, sample(s) will be obtained and stored for research purposes.

The same blood tests will be taken at each follow-up visit. In addition, blood samples will be taken, processed and stored. If the participant has an indwelling pleural catheter in situ, drainage diaries will be reviewed at each follow-up visit, and a sample of pleural fluid obtained and stored.

Imaging

Thoracic ultrasound, chest X-ray (CXR) will be performed at baseline. The presence of non-expandable lung will be recorded. Diagnostic CT thorax will have been performed prior to the baseline assessment during initial clinical investigation, and the results of this will be recorded. At follow-up visits, imaging will be undertaken at the discretion of the clinician, as clinically indicated. All clinically indicated radiological investigations will be recorded for ASSESS-meso. It is anticipated that most participants will have a CXR at every clinic appointment and a CT scan every 6 months.

Screening for TwiCs

If a TwiC is underway, participants will be screened for eligibility at each study visit. Eligible participants will be randomly selected to participate, and those who are selected will be provided with a PIS for the trial. Having had the chance to discuss the trial with a member of the team, participants selected for the TwiC will be asked to

provide consent to enrol in the trial. Eligible participants who are not selected for the TwiC will provide control data from within ASSESS-meso. Participants in ASSESS-meso who are enrolled in, have completed or are providing control data for a TwiC will undergo adverse event monitoring at each ASSESS-meso visit to ensure ongoing safety monitoring for participants and to allow collection of data on late complications.

Telephone or virtual follow-up
Participants who are unable to attend regular in-person follow-up appointments may undergo telephone or virtual follow-up. Telephone and virtual appointments will be undertaken by a research nurse or any member of the research team. Assessments will include a clinical evaluation and review of pleural fluid drainage diaries. Any recent blood test results or imaging relevant to the current follow-up assessment will be imported and recorded. QoL questionnaires (EQ-5D-5L QoL) and symptom VAS scores will be sent via post or email for completion by the participant in their own time.

Cessation of follow-up and death
Follow-up assessments will cease if the participant dies or withdraws from the study. Mortality data will be cross-checked with National Health Service (NHS) Digital. A mortality form will be completed for each deceased patient.

Sample size
The sample size necessary to detect a difference in survival between different patient groups is 266 participants per group (532 in total). A recruitment target of 700 allows for approximately 20% withdrawal from the study, incomplete data and lost to follow-up. This calculation is based on the survival outcomes from previous chemotherapy trials in mesothelioma, in which chemotherapy increased 1-year survival from 38% to 50%.[4] A cohort of this size will provide 80% power (alpha 0.05) to detect a similar difference in 1-year survival, based on an individual patient characteristics (split at the median) or treatment received (binary yes/no).

Statistical analysis
The aim of ASSESS-meso is to describe phenotypes of disease and explore factors associated with prognosis. Descriptive statistics will be used to summarise characteristics. Factors associated with survival will use adjusted and non-adjusted Cox proportional hazards model. Multiple linear regression will be used to compare continuous outcomes and logistic regression used to compare dichotomous outcomes. We will use random effects models or robust estimates to allow for clustering between centres. Outcomes with repeat measurements will be analysed using regression modelling with adjustment for baseline values.

The sensitivity, specificity, negative predictive value and positive predictive value for predicting disease progression will be assessed at established cut-off levels for serum and pleural fluid biomarkers, cytokines, immune profile, receptor status and epigenetic markers. Receiver operator characteristic curves will be drawn. The gold standard for disease progression will be confirmation of progressive disease made at the regional mesothelioma MDT meeting.

End of trial
The study will end when the final participant (n=700) has been followed up for 12 months (or until death), or until the study has run for 10 years. An interim analysis is planned to be undertaken when recruitment reaches 25% of target to evaluate recruitment efforts and the demographicsand disease features of the cohort.

ETHICS AND DISSEMINATION
This study is run in accordance with the International Conference on Harmonisation Good Clinical Practice. All participants provided written informed consent or witnessed verbal informed consent. The research sponsor is North Bristol NHS Trust, who will oversee annual monitoring of sites. A study steering committee (SSC) has been formed to review study progress and review emerging data. All proposed substudies, amendments to the study protocol and publications generated through ASSESS-meso are reviewed for approval by the SSC. The study has been approved by the Research Ethics Committee South West—Central Bristol (17-SW-0019) and Health Research Authority (IRAS ID 220360). Results will be published in peer-reviewed OpenAccess journals.

PATIENT AND PUBLIC INVOLVEMENT
The SSC includes a patient/participant representative, who were involved in the study and study protocol design. They contribute to reviews of study progress and emerging data.

DISCUSSION
Mesothelioma continues to have a poor prognosis, with few tools for predicting survival or monitoring response to disease. ASSESS-meso is a pragmatic observational study that has been designed to address the need for longitudinal data from a representative cohort. By describing the variety of clinical phenotypes, it will provide insight into different disease pathways and outcomes. The repository of serial biological samples will provide a resource for exploring unanswered questions about blood and pleural biomarkers of diagnosis,[28] prognostication[29–34] and treatment response.[35 36] Biological samples will also enable investigation into the pathological, immunological and genetic processes involved in disease evolution and progression. Finally, ASSESS-meso will provide a resource for future clinical trials and substudies, providing high generalisability and external validity due to its pragmatic inclusion criteria.

