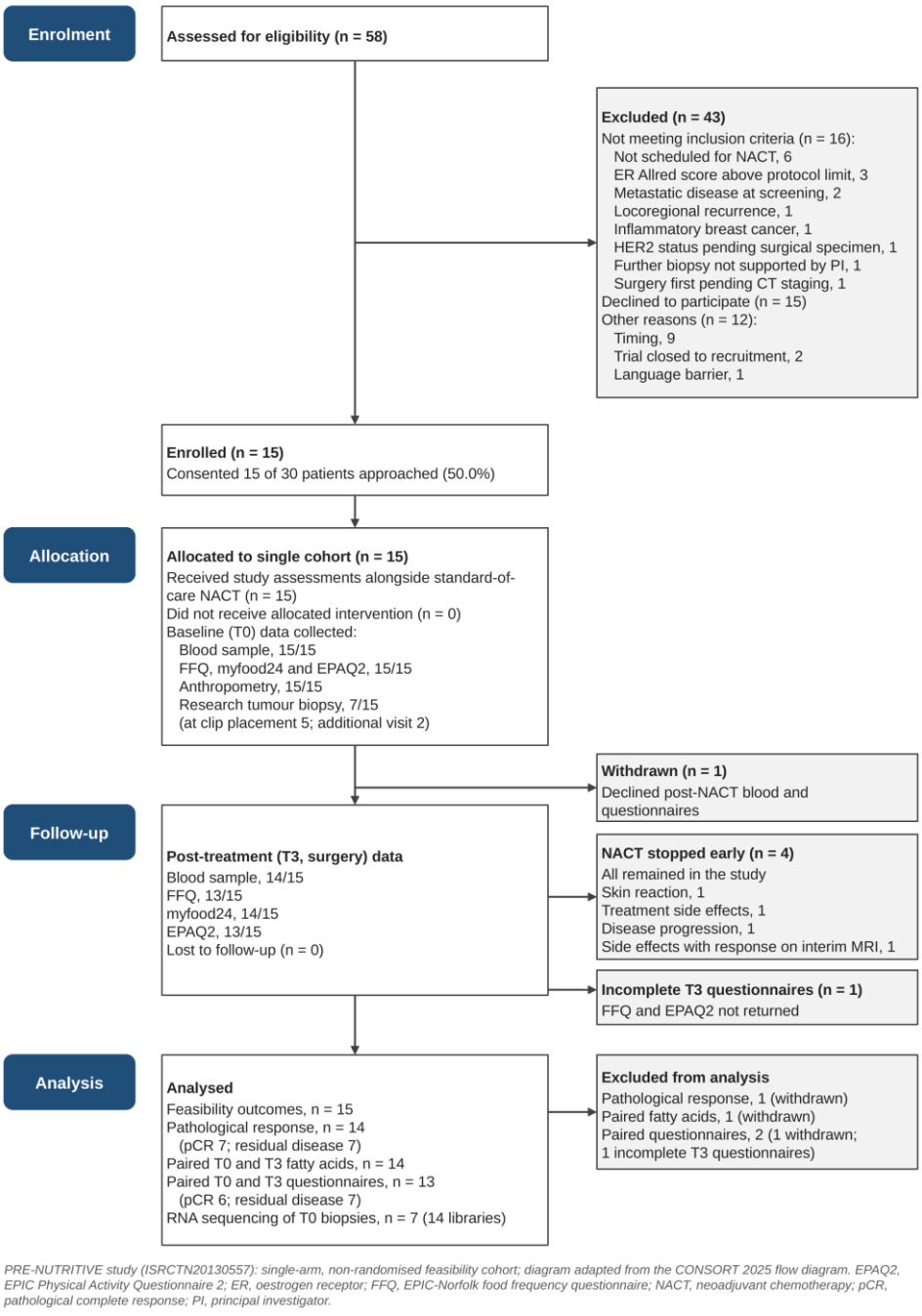
Summary of results: ISRCTN20130557

Predicting responses to chemotherapy from nutrition in triple negative breast cancer patients (the PRE-NUTRITIVE study): a prospective feasibility study. Protocol version 1.4, 4 April 2024.

