

Study Title: Peri-Operative wearabLe-based Assessment and patient Reported Outcomes In Surgery for Oesophago-Gastric cancer (POLARIS-OG)

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Principal Investigator (Please print name)	**Signature**	**Site name or ID number**	**Date**

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TABLE OF CONTENTS

1. KEY CONTACTS 7
2. LAY SUMMARY 7
3. SYNOPSIS 8
4. ABBREVIATIONS 11
5. BACKGROUND AND RATIONALE 12
6. OBJECTIVES AND OUTCOME MEASURES 15
7. STUDY DESIGN 17
8. PARTICIPANT IDENTIFICATION 19
8.1. Study Participants 19
8.2. Inclusion Criteria 19
8.3. Exclusion Criteria 19
9. PROTOCOL PROCEDURES 19
9.1. Recruitment 19
9.2. Screening and Eligibility Assessment 19
9.3. Informed Consent 20
9.4. Randomisation 20
9.5. Blinding and code-breaking 20
9.6. Description of study intervention(s), comparators, and clinical procedures 20
9.6.1. Description of study intervention(s) 20
9.6.2. Description of comparator(s) 22
9.6.3. Description of clinical procedure(s) undertaken as part of the study 22
9.7. Medical Devices 23
9.8. Baseline Assessments 25
9.9. Subsequent Visits 25
9.10. Sample Handling 26
9.11. Early Discontinuation/Withdrawal of Participants 26
9.12. Definition of End of Study 27
10. SAFETY REPORTING 27
10.1. Definition of Serious Adverse Events 28
10.2. Reporting Procedures for Serious Adverse Events 28
10.3 Serious Incidents involving Medical Devices 28
11. STATISTICS AND ANALYSIS 29

11.1. Description of the Statistical Methods 29
Primary outcome – prediction of CPET-derived VO_2peak using wearable-derived measures 29
Secondary outcomes and analyses 31
11.2. Sample Size Determination 34
11.3. Analysis populations 35
11.4. Decision points 36
11.5. Stopping rules 36
11.6. The Level of Statistical Significance 37
11.7. Procedure for Accounting for Missing, Unused, and Spurious Data. 37
11.8. Procedures for Reporting any Deviation(s) from the Original Statistical Plan 37
11.9. Health Economics Analysis 37
12. DATA MANAGEMENT 37
12.1. Source Data 37
12.2. Access to Data 38
12.3. Data Recording and Record Keeping 38
13. QUALITY ASSURANCE PROCEDURES 38
13.1. Risk assessment 39
13.2. Study monitoring 39
13.3. Study Committees 39
14. PROTOCOL DEVIATIONS 39
15. SERIOUS BREACHES 39
16. ETHICAL AND REGULATORY CONSIDERATIONS 40
16.1. Declaration of Helsinki 40
16.2. Guidelines for Good Clinical Practice 40
16.3. Approvals 40
16.4. Other Ethical Considerations 40
16.5. Reporting 41
16.6. Transparency in Research 41
16.7. Participant Confidentiality 41
16.8. Expenses and Benefits 41
17. FINANCE AND INSURANCE 41
17.1. Funding 41
17.2. Insurance 41
17.3. Contractual arrangements 42

18. PUBLICATION POLICY 42
19. DEVELOPMENT OF A NEW PRODUCT/ PROCESS OR THE GENERATION OF INTELLECTUAL PROPERTY 42
19. ARCHIVING 42
20. REFERENCES 42
21. APPENDIX A: STUDY FLOW CHART 44
22. APPENDIX B: SCHEDULE OF STUDY PROCEDURES 46
23. APPENDIX C: AMENDMENT HISTORY 47
24. APPENDIX D: POTENTIAL SITE COLLABORATORS 48

1. KEY CONTACTS

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Statistician	Not applicable
Committees	Not applicable

2. LAY SUMMARY

Cancer of the oesophagus (food pipe) and stomach are serious conditions that often require major surgery as part of curative treatment. These are among the most complex operations performed in cancer surgery and carry a significant risk of complications. Understanding how fit a patient is before their operation helps surgeons and anaesthetists anticipate who may be at higher risk, plan their care more carefully, and have better conversations with patients about what to expect.

At present, the standard way of measuring fitness before this type of surgery is cardiopulmonary exercise testing (CPET). During CPET, a patient cycles on a stationary bike while their heart and lung function are carefully measured. While CPET provides valuable information, it is a single snapshot taken in a hospital setting and does not capture how a person functions in their normal daily life.

Wearable devices can continuously record information about a person's heart rhythm, physical activity, and sleep in their own home environment over days or weeks. This may give a more complete and realistic picture of a patient's fitness and how it changes throughout their treatment and recovery.

In this study, we aim to develop and internally validate a model that uses wearable-device data to estimate CPET-measured VO_2peak, a marker of cardiorespiratory fitness. We will also explore how wearable-derived measures relate to patient-reported symptoms, physical function and recovery across the treatment pathway. Participants will wear two wearable devices – one on the chest and one on the wrist – at several time points before and after their surgery and complete short questionnaires about their quality of life and general health. No additional hospital visits will be required solely for the purpose of this study.

The study will take place across several specialist cancer surgery centres in England. The findings will help us understand whether wearable devices could be used alongside CPET in the future, and whether they can provide additional information about patients' day-to-day physical activity, physiology, and recovery that is not captured by a single hospital-based assessment.

3. SYNOPSIS

Study Title	Peri-Operative wearabLe-based Assessment and patient Reported Outcomes In Surgery for Oesophago-Gastric cancer (POLARIS-OG): A prospective multi-centre observational study
Internal ref. no. / short title	POLARIS-OG
Study registration	N/A – Non-interventional study
Sponsor	University of Oxford Research Governance, Ethics & Assurance Team Boundary Brook House, Churchill Drive, Headington, OX3 7GB University of Oxford Email: rgea.sponsor@admin.ox.ac.uk
Funder	Oxford Cancer | CRUK Oxford Centre University of Oxford Churchill Hospital OX3 7LE cancer@medsci.ox.ac.uk
Study Design	Prospective Multi-Centre Non-Interventional Observational Study
Study Participants	Individuals aged 18 or over with oesophagogastric cancer, due to undergo elective curative-intent oesophagogastric cancer resection surgery
Sample Size	200 Participants
Planned Study Period	Total study period: approximately 33 months Individual study period: approximately 15 months (active participation ~6 months; clinical follow-up to 1 year post-surgery)
Planned Recruitment period	September 2026 – February 2028 (18 Months)