Author affiliations
[1]Department of Medicine, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK
[2]Academic Respiratory Unit, University of Bristol, Bristol, UK
[3]Department of Respiratory Medicine, North Bristol NHS Trust, Westbury on Trym, UK
[4]Bristol Haematology and Oncology Centre, Bristol Royal Infirmary, Bristol, UK
[5]Institute of Cancer Sciences, University of Glasgow, Glasgow, UK
[6]Beatson Institute, Cancer Research UK Beatson Institute, Glasgow, UK

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

ORCID iD
Ruairi J H Conway http://orcid.org/0000-0003-0025-7060

REFERENCES

1 Bibby AC, Tsim S, Kanellakis N, et al. Malignant pleural mesothelioma: an update on investigation, diagnosis and treatment. *Eur Respir Rev* 2016;25:472–86.
2 Beckett P, Edwards J, Fennell D, et al. Demographics, management and survival of patients with malignant pleural mesothelioma in the National lung cancer audit in England and Wales. *Lung Cancer* 2015;88:344–8.
3 Woolhouse I, Bishop L, Darlison L, et al. British thoracic Society guideline for the investigation and management of malignant pleural mesothelioma. *Thorax* 2018;73:i1-i30.
4 Vogelzang NJ, Rusthoven JJ, Symanowski J, et al. Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma. *J Clin Oncol* 2003;21:2636–44.
5 Zalcman G, Mazieres J, Margery J, et al. Bevacizumab for newly diagnosed pleural mesothelioma in the mesothelioma Avastin cisplatin pemetrexed study (maps): a randomised, controlled, open-label, phase 3 trial. *Lancet* 2016;387:1405–14.
6 Cao C, Tian DH, Pataky KA, et al. Systematic review of pleurectomy in the treatment of malignant pleural mesothelioma. *Lung Cancer* 2013;81:319–27.
7 Rintoul RC, Ritchie AJ, Edwards JG, et al. 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;384:1118–27.
8 Treasure T, Lang-Lazdunski L, Waller D, et al. 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;12:763–72.
9 Taioli E, Wolf AS, Flores RM. Meta-Analysis of survival after pleurectomy decortication versus extrapleural pneumonectomy in mesothelioma. *Ann Thorac Surg* 2015;99:472–80.
10 Davies HE, Mishra EK, Kahan BC, et al. Effect of an indwelling pleural catheter vs chest tube and talc pleurodesis for relieving dyspnea in patients with malignant pleural effusion: the TIME2 randomized controlled trial. *JAMA* 2012;307:2383–9.
11 Baas P, Scherpereel A, Nowak AK, et al. First-Line nivolumab plus ipilimumab in unresectable malignant pleural mesothelioma (CheckMate 743): a multicentre, randomised, open-label, phase 3 trial. *Lancet* 2021;397:375–86.
12 Calabrò L, Morra A, Fonsatti E, et al. Tremelimumab for patients with chemotherapy-resistant advanced malignant mesothelioma: an open-label, single-arm, phase 2 trial. *Lancet Oncol* 2013;14:1104–11.
13 Calabrò L, Morra A, Fonsatti E, et al. Efficacy and safety of an intensified schedule of tremelimumab for chemotherapy-resistant malignant mesothelioma: an open-label, single-arm, phase 2 study. *Lancet Respir Med* 2015;3:301–9.
14 Nowak AK, Lesterhuis-Vasbinder D, Lesterhuis WJ. New directions in mesothelioma treatment. *Lung Cancer Manag* 2015;4:299–307.
15 Scherpereel A, Mazieres J, Greillier L, et al. Nivolumab or nivolumab plus ipilimumab in patients with relapsed malignant pleural mesothelioma (IFCT-1501 MAPS2): a multicentre, open-label, randomised, non-comparative, phase 2 trial. *Lancet Oncol* 2019;20:239–53.
16 Lau B, Boyer M, Lee JH, et al. Clinical trials eligibility of patients with malignant pleural mesothelioma: use of novel therapies and outcomes. *Clin Lung Cancer* 2020;21:378–83.
17 Bibby AC, De Fonseka D, Morley AJ, et al. Exploring the characteristics of patients with mesothelioma who chose active symptom control over chemotherapy as first-line treatment: a prospective, observational, single centre study. *BMC Palliat Care* 2017;16:71.
18 Byrne MJ, Nowak AK. Modified RECIST criteria for assessment of response in malignant pleural mesothelioma. *Ann Oncol* 2004;15:257–60.
19 Oxnard GR, Armato SG, Kindler HL. Modeling of mesothelioma growth demonstrates weaknesses of current response criteria. *Lung Cancer* 2006;52:141–8.
20 Relton C, Torgerson D, O'Cathain A, et al. Rethinking pragmatic randomised controlled trials: introducing the "cohort multiple randomised controlled trial" design. *BMJ* 2010;340:c1066.
21 Longworth L, Rowen D. Mapping to obtain EQ-5D utility values for use in NICE health technology assessments. *Value Health* 2013;16:202–10.
22 Groenvold M, Petersen MA, Aaronson NK, et al. The development of the EORTC QLQ-C15-PAL: a shortened questionnaire for cancer patients in palliative care. *Eur J Cancer* 2006;42:55–64.
23 Cleeland CS, Ryan KM. Pain assessment: global use of the brief pain inventory. *Ann Acad Med Singap* 1994;23:129-38.
24 Portenoy RK, Payne D, Jacobsen P. Breakthrough pain: characteristics and impact in patients with cancer pain. *Pain* 1999;81:129–34.
25 Hopwood P, Howell A, Maguire P. Screening for psychiatric morbidity in patients with advanced breast cancer: validation of two self-report questionnaires. *Br J Cancer* 1991;64:353–6.
26 Mishra EK, Corcoran JP, Hallifax RJ, et al. Defining the minimal important difference for the visual analogue scale assessing dyspnea in patients with malignant pleural effusions. *PLoS One* 2015;10:e0123798.
27 Mishra EK. Measurement of breathlessness in patients with malignant pleural effusions. *Curr Pulmonol Rep* 2016;5:1–6.
28 Tsim S, Alexander L, Kelly C, et al. Serum proteomics and plasma Fibulin-3 in differentiation of mesothelioma from asbestos-exposed controls and patients with other pleural diseases. *J Thorac Oncol* 2021;16:1705–17.
29 Linch M, Gennatas S, Kazikin S, et al. A serum mesothelin level is a prognostic indicator for patients with malignant mesothelioma in routine clinical practice. *BMC Cancer* 2014;14:674.
30 Hassan R, Remaley AT, Sampson ML, et al. Detection and quantitation of serum mesothelin, a tumor marker for patients with mesothelioma and ovarian cancer. *Clin Cancer Res* 2006;12:447–53.