Funder: World Cancer Research Fund (grant IIG_FULL_2021_019). Ethics: West Midlands, Solihull Research Ethics Committee (22/WM/0087). Chief Investigator: Dr James L Thorne, University of Leeds.

Single-arm, non-randomised feasibility cohort of patients with triple-negative breast cancer receiving neoadjuvant chemotherapy (NACT) at Leeds Teaching Hospitals NHS Trust. There was no randomised allocation; all 15 enrolled participants form one cohort. Where results are shown by comparison group, the groups are defined by pathological response at surgery and are descriptive only.

1. Participant flow



PRE-NUTRITIVE study (ISRCTN20130557): single-arm, non-randomised feasibility cohort; diagram adapted from the CONSORT 2025 flow diagram. EPAQ2, EPIC Physical Activity Questionnaire 2; ER, oestrogen receptor; FFQ, EPIC-Norfolk food frequency questionnaire; NACT, neoadjuvant chemotherapy; pCR, pathological complete response; PI, principal investigator.

Figure 1. Flow of participants through the study (adapted from the CONSORT 2025 flow diagram for a single-arm cohort).

2. Baseline characteristics

Table 1. Baseline characteristics, all participants and by pathological response group

Characteristic	All participants (n = 15)	pCR (n = 7)	Residual disease (n = 7)
Demographics			
Age, years, median (IQR)	51.0 (50.5 to 58.0)	51.0 (49.5 to 51.5)	57.0 (51.0 to 62.0)
Female sex, n (%)	15 (100%)	7 (100%)	7 (100%)
Anthropometry			
BMI, kg/m², median (IQR)	26.5 (24.0 to 32.8)	26.3 (24.0 to 26.9)	29.4 (24.1 to 33.1)
BMI category, n (%)			
Healthy weight (18.5 to 24.9)	6 (40%)	3 (43%)	3 (43%)
Overweight (25.0 to 29.9)	4 (27%)	3 (43%)	1 (14%)
Obesity class I (30.0 to 34.9)	3 (20%)	1 (14%)	2 (29%)
Obesity class II (35.0 to 39.9)	1 (7%)	0 (0%)	1 (14%)
Obesity class III (40.0 or above)	1 (7%)	0 (0%)	0 (0%)
Waist circumference, cm, median (IQR)	94.0 (79.0 to 100.0)	90.0 (79.0 to 96.0)	95.0 (84.8 to 100.5)
Hip circumference, cm, median (IQR)	106.0 (101.5 to 119.0)	102.0 (101.0 to 106.5)	107.0 (106.0 to 122.0)
Waist to hip ratio, median (IQR)	0.86 (0.77 to 0.90)	0.87 (0.78 to 0.90)	0.86 (0.75 to 0.88)
Reproductive and lifestyle history			
Menopausal status, n (%)			
Pre-menopausal	4 (27%)	3 (43%)	1 (14%)
Peri-menopausal	4 (27%)	2 (29%)	2 (29%)
Post-menopausal	7 (47%)	2 (29%)	4 (57%)
History of breastfeeding, n (%)	10 (67%)	3 (43%)	7 (100%)
Smoking status, n (%)			
Never smoked	10 (67%)	4 (57%)	5 (71%)
Ex-smoker	3 (20%)	2 (29%)	1 (14%)
Current smoker	2 (13%)	1 (14%)	1 (14%)
Clinical and tumour characteristics			
ECOG performance status, n (%)			
0	14 (93%)	7 (100%)	6 (86%)
Not recorded	1 (7%)	0 (0%)	1 (14%)
Histology, n (%)			
Invasive ductal carcinoma	12 (80%)	7 (100%)	4 (57%)
Invasive lobular carcinoma	1 (7%)	0 (0%)	1 (14%)
Other subtypes (including metaplastic)	2 (13%)	0 (0%)	2 (29%)
Tumour grade, n (%)			
Grade 2	6 (40%)	3 (43%)	3 (43%)
Grade 3	8 (53%)	4 (57%)	3 (43%)
Not stated	1 (7%)	0 (0%)	1 (14%)
Maximum tumour dimension on baseline MRI, mm, median (IQR)	34 (26 to 42)	34 (24 to 48)	34 (27 to 39)
Multifocal or multicentric disease, n (%)	3 (20%)	2 (29%)	1 (14%)
Lymphovascular invasion, n (%)			
Present	2 (13%)	1 (14%)	1 (14%)