	Objectives	Outcome Measures	Timepoint(s)
Primary	To develop and internally validate a prediction model for CPET-derived peak oxygen uptake, measured as VO_2peak, using wearable-derived physiological and activity parameters collected during real-world monitoring.	The primary outcome will be root mean squared error (RMSE) between wearable-predicted VO_2peak and CPET-measured VO_2peak, expressed in $ml \cdot kg^{-1} \cdot min^{-1}$. Secondary performance measures will include mean absolute error, coefficient of determination, calibration intercept and slope, mean prediction bias, Bland–Altman limits of agreement, and the proportion of predictions falling within pre-specified clinically acceptable error margins, for example ±2 and ±3 $ml \cdot kg^{-1} \cdot min^{-1}$.	Pre-operative baseline or post-neoadjuvant chemotherapy. If more than one CPET, the closest test to index surgery will be selected.
Secondary	To develop and internally validate a prediction model for CPET-derived Anaerobic Threshold (AT), using wearable-derived physiological and activity parameters collected during real-world monitoring.	Performance measures will include RMSE, mean absolute error, coefficient of determination, calibration intercept and slope, mean prediction bias, Bland–Altman limits of agreement, and the proportion of predictions falling within pre-specified clinically acceptable error margins.	Pre-operative baseline or post-neoadjuvant chemotherapy. If more than one CPET, the closest test to index surgery will be selected.
	To evaluate the relationship between pre-operative wearable-derived cardiorespiratory fitness and CPET-derived cardiorespiratory fitness in patients undergoing surgery for oesophago-gastric cancer.	Pearson or Spearman correlation coefficients, with 95% confidence intervals, between pre-operative wearable-derived metrics and CPET-derived variables including VO_2peak, anaerobic threshold and VE/VCO_2 slope. Wearable-derived metrics will included daily step count, activity averages, minimum heart rate, resting heart rate, heart rate variability (RMSSD,	Pre-operative baseline or post-neoadjuvant chemotherapy. If more than one CPET, the closest test to index surgery will be selected.

		SDNN), heart rate reserve, and chronotropic index	
	To describe different trajectory clusters of patients' wearable-derived features across the clinical course from baseline to post-operative	Time series evaluation of wearable derived features including activity time, daily step count, chronotropic incompetence, HRV, resting heart rate, heart rate reserve, and sleep metrics where derivable.	Baseline, Post-neoadjuvant chemotherapy, 30- and 90-day post-operation
	To assess agreement between VO_2peak estimated using a published wearable-derived algorithm[1] and CPET-derived VO_2peak.	Bland–Altman agreement, RMSE, MAE, prediction bias and Pearson or Spearman correlation between published algorithm-derived VO_2peak and CPET-derived VO_2peak.	(1) Baseline, (2) post-neoadjuvant chemotherapy (if multiple CPET tests, the test closest to index surgery will be selected for the primary analysis)
	To evaluate the association of wearable-derived measures with patient-reported outcome measures	Health-related quality of life and health utility (EQ-5D-5L; SF-36)	Baseline, Post-neoadjuvant chemotherapy, 30- and 90-day post-operation
	To determine usability and acceptability of wearable devices	Device wear-time adherence; participant-reported acceptability and tolerability	Baseline, Post-neoadjuvant chemotherapy, 30- and 90-day post-operation
Intervention(s)	This is a non-interventional observational study. No investigational medicinal products, surgical procedures, or therapeutic interventions are administered as part of the study. All devices used are CE/UK CA marked and no data will be shared with the device suppliers. The study procedures comprise: (1) Continuous physiological monitoring using two wearable devices — a chest-worn patch and a wrist-worn device — during the pre-operative, peri-operative, and post-discharge periods (2) Cardiopulmonary exercise testing (CPET) performed as part of standard pre-operative assessment (3) Completion of patient-reported outcome measures (EQ-5D-5L; SF-36) at designated timepoints		

	All clinical management decisions, including surgical approach and perioperative care, remain entirely at the discretion of the treating clinical team.
Comparator	There is no comparator intervention. As an observational cohort study, POLARIS-OG does not randomise participants or assign comparator treatments. The study evaluates the agreement of wearable-derived measures against the current standard of pre-operative fitness assessment, cardiopulmonary exercise testing (CPET), which serves as the reference standard for comparison of wearable device metrics.

4. ABBREVIATIONS

Abbreviation	Definition
AJCC	American Joint Committee on Cancer
ASA	American Society of Anesthesiologists physical status classification
AT	Anaerobic Threshold
AUGIS	Association of Upper Gastrointestinal Surgery of Great Britain and Ireland
AUROC	Area Under the Receiver Operating Characteristic Curve
CI	Chief Investigator
CPET	Cardiopulmonary Exercise Testing
CRF	Case Report Form
ECCG	Esophagectomy Complications Consensus Group
eCRF	Electronic Case Report Form
EDF	European Data Format
EQ-5D-5L	EuroQol Five-Dimension Five-Level questionnaire
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
HDU	High Dependency Unit
HRA	Health Research Authority
HRV	Heart Rate Variability
ICF	Informed Consent Form
ICU	Intensive Care Unit
IRR	Incidence Rate Ratio
MCTQ	Munich ChronoType Questionnaire
MDT	Multidisciplinary Team
METs	Metabolic Equivalents of Task
MHRA	Medicines and Healthcare products Regulatory Agency
NACT	Neoadjuvant Chemotherapy
NHS	National Health Service
OG	Oesophagogastric
OR	Odds Ratio
PI	Principal Investigator
PIL	Participant Information Leaflet
PIS	Participant Information Sheet
PROM	Patient-Reported Outcome Measure
R&D	NHS Trust Research and Development Department
REC	Research Ethics Committee
REDCap	Research Electronic Data Capture
RGEA	Research Governance, Ethics and Assurance

RMSSD	Root Mean Square of Successive Differences
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SDNN	Standard Deviation of Normal-to-Normal Intervals
SF-36	Short Form 36 Health Survey
SOP	Standard Operating Procedure
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TRIPOD	Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis
UKCA	United Kingdom Conformity Assessed
VO_2peak	Peak Oxygen Uptake

5. BACKGROUND AND RATIONALE

Oesophagogastric cancer surgery induces a profound physiological stress response, characterised by increased tissue oxygen consumption, systemic inflammation, and significant muscle wasting.[2] The volume of oesophagogastric surgery is rising in an ageing population with increasing comorbidity burden and both surgery and post-operative complications are associated with substantial short- and long-term consequences. These include reduced quality of life, increased medical and social care needs, prolonged healthcare utilisation, and reduced overall survival.[2]

A patient's peri-operative cardiorespiratory fitness and functional reserve play a critical compensatory role in determining their ability to tolerate surgery and recover.[2] Large multicentre cohort studies have consistently demonstrated strong associations between pre-operative functional reserve and post-operative morbidity and mortality.[3,4] As a result, cardiopulmonary exercise testing (CPET) is regarded as the gold standard for objective assessment of cardiorespiratory fitness and pre-operative physiological risk in patients undergoing high risk surgery in the elective setting.[5] CPET provides a comprehensive evaluation of aerobic capacity under physiological stress, including measurement of peak oxygen uptake, and has strong discriminative ability for predicting post-operative outcomes.[5–7]

However, CPET has several limitations that restrict its scalability and broader clinical application within contemporary peri-operative care pathways. It is resource-intensive, requiring specialist equipment, dedicated laboratory facilities, and trained personnel, which limits accessibility across healthcare systems and constrains its routine use at scale.[5] CPET also provides only a single time-point assessment performed within a highly controlled clinical environment and may therefore fail to reflect functional capacity and physiological reserve during normal daily activities.[5] Furthermore, successful completion of CPET is highly dependent on patient effort and co-operation, which may be compromised in patients who are frail, nutritionally depleted, sarcopenic, or recovering from neoadjuvant chemotherapy.[5] As a result, some patients may be unable to complete maximal exercise testing reliably, while others may experience additional physical or psychological burden associated with the assessment. These limitations may disproportionately affect patients at highest peri-operative risk and highlight the need for complementary approaches capable of delivering objective, scalable, and longitudinal assessment of physiological function in real-world settings.

