the RESPECT-Meso investigators (2019). A randomised controlled trial of regular early specialist palliative care on quality of life in malignant pleural mesothelioma – 'RESPECT-Meso': A randomised controlled trial. *Thorax*, *74*(4), 354-361. https://doi.org/10.1136/thoraxjnl-2018-212380

RESPECT-Meso

ONLINE SUPPLEMENT

Study visit schedule

At 12 weeks (primary end point) and 24 weeks, participants and carers from both the intervention and control groups were reviewed in clinic by the study team and recent treatments and hospital/healthcare utilisation, medication use, participant and carer HRQoL and mood, satisfaction with care documented. A summary of the visit and data collection schedule is provided in table 1.

Telephone consultations with participants in both the intervention and control group were performed at 4, 8, 16 and 20 weeks to review recent treatments and healthcare utilisation, medication use, HRQoL questionnaires. After participant death, the carer was approached by the study team to complete the final questionnaires, 24 weeks after bereavement.

Table 1. Summary of the study visit and data collection schedule. QLQ-C30 = (EORTC) Quality of Life questionnaire Core 30; GHQ-12 = General Health Questionnaire-12; SF-36 = short form 36 health survey.

Outcome measure	Baseline	4 weeks	8 weeks	12 weeks	16 weeks	20 weeks	24 weeks	24 weeks post bereavement
QLQ-C30 (participant)	✓	✓	✓	✓	✓	✓	✓	
GHQ-12 (participant)	✓			✓			✓	
GHQ-12 (caregiver)	✓			✓			✓	✓
SF-36 (caregiver)	✓			✓			✓	✓
FAMCARE-2 (caregiver)	✓			✓			✓	✓

Exploratory Analysis

Symptom burden using the EORTC QLQ-C30 and LC13. A chi^2 test was performed for each of the questions to compare the numbers who answered Quite a Bit/ Very Much vs Not at All/ A Little between treatment groups at 12 weeks. Data presented in Table 3.

RESULTS

Recruitment by centre is presented in Table 2.

Table 2. List of centres recruiting to the study. All centres are based in England with the exception of Sir Charles Gairdner Hospital

	Regular Early Specialist Palliative Care (N=87)	**Standard Care (N=87)**
Centre:		
Basildon and Thurrock University Hospitals NHS Foundation Trust	4 (4.6)	3 (3.5)
Broomfield Hospital, Mid Essex Hospital NHS Trust	2 (2.3)	2 (2.3)
Ipswich Hospital NHS Trust	2 (2.3)	1 (1.2)
Kings Mill Hospital, Sherwood Forest Hospitals NHS Foundation Trust	2 (2.3)	2 (2.3)
Musgrove Park, Taunton and Somerset NHS Foundation Trust	3 (3.5)	2 (2.3)
County Durham and Darlington NHS Foundation Trust	3 (3.5)	2 (2.3)
North Manchester General Hospital, Pennine Acute Hospitals NHS Trust	5 (5.8)	5 (5.8)
North Tyneside General, Northumbria Healthcare NHS Foundation Trust	1 (1.2)	1 (1.2)
Sir Charles Gairdner Hospital, Perth, Australia	18 (20.7)	18 (20.7)
South Tyneside NHS Foundation Trust	4 (4.6)	1 (1.2)
University Hospital Southampton NHS Foundation Trust	1 (1.2)	2 (2.3)
Southmead Hospital, North Bristol NHS Trust	4 (4.6)	3 (3.5)
Basingstoke and North Hampshire Hospital - Hampshire Hospitals NHS Foundation Trust	0 (0.0)	1 (1.2)
Great Western Hospitals NHS Foundation Trust	3 (3.5)	0 (0.0)
New Cross Hospital, The Royal Wolverhampton NHS Trust	0 (0.0)	1 (1.2)
Norfolk & Norwich University Hospitals NHS Foundation Trust	3 (3.5)	6 (6.9)
Queen Alexandra Hospital, Portsmouth Hospitals NHS Trust	17 (19.5)	18 (20.7)
Royal Hampshire County Hospital, Hampshire Hospitals NHS Foundation Trust	5 (5.8)	3 (3.5)
Wythenshawe Hospital, University Hospital of South Manchester NHS Foundation Trust	9 (10.3)	13 (14.9)
Wansbeck General, Northumbria Healthcare NHS Foundation Trust	1 (1.2)	3 (3.5)