Characteristic	All participants (n = 15)	pCR (n = 7)	Residual disease (n = 7)
Absent	4 (27%)	2 (29%)	2 (29%)
Not stated or not recorded	9 (60%)	4 (57%)	4 (57%)
Inflammatory breast cancer, n (%)	0 (0%)	0 (0%)	0 (0%)
Planned neoadjuvant chemotherapy			
NACT regimen, n (%)			
Paclitaxel and carboplatin, then epirubicin and cyclophosphamide	7 (47%)	5 (71%)	2 (29%)
As above with pembrolizumab	6 (40%)	1 (14%)	4 (57%)
Paclitaxel or nab-paclitaxel and carboplatin, then epirubicin and cyclophosphamide	2 (13%)	1 (14%)	1 (14%)
Any pembrolizumab recorded, n (%)	7 (47%)	1 (14%)	5 (71%)
Study-specific measures at baseline (T0)			
WCRF/AICR score, FFQ (six recommendations, 0 to 6), median (IQR)	3.0 (2.8 to 3.8)	3.0 (2.5 to 3.4)	3.8 (3.0 to 3.8)
WCRF/AICR score, myfood24 (six recommendations, 0 to 6), median (IQR)	3.8 (3.4 to 4.6)	4.2 (3.9 to 4.6)	3.5 (3.0 to 4.2)

Continuous variables are median (interquartile range). The all participants column includes the participant who withdrew before T3 (n = 1), whose pathological response was not assessed. Categorical variables are n (% of column total). No significance tests of baseline differences were performed, in line with CONSORT guidance.

Pathological response groups follow the pathology report (pCR, n = 7; residual disease, n = 7, comprising partial response 4, stable disease 1, progressive disease 2). The paired T0 and T3 questionnaire analyses used 13 participants (pCR 6; residual disease 7). The withdrawn participant provided no T3 questionnaires, and one pCR participant did not return the T3 FFQ or EPAQ2.

One participant in the nab-paclitaxel group received one cycle of pembrolizumab before it was discontinued. Waist to hip ratio was calculated from recorded waist and hip circumferences.

Abbreviations: BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; FFQ, EPIC-Norfolk food frequency questionnaire; IQR, interquartile range; MRI, magnetic resonance imaging; NACT, neoadjuvant chemotherapy; pCR, pathological complete response; WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research.

3. Outcome measures

Table 2. Registered primary and secondary outcome measures (single cohort, n = 15)

