

## Supplementary Information

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### Pre-EMPT trial Eligibility Criteria

Eligibility criteria:

Inclusion

1. Participants must be diagnosed with operable oesophageal and gastro-oesophageal adenocarcinoma and scheduled to undergo standard neo-adjuvant chemotherapy and oesophago-gastric surgery as recommended by the Multidisciplinary Meeting decision.
2. 18+
3.  $\leq 79$  (patients above this age may be included in studies after the feasibility study has been completed)
4. Participants must be able to understand and independently consent to participation in the study.
5. Participants must be able to understand and complete the questionnaires.
6. Participants must be willing to undergo all the standard assessments and interventions included in this study - CPEX testing, blood sampling, questionnaires and exercise intervention where appropriate.
7. Participants must be willing to wear the Fitbit monitoring device and agree with its use.
8. Participants must be ASA 1-3 and fit for surgical resection.
9. Patients should have a Body Mass Index (BMI) equal to or above 18.5 with less than 10% self-reported unintentional weight loss at diagnosis.

Exclusion

Participants will be excluded if they:

1. Are not considered medically fit for surgery at diagnosis, as decided by the Multidisciplinary team
2. Will undergo primary or palliative chemotherapy
3. Are recommended to have chemoradiotherapy
4. Are under 18 years old
5. Are over 79 years old
6. Are unable to undergo CPEX testing
7. Do not wish to take part in selected aspects of the study
8. Cannot or do not wish to attend the CHHP for assessment and/or advice on exercise
9. Cannot understand and give informed consent to the study
10. Cannot understand and complete the questionnaires
11. Do not wish to wear a Fitbit monitoring device
12. ASA 4+
13. Patients with BMI of less than 18.5 with self-reported unintentional weight loss of 10% or more at diagnosis.

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**Exercise Prehabilitation Program:**

Provided by Centre for Health and Human Performance, London

4 Week, 30 minutes walking programme, with additional Core Strength &amp; Stability, Flexibility and Band Strength Exercises

<b>Week 1</b>	<b>SESSION 1</b>	30 minutes moderate walk including; 10 x (30s hard walk with 1min 30s easy)
	<b>SESSION 2</b>	30 minutes moderate walk including; 2 x (5 x 1 minute hard walk with 1 minute easy) 5 minutes between sets
	<b>SESSION 3</b>	30 minutes moderate walk including; 2 x (10 x 30s hard walk with 1min 30s easy) 5 minutes between sets
	<b>SESSION 4</b>	30 minutes moderate walk
	<b>SESSION 5</b>	30 minutes moderate walk
<b>Week 2</b>	<b>SESSION 1</b>	30 minutes moderate walk including; 2 x (6 x 1 minute hard walk with 1 minute easy) 5 minutes between sets
	<b>SESSION 2</b>	30 minutes moderate walk including; 5 x (2 minutes hard walk with 1 minute easy) 5 minutes between sets
	<b>SESSION 3</b>	30 minutes moderate walk including; 10 x (1 minute hard walk with 1 minute easy) 5 minutes between sets
	<b>SESSION 4</b>	30 minutes moderate walk
	<b>SESSION 5</b>	30 minutes moderate walk
<b>Week 3</b>	<b>SESSION 1</b>	30 minutes moderate walk including; 2 x (10 x 30s hard walk with 1 minute 30s easy) 15 minutes between sets
	<b>SESSION 2</b>	30 minutes moderate walk including; 5 x (3 minutes hard walk with 2 minutes easy) 10 minutes between sets
	<b>SESSION 3</b>	30 minutes moderate walk including; 10 x (1 minute hard walk with 1 minute easy) 10 minutes between sets
	<b>SESSION 4</b>	30 minutes moderate walk
	<b>SESSION 5</b>	30 minutes moderate walk
<b>Week 4</b>	<b>SESSION 1</b>	30 minutes moderate walk including; 3 x (5 x 30s hard walk with 1 minute 30s easy) 5 minutes between sets
	<b>SESSION 2</b>	30 minutes moderate walk including; 10 x (2 minutes hard walk with 1 minute easy) 10 minutes between sets
	<b>SESSION 3</b>	30 minutes moderate walk including; 15 x (1 minute hard walk with 1 minute easy)
	<b>SESSION 4</b>	30 minutes moderate walk
	<b>SESSION 5</b>	30 minutes moderate walk

*N.B. easy = able to hold full conversation; moderate = brisk walking, concentrating to maintain pace; hard = fast/power walking*

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Table 4 Body composition changes

