RESPECT-Meso frequently asked questions

Why recruit to RESPECT-Meso?
The UK has the highest prevalence of mesothelioma worldwide and incidence is increasing and predicted to peak in 2015-2025. The UK also has the highest death rate from malignant mesothelioma in the world, accounting for 1 in 170 of all deaths.

RESPECT-Meso has been peer reviewed by a competitive grant process, and, as a high quality study, we hope it will be of significant benefit to patients and their carer's.

This study is on the National Institute of Health and Research (NIHR) portfolio and as such will generate benefits of associated NIHR network support and activity based funding. This study also involves recruiting the patient's primary caregiver as a separate participant, giving centres the opportunity to generate double the number of accruals for this RCT. In addition there will be a per patient tariff at randomisation. Details regarding this can be obtained from the study trial manager Laura Marshall (email: laura.marshall2@porthosp.nhs.uk).

Why is this research important?

Mesothelioma is an aggressive, incurable cancer which often presents late limiting treatment options. Recent research examining non small cell lung cancer and early specialist palliative care intervention (*Temel et al 2010)* demonstrated improved quality of life and survival benefits for patients. The research team are studying whether similar outcomes might be achieved for patients with mesothelioma.

This comprehensive, randomised, multicentre study will examine the impact of regular early specialist symptom control intervention provided by Specialist Palliative Care professionals on both patient and caregiver quality of life, and the healthcare economic consequences of providing such an intervention. The results of the study will be widely applicable to many institutions and patients throughout the UK.

What is the study intervention?
The study intervention is regular early specialist symptom control treatment provided by Specialist Palliative Care professionals. The first contact with Specialist Palliative Care will be within 3 weeks of randomisation followed by 4 weekly follow up.

Will this study represent a change in practice for palliative care services?

Early palliative care intervention in patients with mesothelioma might represent a change in practice in the United Kingdom, however practice does vary in different centres. Studies have shown that more than 85% of patients have symptoms at presentation, usually fatigue, dyspnoea, loss of appetite and pain. This study seeks to randomise patients who are asymptomatic or

symptomatic but fully ambulatory to usual care or early palliative care referral. Many such patients will receive chemotherapy, and traditionally patients have not been referred to palliative care services whilst they are having active treatment. Whether patients would benefit from palliative care input during this time, and therefore whether practice *should* change, is one of the questions this study is seeking to answer.

Is the study economically viable for palliative care departments?

For a hospitals seeing 50 new mesothelioma patients per annum based on the protocol's assumptions and a 1:1 randomisation ratio to intervention each site might receive 12 extra patients over the two year study period. Each patient should receive a monthly palliative care review. Some of these patients will not survive for the entire study period and some would have been referred to palliative care, so are not entirely 'new' costs. Should this funding be insufficient, centres will be able to bid for NHS Support Costs for palliative care time through their CLRNs (in accordance with Department of Health ARCO guidance).

How much Specialist Palliative Care time will be required per patient?
The initial patient and carer contact with Specialist Palliative Care will take approximately 1 hour. Subsequent follow up visits will take about 30 minutes. Based on existing median survival data we estimate that each patient in the intervention arm will require a total of 5 hours of Specialist Palliative Care time for the duration of the trial.

Why are patients with an ECOG status of only 0-1 included in the study?
Only patients with an ECOG PS of 0-1 will be eligible to enter the study. The majority of these patients would not normally require specialist palliative care for the management of their symptoms at the time of diagnosis.

Patients with higher ECOG scores are perceived as being much more likely to have troublesome symptoms at presentation and therefore likely to need specialist palliative care services for symptom control which would make them ineligible for study participation. As it is likely that patients with poorer performance statuses will already be seeing palliative care services based on clinical need we do not think this group of patients will be missing out in any way.

Furthermore patients with ECOG score of 2 and more have a much higher mortality (even at 3 months), making study follow up difficult making power calculations and analysis difficult and potentially unreliable.

How has the ethical question of early intervention for this group and not for patients ECOG 2 – 4 been addressed?

Those caring for patients with mesothelioma have always been welcome to refer patients with complex needs to specialist palliative care. These patients are likely to have poor performance status. The study does not seek to alter usual referral practice for these patients, rather to see whether palliative care input for patients who still have a good performance status at diagnosis alters their outcome.

Will referring teams not wish to afford all patients the same intervention of early specialist palliative care - even if of unproven value?