Table 3. Reported symptoms from EORTC QLQ-C30 and EORTC QLQ-LC13 at week 12. For each question: n=no. of responses received, **0**= **1** Not at All or **2** A Little; **1**= **3** Quite a Bit or **4** Very Much

	Early Specialist Palliative Care	**Standard Care**	**Chi^2(1) P-value**
EORTC QLQ-C30			
Q8: Were you short of breath? n= 150 0/1 (% 0/1)	n=77 51/26 (66.2/33.8)	n=73 48/25 (65.8/34.2)	0.95
Q9: Have you had pain? n= 150 0/1 (%0/1)	n=77 66/11 (85.7/14.3)	n=73 58/15 (79.5/20.5)	0.31
Q18: Were you tired? n=148 0/1 (%0/1)	n=76 47/29 (61.8/38.2)	n=72 45/27 (62.5/37.5)	0.93
EORTC QLQ-LC13			
Q33: Were you short of breath when you rested? n=151 0/1 (%0/1)	n=77 74/3 (96.1/3.9)	n=74 70/4 (94.6/5.4)	0.66
Q34: Were you short of breath when you walked? n=151 0/1 (%0/1)	n=77 57/20 (74.0/26.0)	n=74 54/20 (73.0/27.0)	0.88
Q35: Were you short of breath when you climbed stairs? n=145 0/1 (%0/1)	n=73 51/22 (69.9/ 30.1)	n=72 47/25 (65.3/34.7)	0.56
Q40: Have you had pain in your chest? n=151 0/1 (%0/1)	n=77 69/8 (89.6/10.4)	n=74 63/11 (85.1/14.9)	0.41

Table 4. Pre-specified sub group analyses using the Global Health Status of the EORTC QLQ-C30 quality of life questionnaire. GHS = Global Health Status; NLR = Neutrophil to lymphocyte ratio; IASLC = International Association for the Study of Lung Cancer; AUS = Australia; UK = United Kingdom; ECOG = European Collaborative Oncology Group; SD = standard deviation; CI = confidence intervals