Wearable devices may provide a scalable and patient-centred method of measuring physical activity, heart rate, sleep, and physiological recovery during daily life.[8] Unlike laboratory-based exercise testing, wearable technologies permit longitudinal assessment in free-living environments and may capture aspects of habitual function, cardiovascular response, and recovery that are not assessed by single time-point hospital-based testing. Small single-centre studies in high-risk surgical cohorts have demonstrated associations between wearable-derived activity metrics, such as step count, and post-operative complications and length of stay.[9–11] Further validation studies in healthy cohorts have shown concordance between wearable-derived features and CPET metrics of aerobic fitness,[1] suggesting that wearables may capture meaningful physiological signals relevant to cardiorespiratory fitness and surgical risk.

Despite this promise, a critical knowledge gap remains. There has been limited large-scale, multi-centre evaluation of advanced wearable devices in complex surgical oncology populations, particularly alongside gold-standard CPET. Importantly, it remains unclear whether wearable-derived physiological and activity parameters can be combined to accurately estimate CPET-derived peak oxygen uptake, measured as VO_2peak, in patients undergoing curative-intent oesophagogastric cancer surgery. Developing and internally validating such a model would provide important evidence on whether real-world wearable data can act as a scalable marker of cardiorespiratory fitness, while retaining CPET-derived VO_2peak as the reference standard.

Peri-operative physiological reserve is also a dynamic rather than static phenomenon. Patients may experience substantial changes in fitness, functional capacity, and physiological reserve during neoadjuvant treatment, prehabilitation, surgery, and post-operative recovery; yet current assessment strategies largely rely on isolated single snapshot clinic-based measurements. There is limited evidence to describe how physiological reserve evolves across the entire treatment pathway. Whether wearable-derived measures can characterise these changes in a clinically meaningful manner, and how these measures related to CPET-derived fitness, patient-reported symptoms, functional recovery, and quality of life.

Unpublished work from our group involving large UK and US peri-operative cohorts comprising more than 7,000 patients has demonstrated that pre-operative step count measured using wearable devices is strongly associated with post-operative outcomes and hospital length of stay. Patients recording fewer than 2,500 steps per day pre-operatively demonstrated a 2.6-fold increased risk of 30-day post-operative complications (adjusted OR 2.60; 95% CI 1.55-4.36) and a 1.77-fold longer hospital length of stay (adjusted IRR 1.77; 95% CI 1.42-2.20) compared with patients achieving more than 10,000 steps per day. These findings suggest that wearable-derived activity metrics may provide clinically meaningful markers of physiological reserve and surgical risk in real-world settings.

In parallel, ongoing pilot work from our group (IRAS 344980) provides encouraging early evidence for the feasibility and acceptability of wearable monitoring in patients with oesophagogastric cancer using chest-worn devices. Over 5 months, 45 patients were approached, 32 agreed to receive the participant information sheet and consent form, and 23 were confirmed as eligible and consented following second-stage clinical review. Eighteen participants have completed baseline wearable monitoring, with a further two awaiting baseline measurement. Wearable uptake and adherence have been high. Reasons for non-wear were logistical or clinical rather than acceptability-related, including inability to receive the device before chemotherapy (n = 2) and withdrawal following subsequent evidence of metastatic disease (n = 1).

Across 18 baseline measurements, mean wear time was 89.4% (± 2.3% SD), with a median proportion of data passing quality control constraints of 81.1% (IQR 69.8–87.3%). Participant feedback was also favourable: among 13 returned acceptability questionnaires, all participants reported that the instructions were clearly explained, that they understood what the device was measuring, and that they would be willing to wear the device again. Eleven participants found the device comfortable or very comfortable during daily activities and sleep. Importantly, linkage with the clinical pathway is already underway. Seven participants have completed baseline CPET, two have undergone post-NACT CPET, and three have proceeded to both CPET testing and surgery. As expected in this clinical pathway, nine participants have been withdrawn due to subsequent clinical ineligibility, including metastatic disease or becoming too unwell for a curative surgical pathway, while six are awaiting CPET and surgery. These early findings support the feasibility and acceptability of wearable monitoring in this population and provide valuable practical insight into recruitment, device logistics, longitudinal CPET follow-up, data quality, and expected attrition in a prospective oesophagogastric cancer surgical cohort.

The proposed study will recruit adults undergoing curative-intent surgery for oesophageal or gastric cancer within specialist Upper Gastrointestinal cancer centres. Findings from this work are expected to be generalisable to patients undergoing major elective oesophagogastric cancer surgery within similar tertiary surgical oncology settings and may inform similar work in other high-risk surgical and oncological populations. Participants will undergo longitudinal monitoring using chest-worn electrocardiogram (ECG) and accelerometry devices, together with wrist-worn photoplethysmography (PPG) and accelerometry devices, during the peri-operative pathway.

The primary aim of this study is to develop and internally validate a model that predicts CPET-derived VO_2peak using wearable-derived physiological and activity parameters collected during real-world monitoring. CPET-derived VO_2peak will be treated as the reference standard outcome. Wearable-derived predictors may include measures of physical activity, sedentary behaviour, acceleration-derived movement, heart rate, heart rate variability, chronotropic response, sleep, physiological recovery, and day-to-day variability. Model performance will be assessed using measures of prediction accuracy and agreement, including root mean squared error, mean absolute error, coefficient of determination, calibration, prediction bias and Bland–Altman limits of agreement.

In addition to the primary prediction modelling objective, the study will evaluate the peri-operative trajectory of wearable-derived physiological function and activity across the treatment pathway. Wearable-derived measures will be compared with CPET variables and patient-reported outcome measures, and exploratory associations between wearable-derived parameters and clinical outcomes will be investigated. This will allow assessment not only of whether wearable data can estimate CPET-derived VO_2peak, but also whether wearables provide additional information regarding free-living functional status, treatment-related physiological decline, recovery, and patient experience.

This study will therefore evaluate whether wearable-derived measures can be used to develop a predictive model of CPET-derived VO_2peak, while also providing complementary information beyond CPET through objective, repeated, and longitudinal assessment in real-world settings. If validated, wearable monitoring could extend physiological assessment beyond isolated hospital-based testing and support repeated measurement throughout the peri-operative pathway, including during neoadjuvant treatment, prehabilitation, pre-operative optimisation, and post-operative recovery. This may ultimately support

more personalised risk stratification, earlier identification of treatment-related physiological decline, and objective evaluation of recovery following major cancer surgery.

The work from this study does not aim to replace CPET, which remains the gold-standard for objective assessment of cardiorespiratory fitness under controlled physiological stress. Rather, it aims to investigate whether wearable-derived physiological and activity data can be used to estimate CPET-derived VO_2peak and provide additional clinically relevant information that CPET cannot readily capture, including free-living physical activity, physiological response during daily life, longitudinal change over time, and recovery after treatment. Variation in adherence to wearable use, differences in peri-operative treatment pathways between centres, and missing longitudinal data may influence data completeness and generalisability. Nevertheless, this study is intended to provide important feasibility, acceptability, prediction modelling and exploratory physiological data to inform the design of future interventional, recovery-monitoring, and risk-stratification studies.