Parameters	Intervention Group (n=13) Median (IQR)	Control Group (n=14) Median (IQR)	p-value = *
<b>FFM index (kg/m<sup>2</sup>)</b>			
Baseline	17.8 (14.4-20.9)	16.3 (11.8-18.5)	.225
Post-treatment	18.7 (15.0-20.2)	14.7 (12.3-17.3)	.026
<b>FM index (kg/m<sup>2</sup>)</b>			
Baseline	9.1 (6.4-9.6)	8.1 (7.1-10.4)	.961
Post-treatment	8.2 (6.8-9.2)	8.2 (7.4-10.5)	.698
<b>FMR</b>			
Baseline	1.08 (0.67-1.75)	1.07 (0.90-1.58)	.846
Post-treatment	0.91 (0.59-1.94)	1.11 (0.88-2.16)	.409
<b>Visceral fat (cm<sup>2</sup>)</b>			
Baseline	204 (41-256)	206 (141-274)	.698
Post-treatment	154 (104-228)	214 (163-249)	.207
<b>Subcutaneous fat (cm<sup>2</sup>)</b>			
Baseline	153 (109-214)	165 (112-183)	.808
Post-treatment	147 (111-227)	158 (129-190)	.771
<b>VA/SA ratio</b>			
Baseline	0.83 (0.61-1.51)	1.24 (0.84-1.50)	.308
Post-treatment	0.83 (0.59-1.39)	1.22 (0.99-1.41)	.357
<b>Weight (kg)</b>			
Baseline	80.1 (64.3-84.3)	87.5 (68.7-94.5)	.052
Post-treatment	76.4 (69.2-79.9)	88.2 (74.0-95.6)	.053

\* p-values derived from Wilcoxon-signed rank test

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Table 5 Immunity Markers - Baseline versus Post-NAC

	Intervention Group		Control Group		p-value =
	Mean (SD)	Range	Mean (SD)	Range	
<b>CD3</b>					
Baseline	1474.38 (649.65)	(683-2793)	964.94 (350.45)	(582-1587)	
Post-NAC	1681.2 (504.36)	(733-2861)	981.08 (349.75)	(516-1686)	
<b>Participant change Baseline Post-NAC (%)</b>	34.26 (36.58)	(-16.78-111.57)	4.53 (25.67)	(-23.00-63.41)	<b>.034</b>
<b>CD4</b>					
Baseline	960.60 (403.63)	(292-2031)	550.88 (172.49)	(337-971)	
Post-NAC	1117.73 (323.09)	(471-1625)	584.92 (249.27)	(327-1231)	
<b>Participant change Baseline Post-NAC (%)</b>	42.08 (51.40)	(-22.45-179.45)	9.36 (37.90)	(-26.30-112.17)	.095
<b>CD8</b>					
Baseline	548.50 (394.68)	(174-1678)	376.75 (227.63)	(134-877)	
Post-NAC	551.47 (297.64)	(182-1267)	363.33 (179.24)	(120-675)	
<b>Participant change Baseline Post-NAC (%)</b>	29.41 (31.19)	(2.82-89.66)	0.98 (19.69)	(-23.03-50.89)	<b>.033</b>

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Table 6 Inflammatory Markers - Baseline versus Post-NAC

	Intervention Group		Control Group		p-value =
	Mean (SD)	Range	Mean (SD)	Range	
<b>IL-6</b>					
Baseline	2.68 (3.76)	(0.16-16.1)	1.13 (0.65)	(0.41-3.03)	
Post-NAC	3.20 (4.63)	(0.6-19.5)	2.31 (1.56)	(0.86-6.73)	
<b>Participant change Baseline Post-NAC (%)</b>	+27.93 (97.02)	(-55.94-275.00)	+126.41 (107.59)	(-53.14-282.39)	.041
<b>VEGF</b>					
Baseline	12.61 (11.98)	(2.66-53.51)	7.79 (3.43)	(2.92-15.5)	
Post-NAC	9.79 (5.13)	(3.64-21.26)	9.21 (4.16)	(5.1-17.35)	
<b>Participant change Baseline Post-NAC (%)</b>	-10.51 (62.09)	(-60.27-149.58)	+51.79 (99.54)	(-67.10-300.34)	.274
<b>INF-<math>\gamma</math></b>					
Baseline	0.34 (0.38)	(0.1-1.34)	0.15 (0.17)	(0.01-0.7)	
Post-NAC	0.39 (0.59)	(0.1-2.29)	0.23 (0.22)	(0.07-0.9)	
<b>Participant change Baseline Post-NAC (%)</b>	+57.24 (140.13)	(-80.60-300)	+223.64 (562.36)	(-50-1900)	.364
<b>TNF<math>\alpha</math></b>					
Baseline	1.53 (3.92)	(0.21-16.2)	0.58 (0.18)	(0.36-0.88)	
Post-NAC	1.76 (4.77)	(0.3-18.99)	0.74 (0.31)	(0.41-1.5)	
<b>Participant change Baseline Post-NAC (%)</b>	-1.77 (33.23)	(-53.03-45.45)	+28.31 (74.51)	(-30.99-233.33)	.245
<b>MCP-1</b>					

Baseline	54.14 (32.62)	(12.73- 136.33)	39.98 (27.82)	(4.24-95.7)	
Post-NAC	60.94 (21.18)	(16.8- 97.63)	63.37 (33.18)	(24.68- 137.2)	
<b>Participant change Baseline Post-NAC (%)</b>	+52.11 (58.18)	(-34.01- 174.16)	+163.69 (193.53)	(-45.56- 482.08)	.093
<b>EGF</b>					
Baseline	2.71 (3.13)	(0.34-12.4)	6.96 (7.32)	(0.5-24.5)	
Post-NAC	3.38 (6.25)	(0.4-25.2)	2.87 (3.30)	(0.6-12.5)	
<b>Participant change Baseline Post-NAC (%)</b>	+20.06 (80.48)	(-62.72- 176.47)	-8.23 (152.86)	(-95.21- 440.00)	.607