GHS score on the EORTC QLQ-C30 for participants at 12 weeks												
	Neutrophil/ lymphocyte ratio (<5/≥5)		**IASLC Radiological stage (1/2/3/4)**		**Country (AUS/UK)**		**Age at baseline (<75/≥75)**		**ECOG at baseline (0/1)**		**Presence of carer (Yes/No)**	
	Standard care	Early Specialist palliative care	Standard care	Early Specialist palliative care	Standard care	Early Specialist palliative care	Standard care	Early Specialist palliative care	Standard care	Early Specialist palliative care	Standard care	Early Specialist palliative care
n=	72	75	46	42	73	75	73	75	73	75	73	75
Mean score (SD)	59.6 (21.3)	60.2 (23.6)	59.1 (20.2)	59.1 (27.5)	59.5 (21.2)	60.2 (23.6)	59.5 (21.2)	60.2 (23.6)	59.5 (21.2)	60.2 (23.6)	59.5 (21.2)	60.2 (23.6)
Modelled mean difference (95% CI)	<5 NLR (n=104):	3.0 (-5.0, 11.1)	Stage 1 (n=30):	4.8 (-11.5, 21.1)	UK (n=114):	-0.31 (-8.0, 7.3)	<75 (n=90):	1.7 (-7.0, 10.3)	ECOG 0 (n=58):	4.9 (-5.9, 15.6)	Carer did not Consent (n=23)	-1.4 (-18.7, 15.9)
			Stage 2 (n=9):	17.6 (-14.2, 49.4)								
	≥5 NLR (n=43):	-1.7 (-14.2, 10.8)	Stage 3 (n=29):	-5.7 (-22.3, 10.8)	AUS (n=34):	8.9 (-5.1, 23.0)	≥75 (n=58):	1.7 (-9.1, 12.5)	ECOG 1 (n=90):	-0.1 (-8.7, 8.5)	Carer consented (n=125)	2.3 (-5.0, 9.7)
			Stage 4 (n=20):	-2.9 (-22.8, 17.0)								
P-Value for interaction	0.52		0.51		0.24		1.00		0.47		0.69	
GHS score on the EORTC QLQ-C30 for participants at 24 weeks												
n=	64	60	42	28	65	60	65	60	65	60	65	60
Mean score (SD)	63.9 (19.9)	61.3 (20.7)	64.7 (20.0)	62.5 (24.1)	63.7 (19.8)	61.3 (20.7)	63.7 (19.8)	61.3 (20.7)	63.7 (19.8)	61.3 (20.7)	63.7 (19.8)	61.3 (20.7)
Modelled mean difference (95% CI)	<5 NLR (n=90):	-1.3 (-9.1, 6.5)	Stage 1 (n=28):	-6.7 (-22.2,8.8)	UK (n=96):	-0.2 (-7.8, 7.3)	<75 (n=80):	-2.3 (-10.6, 6.0)	ECOG 0 (n=54):	-7.3 (-17.3, 2.7)	Carer did not Consent (n=22)	-0.3 (-16.2, 15.5)
			Stage 2 (n=7):	17.2 (-16.6, 50.9)								
	≥5 NLR (n=34):	-4.3 (-17.3, 8.8)	Stage 3 (n=22):	-7.5 (-24.8,9.8)	AUS (n=29):	-7.1 (-20.9, 6.8)	≥75 (n=45):	-1.5 (-12.6, 9.6)	ECOG 1 (n=71):	2.0 (-6.7, 10.8)	Carer consented (n=103)	-2.2 (-9.5, 5.0)
			Stage 4 (n=13):	8.0 (-14.9, 31.0)								
P-Value for interaction	0.70		0.38		0.38		0.90		0.16		0.83	

Table 5. Baseline characteristics of study participants with data for the primary analysis (n=148).

	Early Specialist Palliative Care (n=75)		**Standard Care (n=73)**		**Patients with vs without primary outcome[1]** (p-value from t-test/chi-squared test)
	n=				
Age median (LQ, UQ)	75	72.0 (66.4, 77.0)	73	72.8 (68.9, 78.1)	0.01
Gender *Male (%)*	75	58 (77.3)	73	60 (82.2)	0.90
Neutrophil to Lymphocyte Ratio *Median (LQ, UQ)*	75	3.5 (2.7, 5.1)	72	3.9 (2.7, 6.8)	0.02
Minimisation factors:					
Plan for chemotherapy *Yes (%)*	75	40 (53.3)	72	38 (52.8)	0.94
ECOG performance status 0 1	75	 30 (40.0) 45 (60.0)	73	 28 (38.4) 45 (61.6)	0.41
Histological subtype *Non-Epithelioid/Epithelioid (% Non-Epithelioid/Epithelioid)*	75	13/62 (17.3/82.7)	73	14/59 (19.2/80.8)	<0.01

UQ = upper quartile; LQ = lower quartile; ECOG = Eastern Collaborative Oncology Group

[1]This column compares patients with the primary outcome (n=148) vs patients missing the primary outcome (n=26). For each baseline factor, the number of patients with available baseline data out of 148 *with the primary outcome* is shown in the table i.e. n (sum of both arms), the number of patients with available baseline data out of 26 *missing the primary outcome* is n (sum of both arms) in Table2 minus n (sum of both arms) shown here.

Table 5 shows that the randomised groups are well-balanced for baseline characteristics. P-values are shown for comparing those included vs excluded from the primary analysis, the mean age for those missing the primary outcome was higher which was to be expected but this does not cause an imbalance between treatment groups in patients with available primary outcome. Similarly, there are some differences in neutrophil to lymphocyte ratio and histological subtype between those with and without the primary outcome but the balance between treatment groups was unaffected.

Figure 1

CONSORT diagram of the full study period (24 weeks), including carers

Figure 2

Kaplan Meier graph of overall survival by treatment arms censored at the last known date of contact in the study