The risks associated with participation are anticipated to be minimal and relate primarily to mild discomfort, skin irritation, or inconvenience associated with wearable device use and questionnaire completion. Participants are not expected to derive direct clinical benefit from participation. However, the study may contribute to the development of improved peri-operative risk assessment, personalised peri-operative care pathways, and future wearable-guided interventions for patients undergoing major cancer surgery. Further detail regarding safety considerations and adverse event reporting is provided in the relevant safety reporting sections of this protocol.

6. OBJECTIVES AND OUTCOME MEASURES

Objectives	**Outcome Measures**	**Timepoint(s) of evaluation of this outcome measure (if applicable)**
Primary Objective		
To develop and internally validate a prediction model for CPET-measured peak oxygen uptake, measured as VO_2peak, using wearable-derived physiological and activity parameters collected during real-world monitoring.	The primary outcome will be root mean squared error (RMSE) between wearable-predicted VO_2peak and CPET-measured VO_2peak, expressed in $ml \cdot kg^{-1} \cdot min^{-1}$. Secondary performance measures will include mean absolute error, coefficient of determination, calibration intercept and slope, mean prediction bias, Bland–Altman limits of agreement, and the proportion of predictions falling within pre-specified clinically acceptable error margins, for example ±2 and ±3 $ml \cdot kg^{-1} \cdot min^{-1}$.	Pre-operative baseline or post-neoadjuvant chemotherapy. If more than one CPET, the closest test to index surgery will be selected.

Secondary Objectives		
To develop and internally validate a prediction model for CPET-derived anaerobic threshold (AT), using wearable-derived physiological and activity parameters collected during real-world monitoring.	Performance measures will include RMSE, mean absolute error, coefficient of determination, calibration intercept and slope, mean prediction bias, Bland–Altman limits of agreement, and the proportion of predictions falling within pre-specified clinically acceptable error margins, for example ±2 and ±3 $ml \cdot kg^{-1} \cdot min^{-1}$.	Pre-operative baseline or post-neoadjuvant chemotherapy. If more than one CPET, the closest test to index surgery will be selected.
To evaluate exploratory associations between pre-operative wearable-derived physiological and activity metrics and CPET-derived cardiorespiratory fitness variables in patients undergoing surgery for oesophago-gastric cancer.	Pearson or Spearman correlation coefficients, with 95% confidence intervals, between pre-operative wearable-derived metrics and CPET-derived variables including VO_2peak, anaerobic threshold and VE/VCO_2 slope. Wearable-derived metrics will include daily step count, activity averages, minimum heart rate, resting heart rate, heart rate variability (RMSSD, SDNN), heart rate reserve, and chronotropic index	Pre-operative baseline or post-neoadjuvant chemotherapy. If more than one CPET, the closest test to index surgery will be selected.
To describe the peri-operative trajectory of wearable-derived physiological metrics across the surgical episode	Time-series description of heart rate, heart rate variability (RMSSD, SDNN), daily step count, active minutes, and sleep metrics (total sleep time, sleep efficiency, number of awakenings, circadian disruption)	Pre-operative baseline, post-NACT, 30-days post-operative, and 90-days post-operative
To assess agreement between VO_2peak estimated using a published[1] wearable-derived algorithm and CPET-derived VO_2peak.	Bland–Altman agreement, RMSE, MAE, prediction bias and Pearson or Spearman correlation between published algorithm-derived VO_2peak and CPET-derived VO_2peak.	(1) Baseline, (2) post-neoadjuvant chemotherapy (if multiple CPET tests, the test closest to index surgery will be selected for the primary analysis)
To evaluate the association between wearable-derived measures of physical activity and physiological fitness and patient-reported health-related quality of life and functional status	Domain scores and summary indices of the EQ-5D-5L (utility index and visual analogue scale) and SF-36 (physical and mental component summary scores), assessed by Pearson or Spearman correlation with wearable-derived metrics	(1) Baseline, (2) post-neoadjuvant chemotherapy, (3) 30-days post-surgery, (4) 90-days post-surgery

To determine the usability and acceptability of wearable devices for peri-operative monitoring in oesophagogastric cancer surgical patients	Device wear-time adherence (proportion of expected monitoring period with valid data recorded); participant-reported acceptability and tolerability assessed via structured questionnaire at 30 days post-discharge	(1) Baseline, (2) post-neoadjuvant chemotherapy, (3) 30-days post-surgery, (4) 90-days post-surgery
Exploratory Objectives		
To explore associations between wearable-derived measures, CPET-derived variables and post-operative morbidity, hospital length of stay, readmission and mortality following oesophagogastric cancer surgery.	Associations between pre-operative wearable-derived metrics and postoperative clinical outcomes, including major postoperative complications defined as Clavien-Dindo grade ≥ IIIa, hospital length of stay, duration of critical care admission, unplanned readmission at 30 and 90 days, and all-cause mortality. Analyses will be exploratory and hypothesis-generating, using appropriate regression methods to estimate effect sizes with 95% confidence intervals.	30, 90, and 365 days post-operative
To develop and internally validate a multimodal risk-prediction model for major post-operative morbidity combining wearable-derived, CPET, and patient-reported outcome data	AUROC, sensitivity, specificity, and other relevant metrics of a combined predictive model; ORs with 95% confidence intervals for individual predictors retained in the final model; internal validation via bootstrapping or cross-validation	30 and 90 days post-operative

7. STUDY DESIGN

POLARIS-OG is a prospective, multi-centre observational study evaluating the relationship between wearable-derived physiological and activity measures, CPET-derived cardiorespiratory fitness, patient-reported outcomes and postoperative recovery in patients undergoing treatment for oesophago-gastric cancer. The primary analysis will develop and internally validate a model that predicts CPET-derived VO_2peak using wearable-derived physiological and activity parameters collected during real-world monitoring. In addition to the primary prediction modelling objective, the study will evaluate the peri-operative trajectory of wearable-derived physiological function and activity across the treatment pathway. Wearable-derived measures will be compared with CPET variables and patient-reported outcome measures, and exploratory associations between wearable-derived parameters and clinical outcomes will be investigated. A visual summary of the study design is shown in Appendix A.

Participants will be recruited from Upper Gastrointestinal Cancer Centres across England. Appendix D lists all potential participating centres. Recruiting sites will include tertiary referral hospitals and specialist cancer surgery centres responsible for the diagnosis, neoadjuvant treatment, and surgical management of

oesophagogastric cancer. Future recruitment may expand to additional centres in Wales, Scotland, and selected European centres in Germany and the Netherlands.

Potential participants will be identified during routine outpatient or multidisciplinary team (MDT) pathways when a clinical decision has been made to proceed with curative-intent surgery. Recruitment, consent, and clinical follow-up will be undertaken locally by participating site teams. Wearable devices will be distributed centrally by the University of Oxford via mail delivery.

Participants will be involved in the active study period for approximately 6 months, with additional clinical follow-up through review of routine medical records continuing until 1 year after surgery (approximately 15 months total study duration). Eligible patients will be approached in outpatient clinics following diagnosis and treatment planning and will have up to 3 weeks to consider participation, or until 7 days prior to commencing neoadjuvant chemotherapy, whichever occurs sooner.