Registered outcome measure	Timepoint	Participants with data, n/N (%)	95% CI (Wilson), %	Result	Analysis performed
Primary outcome measures					
EPIC-Norfolk FFQ	T0	15/15 (100.0%)	79.6 to 100.0	WCRF/AICR six-recommendation score, median (IQR): 3.0 (2.8 to 3.8)	Descriptive
	T3	13/15 (86.7%)	62.1 to 96.3	Score, median (IQR): 3.2 (2.8 to 3.8) (n = 13). Paired change (n = 13): 5 increased, 5 decreased, 3 unchanged	Descriptive; no hypothesis test
24-hour dietary recall (myfood24)	T0	15/15 (100.0%)	79.6 to 100.0	WCRF/AICR six-recommendation score, median (IQR): 3.8 (3.4 to 4.6)	Descriptive
	T3	14/15 (93.3%)	70.2 to 98.8	Score, median (IQR): 3.5 (3.0 to 4.0) (n = 13 scored). Paired change (n = 13): 4 increased, 9 decreased, 0 unchanged	Descriptive; no hypothesis test
Blood micro- and macronutrient levels	T0	15/15 (100.0%)	79.6 to 100.0	Plasma and serum fatty acid profiles obtained for 15 participants	Descriptive
	T3	14/15 (93.3%)	70.2 to 98.8	Plasma and serum fatty acid profiles obtained for 14 participants (paired n = 14)	Descriptive
Tumour gene expression (RNA sequencing)	T0	7/15 (46.7%)	24.8 to 69.9	14 libraries (two cores per participant) sequenced	Descriptive (see secondary measure 6)
	T3	0/15 (0.0%)	0.0 to 20.4	No tumour tissue collected at surgery	Not applicable
Anthropometric measures (BMI, waist and hip circumference)	T0	15/15 (100.0%)	79.6 to 100.0	Values reported in Table 1	Descriptive
Tumour size by MRI	T0	15/15 (100.0%)	79.6 to 100.0	Maximum dimension, mm, median (IQR): 34 (26 to 42)	Descriptive
	T1 (after cycle 2)	15/15 (100.0%)	79.6 to 100.0	Measurement recorded for all participants (one value queried in the CRF)	Descriptive
	T2 (end of NACT)	14/15 (93.3%)	70.2 to 98.8	One participant: extent not ascertainable on MRI report	Descriptive
	T3 (pathology at surgery)	14/15 (93.3%)	70.2 to 98.8	Pathological complete response 7/14 (50.0%; 95% CI 26.8 to 73.2); partial response 4/14; stable disease 1/14; progressive disease 2/14	Descriptive
Physical activity (EPAQ2)	T0	15/15 (100.0%)	79.6 to 100.0	Questionnaire completed	Descriptive
	T3	13/15 (86.7%)	62.1 to 96.3	Questionnaire completed (paired n = 13)	Descriptive
Secondary outcome measures (assessed at end of study)					
1. Uptake of blood donation	T0	15/15 (100.0%)	79.6 to 100.0	All enrolled participants donated blood at baseline	Proportion with Wilson 95% CI
1. Uptake of tumour tissue donation	T0	7/15 (46.7%)	24.8 to 69.9	Research biopsy at marker clip placement 5; at an additional visit 2	Proportion with Wilson 95% CI
2. Completion of patient surveys (FFQ, myfood24 and EPAQ2 all completed)	T0	15/15 (100.0%)	79.6 to 100.0		Proportion with Wilson 95% CI
	T3	13/15 (86.7%)	62.1 to 96.3	Among participants not withdrawn: 13/14 (92.9%; 95% CI 68.5 to 98.7)	Proportion with Wilson 95% CI
3. Variation in nutritional status	T0 and T3			Between-participant range of six-recommendation score at T0: FFQ 2.25 to 4.75; myfood24 2.50 to 5.25. Plasma and	Descriptive only

Registered outcome measure	Timepoint	Participants with data, n/N (%)	95% CI (Wilson), %	Result	Analysis performed
				serum fatty acid profiles available at T0 (n = 15) and T3 (n = 14)	
4. Accuracy and compliance of WCRF guideline adherence (FFQ and myfood24 methods)	T0			myfood24 score higher than FFQ score in 10/15, lower in 3/15, equal in 2/15 participants	Descriptive; no formal agreement analysis performed
5. RNA yield from tumour biopsies	T0			RNA yield values were not available in the study data files. All 14 libraries passed sequencing quality control (clean reads 36.6 to 54.1 million per library; Q30 95.9% to 97.1%)	Not analysed
6. Predictors of chemoresponse by gene expression	T0	7/15		pCR (n = 1) versus residual disease (n = 6): no gene reached FDR < 0.05 in any of four replicate-handling approaches (blocked, summed, A cores only, B cores only)	Exploratory limma-voom differential expression, Benjamini–Hochberg FDR

Outcome measures are listed as worded in the ISRCTN20130557 registry entry (primary measures current version 21/08/2024). Timepoints: T0, before NACT; T1, after cycle 2; T2, end of NACT; T3, day of surgery. Denominators are all 15 enrolled participants unless stated. Proportions use Wilson score 95% confidence intervals. No inferential tests were applied to the registered outcomes.