Those caring for patients with mesothelioma have always been welcome to refer patients with complex needs to specialist palliative care. This study is set up with true clinical equipoise ie we do not know whether early palliative care will alter patients' outcomes and therefore it would be wrong to alter referral practices until the evidence is acquired to show whether or not early referral alters clinical outcomes.

What are the study outcomes?

The primary outcome of this randomised controlled study is to assess the impact of early specialist symptom control treatment on global quality of life in patients recently diagnosed with malignant pleural mesothelioma (MPM) for 12 weeks post-randomisation, as compared to standard care.

The secondary outcomes are to assess the impact of early specialist symptom control treatment in the care of patients recently diagnosed with MPM on the following:

(a) QOL in patients after 24 weeks.
(b) Patient mood at 12 and 24 weeks.
c) Primary caregiver QOL and mood at 12 and 24 weeks, and 24 weeks after patient death.
(d) Overall survival between the two study groups.
(e) Healthcare utilisation and healthcare costs.
(f) The cost-effectiveness of the intervention when compared to usual practice.

What are the study eligibility criteria?

Inclusion criteria:

1. Histological or cytological confirmation of MPM.
2. ECOG PS of 0-1. (Asymptomatic patients score 0; symptomatic but fully ambulatory patients score 1).
3. The diagnosis of MPM received within the last 6 weeks.
4. Ability to provide written informed consent in English and comply with trial procedures.

Exclusion criteria:

1. Other known malignancy within 5 years (excluding localised squamous cell carcinoma of the skin, cervical intraepithelial neoplasia, grade III and low grade prostate cancer (Gleason score <5, with no metastases)).
2. Significant morbidity which the lead physician (or MDT) feel will unduly confound or influence QOL.
3. Those patients the MDT judge require referral to Specialist Palliative Care professionals at the point of diagnosis.
4. Concurrent, or less than 3 months, since participation in another clinical trial that may affect QOL.
5. Referral at the time of recruitment for cytoreductive, tumour de-bulking, radical decortication or extrapleural pneumonectomy surgery for MPM. (Video Assisted Thoracoscopic Surgery or 'mini' thoracotomy for pleurodesis and diagnosis attempts are permissible.)
6. Chemotherapy treatment for MPM initiated prior to consent.
7. A significant history of depression / anxiety / psychiatric illness requiring specialist hospital care within the last 12 months.

How long does it take to complete each study contact?

Patient	Baseline, weeks 12 & 24:	30 mins
Patient	Telephone – weeks 4, 8, 16, 24:	20 mins
Carer	Baseline, weeks 12 & 24, bereavement + 24 weeks:	20 mins

Are there study support costs?

This study is on the NIHR portfolio and as such will generate benefits of associated NIHR network support and activity based funding. This study also involves recruiting the patient's primary caregiver as a separate participant giving centers the opportunity to generate double the number of accruals for this RCT. In addition there will be a per patient tariff of £200 at randomisation and £50 on completion of all study paperwork amounting to a total of £250.

Will patients in the control group who have Specialist Palliative Care needs miss out as a result of participating in the trial?

Patients in the control group will receive all standard treatments. Most patients are referred to the Specialist Palliative Care Service at some point during their illness. If and when patients in the control group require Specialist Palliative Care they will be referred by their clinical team in line with local arrangements.

What happens if new treatments such as surgery or chemotherapy or radiotherapy become available as part of standard care?

Should new methods of management for MPM become available during the course of the study, we may have to change what treatment and support we are giving. We will discuss these issues at the Trial Steering Committee on a regular basis and also on an ad hoc basis as required. The study may have to be stopped, or changed in some way. We will always do what is best for the patient and their family.

What if the patient cannot nominate a carer or the carer does not want to participate?
The patient may still take part in the study even if they are unable to identify a carer, or if the carer does not want to participate. Even though the carer may not be participating in the study he/she is still welcome to accompany the patient to all study visits.

Can patients participating in RESPECT-Meso co-participate in other studies?
Patients who are currently or within the last 3 months participated in another clinical trial thought to affect patient's quality of life will not be eligible for participation in RESPECT-Meso.

The RESPECT-Meso study team is happy to discuss any queries regarding this on a trial by trial basis.

How is the study funded?
A project grant for this study has been granted by the British Lung Foundation. Grant reference number: APG12-13.

Where can I find further information about the study?
Further information about the study is available at www.respect-meso.org.
Alternatively you may contact a member of the research team.

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