Following consent, participants will complete wearable monitoring and questionnaires at four study timepoints:

- Baseline (at recruitment): chest-worn and wrist-worn devices worn continuously for 7 days; completion of EQ-5D-5L, SF-36, and wearable experience questionnaire
- Post-neoadjuvant therapy / pre-surgery: repeat 7-day monitoring using chest-worn and wrist-worn devices; CPET performed as part of standard care; repeat questionnaires
- 30 days following surgery: wrist-worn device only for 7 days; repeat questionnaires
- 90 days following surgery: wrist-worn device only for 7 days; repeat questionnaires

Wearable devices will be posted directly to participants together with written and diagrammatic instructions and pre-paid packaging for device return. No additional hospital visits will be required specifically for study participation.

Physiological and activity data will be collected using two wearable devices:

- Bittium Faros 180 chest-worn device — collecting single-lead electrocardiogram (ECG) and triaxial accelerometry data
- Garmin® wrist-worn device – collecting photoplethysmography (PPG) derived heart rate and raw triaxial accelerometry data

Patient-reported outcomes will be collected using the validated questionnaires EQ-5D-5L and SF-36. A wearable acceptability and user experience questionnaire will also be administered to assess participant usability and tolerability of the devices.

Clinical data, including CPET variables (e.g. anaerobic threshold and VO_2peak), cancer characteristics, treatment details, surgical outcomes, and postoperative recovery data, will be obtained from routine clinical records and uploaded by local research teams into REDCap electronic case report forms (eCRFs).

These methods have been selected to enable longitudinal assessment of physiological function, physical activity, recovery trajectories, and patient experience within participants' usual living environments, while minimising participant burden and avoiding unnecessary hospital visits. The wearable devices are designed for simple self-application and will not require Bluetooth pairing, smartphone connectivity, or participant-led data transfer. In addition, questionnaires will be available in both electronic and paper formats to ensure broad accessibility and reduce the risk of excluding participants based on digital access or technological literacy.

8. PARTICIPANT IDENTIFICATION

8.1. Study Participants

Participants aged 18 or over undergoing elective curative-intent oesophageal or gastric cancer surgery.

8.2. Inclusion Criteria

- Participant is willing and able to give informed consent for participation in the study.
- Male or Female, aged 18 years or above.
- Participants due to undergo elective oesophagogastric cancer resection surgery (oesophageal, oesophagogastric junction or gastric cancer)

8.3. Exclusion Criteria

The participant may not enter the study if ANY of the following apply:

- Urgent or emergency surgery
- Poor baseline mobility (e.g. wheelchair bound)
- Inability to undergo assessment with wearables or CPET as defined by national guidelines (e.g. active myocardial ischaemia, decompensated heart failure, uncontrolled/untreated arrhythmias, aortic dissection or suspected aortic dissection, endo/peri/myocarditis, acute exacerbation of COPD or asthma, acute pulmonary oedema, acute respiratory failure and pulmonary embolism.)
- Metal allergy or sensitivity to medical adhesives

9. PROTOCOL PROCEDURES

9.1. Recruitment

Patients meeting the inclusion criteria will be identified at the MDT or outpatient clinic where a decision has been made to proceed with surgery. Clinicians or members of the local research team will screen prospective participants to determine if they satisfy the eligibility criteria, after which they will be invited to participate in the study.

Local clinicians/researchers will provide details of the study to the participant by providing a Participant Information Sheet (PIS). The PIS will include details about the study including key time-points, potential adverse effects, and answers to frequently asked questions. The PIS will also confirm the participant's right to withdraw from the study at any time. There will also be contact details for the local research team, and central research team in Oxford, should the participant have any further questions.

If required, local translation services can be adopted to address non-English speaking participants. Translated patient-facing materials can be made upon request from a participating centre.

9.2. Screening and Eligibility Assessment

All participants who satisfy the inclusion and none of the exclusion criteria of the protocol will be invited to participate in the study. Participants will have a window period of three weeks from being informed of the study or until 7 days before commencement of neoadjuvant chemotherapy, whichever is sooner, to deciding participation.

Participation in this study should not delay or interfere with commencement or continuation of routine standard treatment or other required investigations. If a participant is not confirmed in the study at least 7 days prior to commencement of neoadjuvant chemotherapy, they shall be excluded from the study as

they will be unable to provide a baseline measurement. Where participants have radiological imaging or other indications to remove the wearable devices within the 7-day wear period, they should do so for the necessary time before reapplying the devices when safe and appropriate to do so.

9.3. Informed Consent

The participant must personally sign and date the latest approved version of the Informed Consent Form (ICF) before any study specific procedures are performed.

Potential participants will be provided with the current approved Participant Information Sheet (PIS) and given sufficient opportunity to read and consider the information, discuss the study with the research team, and ask any questions before deciding whether to participate. The research team will ensure that participants understand what participation involves and that their decision is voluntary. Participants will be informed that they are free to decline participation or withdraw from the study without this affecting their usual clinical care.

Following discussion of the study and PIS, participants may provide electronic consent via REDCap. Where a participant does not provide consent at that time, and has agreed to further contact, the local research team may contact them by telephone or discuss the study with them at a subsequent agreed hospital visit. This will provide a further opportunity to ask questions and consider participation before consent is obtained.

Written and/or electronic versions of the PIS and ICF will be presented to the participants detailing no less than: the exact nature of the study; what it will involve for the participant; the implications and constraints of the protocol; the known side effects and any risks involved in taking part. It will be clearly stated that the participant is free to withdraw from the study at any time for any reason without prejudice to future care, without affecting their legal rights, and with no obligation to give the reason for withdrawal.

The participant will be allowed as much time as wished to consider the information, and the opportunity to question the Investigator, their GP or other independent parties to decide whether they will participate in the study. Informed consent will then be obtained by means of a written or electronically participant-dated signature and dated signature of the person who presented and obtained the informed consent. The person who obtained the consent must be suitably qualified and experienced and have been authorised to do so by the Chief/Principal Investigator. A copy of the signed Informed Consent will be given to the participant. Electronic versions of the signed form will be stored on REDCap. If the consent form was signed on paper, a copy of the consent form will be uploaded to REDCap and the original signed form will be retained at the study site.

9.4. Randomisation

This is a non-randomised observational study. All participants who provide informed consent and meet the eligibility criteria will be enrolled sequentially. There is no randomisation procedure. Participants will be registered via the REDCap electronic data capture system upon enrolment.

9.5. Blinding and code-breaking

There is no blinding in this study. All participants, site investigators, and the central research team will be aware of the study procedures and devices used. No code-breaking procedure is required.

9.6. Description of study intervention(s), comparators, and clinical procedures

9.6.1. Description of study intervention(s)

This is a non-interventional observational study. No investigational medicinal products, surgical procedures, or therapeutic interventions are administered as part of the study. The study procedures comprise continuous physiological monitoring using two CE/UK CA marked wearable devices — a chest-worn patch and a wrist-worn watch — during the pre-operative and post-operative periods, completion of patient-reported outcome measures at designated timepoints, and collection of clinical data from routine medical records. All clinical management decisions, including surgical approach and perioperative care, remain entirely at the discretion of the treating clinical team.