31 Bonotti A, Simonini S, Pantani E, *et al*. Serum mesothelin, osteopontin and vimentin: useful markers for clinical monitoring of malignant pleural mesothelioma. *Int J Biol Markers* 2017;32:126–31.

32 Cui A, Jin X-G, Zhai K, *et al*. Diagnostic values of soluble mesothelin-related peptides for malignant pleural mesothelioma: updated meta-analysis. *BMJ Open* 2014;4:e004145.

33 Arnold DT, De Fonseka D, Hamilton FW, *et al*. Prognostication and monitoring of mesothelioma using biomarkers: a systematic review. *Br J Cancer* 2017;116:731–41.

34 de Fonseka D, Arnold DT, Stadon L, *et al*. A prospective study to investigate the role of serial serum mesothelin in monitoring mesothelioma. *BMC Cancer* 2018;18.

35 Kao SCH, Pavlakis N, Harvie R, *et al*. High blood neutrophil-to-lymphocyte ratio is an indicator of poor prognosis in malignant mesothelioma patients undergoing systemic therapy. *Clin Cancer Res* 2010;16:5805-13.

36 Yamagishi T, Fujimoto N, Nishi H, *et al*. Prognostic significance of the lymphocyte-to-monocyte ratio in patients with malignant pleural mesothelioma. *Lung Cancer* 2015;90:111–7.

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

BMJ Open

APPENDIX

1. Clinical sites involved in ASSESS-meso

North Bristol NHS Foundation Trust

Oxford University Hospitals Foundation Trust

Hywel Dda University Health Board

University Hospitals of Leicester

Royal United Hospitals Bath NHS Foundation Trust

Somerset NHS Foundation Trust

University Hospitals Plymouth NHS Trust

Manchester University NHS Foundation Trust

Royal Papworth Hospital NHS Foundation Trust

Northumbria Healthcare NHS Foundation Trust

Northern Care Alliance NHS Foundation Trust

University Hospitals of Derby and Burton NHS Foundation Trust

NHS Greater Glasgow & Clyde

Sherwood Forest Hospitals NHS Foundation Trust

Velindre University NHS Trust (Velindre Cancer Centre)

2. Eligibility criteria
Inclusion criteria
Participants must meet *all* of the following criteria:

- histological, cytological, consensus clinico-pathological-radiological diagnosis of mesothelioma, confirmed by local lung cancer or regional mesothelioma multidisciplinary team (MDT).
  - A consensus clinico-pathological-radiological is diagnosis made at MDT in the presence of supportive clinical history and examination findings, with consistent changes on imaging and supportive (but not diagnostic in its own right) cytological or histological findings.
- willing and able to comply with study follow-up assessments.
- willing & able to provide written informed consent.

Exclusion criteria
Participants must meet *none* of the following criteria:

- age <18 years old.
- unable to give written informed consent.
- declines ongoing hospital follow-up.