Missing data: one participant withdrew before T3 and provided no T3 blood sample or questionnaires; one further participant did not return the T3 FFQ or EPAQ2 but completed the T3 myfood24 recall, which was not scored for WCRF/AICR adherence. Two T3 myfood24 recalls had portion-size entry errors and were re-entered in myfood24 before scoring. In one, four of five recorded items had no portion size (0 g); these items were re-entered at the myfood24 standard portion for each item. In the other, five slices of malt loaf had been recorded as 1,225 g; this item was re-entered as five standard slices (245 g).

Blood analytes: the registry lists blood micro- and macronutrients; fatty acid profiles (plasma and serum) are the only blood analyte data held in the study data files.

Abbreviations: BMI, body mass index; CI, confidence interval; CRF, case report form; EPAQ2, EPIC Physical Activity Questionnaire 2; FDR, false discovery rate; FFQ, food frequency questionnaire; IQR, interquartile range; MRI, magnetic resonance imaging; NACT, neoadjuvant chemotherapy; pCR, pathological complete response; WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research.

4. Harms and adverse events

Table 3. Adverse events recorded during the study (single cohort, n = 15)

Category (MedDRA system organ class)	Adverse event	Participants affected, n/15 (%)	Events, n	Attribution recorded in source data	Action or outcome recorded
All-cause mortality					
Death	No deaths recorded	0 (0.0%)	0	Not applicable	Not applicable
Serious adverse events					
Any serious adverse event		2 (13.3%)	3		
Hepatobiliary disorders	Hepatitis, CTCAE grade 3	1 (6.7%)	1	Treatment, agent not specified	Pembrolizumab discontinued
Blood and lymphatic system disorders	Methaemoglobinaemia with haemolysis	1 (6.7%)	1	Secondary to dapsone	Not recorded
Endocrine disorders	Adrenal insufficiency	1 (6.7%)	1	Immunotherapy	Lifelong corticosteroid replacement
Other (non-serious) adverse events					
Any other adverse event		3 (20.0%)	3		
Skin and subcutaneous tissue disorders	Severe skin reaction	1 (6.7%)	1	Chemotherapy (reason for stopping NACT)	NACT stopped early
General disorders and administration site conditions	Chemotherapy side effects, not further specified	2 (13.3%)	2	Chemotherapy (reason for stopping NACT)	NACT stopped early
Adverse events related to study procedures					
Study procedures	Blood sampling, research biopsy, questionnaires	0 (0.0%)	0	Not applicable	Not applicable
Any adverse event (all categories)					
All		5 (33.3%)	6		

Events are reported regardless of causal relation to the study. Participants received standard-of-care neoadjuvant chemotherapy, with or without pembrolizumab, as part of routine care; the study itself involved dietary and physical activity questionnaires, anthropometry, blood sampling and optional research biopsy. No adverse events were recorded in relation to study procedures.

Serious adverse events: one participant had grade 3 hepatitis and methaemoglobinaemia with haemolysis; one participant had adrenal insufficiency. Seriousness is shown as classified by the study team; the CRF does not record the seriousness criteria met.

Other adverse events are those recorded as the reason for stopping NACT early. One further participant stopped NACT because of disease progression; disease progression is not classified as an adverse event in this table. Mortality: no deaths are recorded in the study data; the CRF has no dedicated mortality field.

Abbreviations: CRF, case report form; CTCAE, Common Terminology Criteria for Adverse Events; NACT, neoadjuvant chemotherapy.

5. Conflicts of interest

The authors declare no competing interests.