Chest-worn device — Bittium Faros 180

The Bittium Faros 180 is a CE-marked chest-worn physiological monitoring device collecting single-lead electrocardiogram (ECG) and triaxial accelerometry data. The device will be applied to the anterior chest using an adhesive electrode strip supplied with the device, following manufacturer guidelines. The device will be worn for 7 days at timepoints T1 (baseline) and T2 (pre-operative assessment). Data transfer from the device will be via USB connection to secure servers within the Nuffield Department of Population Health. No data will be shared with the manufacturer. The following metrics will be derived from the continuous physiological signal using in-house validated algorithms developed by the OxWearables group, Nuffield Department of Population Health, University of Oxford:[12] maximum and minimum heart rate, heart rate reserve, resting heart rate, heart rate variability, heart rate recovery relative to activity, and wearable-derived chronotropic response or chronotropic index, where derivable. Physical activity metrics derived from the integrated accelerometer will include time spent in activity zones (sedentary, light, moderate, and vigorous intensity) and sleep metrics. In addition, data quality metrics will be assessed including total wear time, proportion of the expected monitoring period yielding analysable data; and signal quality indicators. Automated quality control checks will be applied to all raw data prior to analysis to identify and exclude periods of non-wear, signal artefact, or data corruption.

Wrist-worn device — Garmin® Activity Watch

Participants will be provided with a Garmin® wrist-worn activity watch, such as a vívoactive® 6, Venu® 3, or Forerunner® 165 model. Garmin® wrist-worn devices are commercially available consumer wearable devices, with relevant model-specific Declarations of Conformity available from Garmin. The device will be worn preferably on the dominant wrist, unless participant preference, comfort, or clinical factors require use of the non-dominant wrist. The device will be used at all four study timepoints (T1–T4).

Participants will be asked to wear the device continuously during each monitoring period, except where removal is required for charging, comfort, clinical care, or participant preference. Data collected will include raw accelerometry, beat-to-beat interval data, and heart rate data. Derived measures will be aligned, where possible, with those obtained from the Bittium Faros device, including assessment of data quality, wear time, and the proportion of analysable data.

Data will be accessed through a secure pathway using Fitrockr software. This platform enables specified data to be downloaded from Garmin® devices without requiring participant linkage to Garmin Connect cloud services. Fitrockr is stated to be compliant with GDPR, relevant EU data protection requirements, and Good Clinical Practice principles (see https://www.fitrockr.com/research/). Devices will be configured using the Fitrockr platform before participant wear. Following device return, data will be synced with the Fitrockr application to process the files and produce downloadable csv files of participant data. Data will then be transferred from the platform to secure servers within the Nuffield Department of Population

Health, and removed from the Fitrockr platform. No participant-identifiable information will be shared with Garmin® or Fitrockr during any part of the process.

Device distribution and return

At each timepoint, devices will be distributed to participants via one of the following pathways, according to participant preference and site logistics:

- Postal distribution: devices will be posted directly to the participant with written and diagrammatic instructions for self-application, and a pre-paid parcel return package for return of the device at the end of the wear period.
- Research team distribution: where preferred by the participant or required by the site, devices will be applied by a member of the research team at a clinic visit or other convenient appointment. Return of the device may be via the participant directly with pre-paid post, or collection by the research team at a pre-defined hospital appointment, then returned via pre-paid post.

No additional hospital visits will be required solely for the purposes of device fitting or return.

The central research team at the University of Oxford will be notified of participants who have been consented by local team via entry of participant details into REDCap following consent. Details including participant name, postal address, telephone number, and email address will be provided to facilitate the postage of wearable devices. Sharing of personal information will be strictly limited to individuals responsible for device postage. Participants will be contacted via email to inform them to expect a device delivery, and a second email will be sent to prompt device return after 7 days of wear.

9.6.2. Description of comparator(s)

There is no comparator intervention. As an observational cohort study, POLARIS-OG does not randomise participants or assign comparator treatments. Cardiopulmonary exercise testing (CPET) serves as the reference standard against which wearable-derived VO_2peak and AT are evaluated, reflecting its current role as the gold-standard method of pre-operative fitness assessment. CPET is performed as part of routine standard care at all participating centres and does not constitute a study-specific intervention. Details of CPET procedures are provided in section 9.6.3.

9.6.3. Description of clinical procedure(s) undertaken as part of the study

Cardiopulmonary exercise testing (CPET)

CPET will be performed as part of routine standard care at the pre-operative assessment timepoint. In accordance with local institutional practice, CPET may be performed prior to commencement of neoadjuvant chemotherapy, following completion of neoadjuvant chemotherapy, or at both timepoints. Where CPET is performed at more than one timepoint, data from all available tests will be recorded and analysed. Testing will follow the American Thoracic Society / American College of Chest Physicians joint statement on cardiopulmonary exercise testing, using an incremental ramp protocol on a cycle ergometer.[13] Each test will be supervised by a clinician and physiologist trained in CPET, with full resuscitation facilities available. The following variables will be recorded: peak oxygen uptake (VO_2peak; $mL \cdot kg^{-1} \cdot min^{-1}$); anaerobic threshold (AT; $mL \cdot kg^{-1} \cdot min^{-1}$) determined by the modified V-slope method; ventilatory equivalent for carbon dioxide at the anaerobic threshold (VE/VCO_2 at AT); peak work rate (Watts); and peak heart rate. CPET is performed as part of routine standard care at all participating centres; no additional visit is required for this procedure.

Baseline Sleep Questionnaire

The validated Munich ChronoType Questionnaire (MCTQ) will be sent to the participant after consent at the baseline timepoint only. The purpose of this questionnaire is to establish regular sleeping patterns of the participant for wearable device sleep detection, and as an important adjustment variable for any sleep related secondary analyses. The questionnaire will be administed via the REDCap study platform. A paper-based alternative will be available for participants unable or unwilling to use digital tools.

Patient-reported outcome measures (PROMs)

Two validated patient-reported outcome measures will be administered at each of the four study timepoints (T1–T4):

- EQ-5D-5L: a generic measure of health-related quality of life and health utility comprising five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) each rated on a five-level scale, and a visual analogue scale for overall health.
- SF-36: a 36-item generic health survey measuring eight domains of health-related quality of life, yielding physical and mental component summary scores.

PROMs will be administered electronically via the REDCap study platform, with automated reminders to participants. A paper-based alternative will be available for participants unable or unwilling to use digital tools.

Wearable experience questionnaire

A brief structured questionnaire assessing participant acceptability, usability, and tolerability of the wearable devices will be administered at each of the four timepoints alongside the PROMs. This questionnaire was developed specifically for use in this study by the research team and has not been formally validated.

Clinical data collection

Clinical and outcome data will be extracted from routine medical records by trained local site research staff and entered into the REDCap eCRF. Data collected will include baseline demographics, comorbidities, tumour staging, neoadjuvant treatment details, operative details, post-operative complications (graded using the Clavien-Dindo classification[14]), hospital and critical care length of stay, readmission, and mortality. Full details of data collected are provided in Section 12 (Data Management).

9.7. Medical Devices

Neither device in this study will be utilised as a medical device. Rather, they will be used as tools to measure physical activity, heart rate metrics, and cardiorespiratory fitness.

Device 1: Bittium Faros 180

The Bittium Faros 180 (Bittium Corporation, Oulu, Finland) is a lightweight chest-worn physiological monitoring device capable of continuous single-lead ECG and triaxial accelerometry recording. The device is CE-marked as a medical device and will be used in accordance with its licensed indications and manufacturer instructions for use. The device will be sourced and held centrally by the University of Oxford research team and distributed to participants as described in section 9.6.1.

User training will be provided to all research staff responsible for device application. Participants will receive written and diagrammatic instructions for device self-application and removal where postal distribution is used. The device is applied using an adhesive electrode strip to the sternum and is designed

for wear periods of up to 7 days. Known risks associated with wear are low and include mild skin irritation or discomfort at the adhesive site. Participants with known metal allergy or sensitivity to medical adhesives are excluded from participation (see section 8.3). Devices will be stored securely at the University of Oxford between use and maintained in accordance with the manufacturer's instructions.

As the Bittium Faros 180 is CE-marked as a medical device and will be used within its licensed indications, the study does not constitute a clinical investigation of a medical device requiring notification to the MHRA. Study data will not be used to support a licensing application or for any commercial purpose. The device manufacturer will have no access to any study data.

Device 2: Garmin® Activity Watch

Garmin® (Garmin International, Inc., Olathe, Kansas, United States) wrist-worn activity watches, such as the vívoactive® 6, Venu® 3, or Forerunner® 165 models, are commercially available consumer wearable devices designed for continuous monitoring of physical activity and physiological parameters in free-living conditions. Relevant model-specific Declarations of Conformity are available from Garmin, including EU Declarations of Conformity for the vívoactive® 6 and Venu® 3, and a UK Declaration of Conformity for the Forerunner® 165. These declarations relate to applicable consumer product regulations, including radio equipment and restriction of hazardous substances requirements, and support CE/UKCA conformity for the relevant models. The devices are not being used in this study for clinical diagnostic, monitoring, or treatment purposes.

The Garmin® watch requires no specialist fitting and will be worn on the dominant wrist, or on the non-dominant wrist if required because of participant preference, comfort, or clinical factors. Participants will receive written instructions for device fitting, charging, wear, and removal. The risks associated with wear are minimal; the device is non-invasive, wrist-worn, and does not require adhesive application. Participants will be asked to remove the device if required for charging, comfort, clinical care, or participant preference. Devices will be stored securely at the University of Oxford between use and maintained in accordance with the manufacturer’s instructions.

The device will be used in this study solely as a research tool for the collection of wearable-derived physiological and activity data, including raw accelerometry, beat-to-beat interval data, and heart rate data. Data will be accessed through a secure pathway using the Fitrockr platform, enabling specified data to be downloaded from Garmin® devices without requiring participant linkage to Garmin Connect cloud services. Following device return, data will be synced with the Fitrockr application to process the files and produce downloadable csv files of participant data. Data will then be transferred from the platform to secure servers within the Nuffield Department of Population Health and removed from the Fitrockr platform. No participant-identifiable information will be shared with Garmin® or Fitrockr during any part of the process.

Serious incidents involving medical devices

In the event of a serious incident involving the Bittium Faros 180, reporting will be undertaken in accordance with Section 10.3 of this protocol. Device faults or unanticipated issues will be reported to the device manufacturer and, where appropriate, to the MHRA via the Yellow Card scheme. All device incidents will be documented and reported to the Sponsor. As Garmin Devices are not classified as medical

devices, formal medical device incident reporting does not apply; however, any device faults or safety concerns will be documented and reported to the Sponsor and device manufacturer.

9.8. Baseline Assessments

The baseline assessment (T1) will take place at the time of recruitment, prior to commencement of neoadjuvant chemotherapy where applicable. This visit will coincide with the participant's pre-operative assessment appointment as part of routine standard care, such that no additional hospital attendance is required. The following assessments will be completed at this timepoint:

Clinical and demographic data

Participant demographics, medical history, and details of the planned elective surgical procedure will be collected by trained site research staff from routine medical records and entered into the REDCap eCRF.

Wearable device monitoring

Both the Bittium Faros 180 chest-worn device and the Garmin® wrist-worn device will be issued to participants at the baseline timepoint. Devices will be worn continuously for 7 days. Device distribution will follow the pathways described in section 9.6.1. Participants will be provided with written and diagrammatic instructions for device fitting, care during the wear period, and return procedures.

Munich ChronoType Questionnaire

The validated Munich ChronoType Questionnaire (MCTQ) will be sent to participants at the first wearable device wear time point to establish usual sleep patterns and chronotype. This will be administered electronically via the REDCap study platform or in paper format when preferred.

Patient-reported outcome measures

Participants will complete the EQ-5D-5L and SF-36 questionnaires at the baseline timepoint, administered electronically via the REDCap study platform or in paper format where preferred. Participants will also complete the study-specific wearable experience questionnaire at the end of the 7-day wear period.

Eligibility confirmation

Final confirmation of eligibility will be completed at the baseline visit prior to device issue, ensuring all inclusion criteria are met and no exclusion criteria apply.

9.9. Subsequent Visits

Following the baseline assessment, participants will complete three further study timepoints (T2, T3, and T4), giving a total of four active study visits. No additional hospital attendance will be required solely for study purposes at any timepoint. The schedule of assessments is summarised in Appendix B.

T2 — Pre-operative assessment (post-neoadjuvant chemotherapy / pre-surgery)

This visit will coincide with the participant's pre-operative assessment appointment as part of routine standard care. The following assessments will be completed:

- Both the Bittium Faros 180 chest-worn device and the Garmin® wrist-worn device will be issued and worn continuously for 7 days, following the distribution pathways described in section 9.6.1
- CPET will be performed as part of routine standard care as described in section 9.6.3

- Participants will complete the EQ-5D-5L and SF-36 questionnaires and the study-specific wearable experience questionnaire at the end of the 7-day wear period

T3 — 30 days post-surgery

At 30 days following surgery, participants will be contacted by the research team. The following assessments will be completed:

- The Garmin® wrist-worn device only will be issued and worn for 7 days, following the distribution pathways described in section 9.6.1. The Bittium Faros 180 chest-worn device will not be used at this timepoint
- Participants will complete the EQ-5D-5L and SF-36 questionnaires and the study-specific wearable experience questionnaire at the end of the 7-day wear period
- Clinical outcome data including post-operative complications, hospital length of stay, critical care utilisation, and readmission will be extracted from routine medical records by site research staff and entered into the REDCap eCRF

T4 — 90 days post-surgery

At 90 days following surgery, participants will again be contacted by the research team. The following assessments will be completed:

- The Garmin® wrist-worn device only will be issued and worn for 7 days, following the distribution pathways described in section 9.6.1
- Participants will complete the EQ-5D-5L and SF-36 questionnaires and the study-specific wearable experience questionnaire at the end of the 7-day wear period
- Clinical outcome data will be extracted from routine medical records by site research staff and entered into the REDCap eCRF

T5 — 1-year follow-up (clinical records review)

At approximately 1 year post-surgery (approximately 15 months total study duration), survival status and any further clinical events will be ascertained through review of routine medical records by site research staff. No active participant contact or device use is required at this timepoint.

9.10. Sample Handling

No biological samples will be collected from participants as part of this study. This section is not applicable.

9.11. Early Discontinuation/Withdrawal of Participants

During the course of the study a participant may choose to withdraw at any time. This may happen for several reasons, including but not limited to:

- The occurrence of what the participant perceives as an intolerable adverse experience related to wearing the devices
- Inability to comply with study procedures
- Participant decision

Participants may choose to discontinue device wear and/or questionnaire completion but remain on study follow-up, permitting continued access to their routine clinical records for outcome data collection.

Participants who wish to withdraw consent completely may do so via one of the following three options, which will be clearly explained in the Participant Information Sheet:

- Withdrawal from active follow-up and further contact, whilst permitting the study team to continue to access routine medical records for clinical outcome data recorded as part of standard care
- Withdrawal from the study whilst permitting data collected up to the point of withdrawal to be retained and used in the study analysis. No further data would be collected after withdrawal
- Complete withdrawal from the study, including withdrawal of all data collected up to the point of withdrawal. Data already collected would not be used in the final study analysis. Where data have already been incorporated into interim analyses, this may not be fully reversible, and this limitation will be explained in the Participant Information Sheet

In addition, the Investigator may discontinue a participant from the study at any time if considered necessary for any reason including, but not limited to:

- Ineligibility arising during the study or retrospectively identified at screening
- Significant protocol deviation
- Significant non-compliance with study requirements
- Clinical decision
- Pregnancy

Participants who withdraw will not be replaced. The type of withdrawal and reason for withdrawal will be recorded in the eCRF. Withdrawal from the study will not affect the participant's clinical care in any way.

9.12. Definition of End of Study

The end of study is defined as the point at which all study data have been entered into the REDCap database, all queries have been resolved, and the database has been locked. This will occur following completion of the 1-year post-surgical clinical records review for the last recruited participant, equating to approximately 15 months following recruitment of the final participant.

The end of study will be reported to the Sponsor, Research Ethics Committee, HRA, and funder within 90 days of completion, accompanied by a final study report.

10. SAFETY REPORTING

POLARIS-OG is a non-interventional observational study. Participants are not exposed to any investigational medicinal product or therapeutic intervention as part of the study. The principal study-specific procedures are the wearing of two non-invasive wearable devices and completion of questionnaires, both of which carry minimal risk. The safety reporting window runs from the point of informed consent to completion of the participant's final study timepoint.

The main foreseeable risks associated with study participation are mild skin irritation or discomfort at the adhesive site of the Bittium Faros 180 chest-worn device. Participants with known metal allergy or sensitivity to medical adhesives are excluded from participation. No risks are anticipated from use of the Garmin® wrist-worn device.

10.1. Definition of Serious Adverse Events

A serious adverse event is any untoward medical occurrence that:

- results in death
- is life-threatening
- requires inpatient hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability/incapacity
- consists of a congenital anomaly or birth defect.

Other 'important medical events' may also be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the participant and may require medical or surgical intervention to prevent one of the outcomes listed above.

NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

10.2. Reporting Procedures for Serious Adverse Events

A serious adverse event (SAE) occurring to a participant should be reported to the REC that gave a favourable opinion of the study where in the opinion of the Chief Investigator the event was 'related' (resulted from administration of any of the research procedures) and 'unexpected' in relation to those procedures. Reports of related and unexpected SAEs should be submitted within 15 working days of the Chief Investigator becoming aware of the event, using the HRA report of serious adverse event form (see HRA website).

10.3 Serious Incidents involving Medical Devices

A serious incident is an event that meets all three criteria:

- An event has occurred, or an issue has been identified. This includes situations where testing performed on the device by the manufacturer, examination of the information supplied with the device, or any scientific information indicates some factor that could lead, or has led, to an event.
- The manufacturer's device is suspected to be a contributory cause of the event, including as a side effect.
- The problem directly or indirectly resulted, or might have resulted, in death or a serious deterioration in state of health of a patient, user or other person.

Incidents with the potential to result in serious harm should be reported even if they have not done so due to a pre-use check by the user. Therefore, the following will also be reported:

- an incident associated with a device happened, and
- if it occurred again, it might lead to death or serious deterioration in health

Where there is doubt about whether to report an incident, it will be reported.

In the event of a serious incident involving the Bittium Faros 180, the incident will be reported to the device manufacturer and to the MHRA via the Yellow Card scheme. All device incidents will be documented in the eCRF and reported to the Sponsor within 24 hours.

As the Garmin® wrist-worn devices are not classified as a medical device, formal medical device incident reporting requirements do not apply. However, any device faults or safety concerns will be documented and reported to the Sponsor and to the device manufacturer.

Incidents with the potential to result in serious harm will be reported even if serious harm did not occur. Where there is doubt about whether to report an incident, it will be reported.

11. STATISTICS AND ANALYSIS

The plan for the statistical analysis of the study is outlined below. There is not a separate SAP document in use for the trial. All analyses will be conducted using R and Python. The SAP will be finalised before any analysis takes place.

11.1. Description of the Statistical Methods

Descriptive statistics

Standard descriptive statistics will be used to characterise the study population. Continuous variables will be reported as mean and standard deviation or median and interquartile range as appropriate to their distribution. Categorical variables will be reported as frequencies and percentages. All comparative outcomes will be presented with 95% confidence intervals.

Primary outcome – prediction of CPET-derived VO_2peak using wearable-derived measures

The primary outcome of the study will be the performance of a prediction model estimating CPET-derived VO_2peak from wearable-derived physiological and activity parameters. CPET-derived VO_2peak, expressed in $ml \cdot kg^{-1} \cdot min^{-1}$, will be treated as the reference standard outcome.

The primary analysis will develop and internally validate a participant-level prediction model using wearable-derived features collected during the pre-operative monitoring period closest to surgery. The index CPET will be defined as the valid CPET performed closest to surgery and before the operation. For participants with CPET performed both prior to neoadjuvant chemotherapy, T1, and following completion of neoadjuvant chemotherapy, T2, the index CPET for the primary analysis will be the pre-operative CPET closest to surgery.

Wearable-derived candidate predictors may include:

- Daily step count
- Minutes active / average acceleration
- Moderate-to-vigorous physical activity, MVPA, minutes
- Sedentary time

- Resting heart rate
- Heart rate variability, including RMSSD and SDNN
- Heart rate reserve, defined as $HR_{max} – HR_{min}$
- Heart rate change relative to activity and recovery
- Wearable-derived chronotropic response or chronotropic index, where derivable
- Sleep metrics, where derivable
- Day-to-day variability in physiological and activity measures
- Wear-time and data-quality metrics

Wearable-derived data will be summarised at participant level prior to modelling to avoid pseudo-replication from repeated within-participant observations. Summary features may include mean, median, minimum, maximum, standard deviation, interquartile range, and proportion of valid monitoring time, as appropriate for each variable. Candidate predictors will be pre-specified where possible and limited according to the available sample size to reduce overfitting.

Additional covariates may include participant features e.g. age, gender, BMI, comorbidities, oncological features e.g. cancer type, stage, location, and other parameters which can affect physical activity levels such as season.

The primary modelling approach will use regression-based prediction modelling, with penalised regression methods, such as ridge regression, LASSO, or elastic net regression, considered where the number of candidate predictors is high relative to the available sample size. Non-linear or machine-learning approaches, such as random forest, support vector regression, or gradient boosting, may be explored as secondary exploratory modelling approaches if sample size and data completeness permit.

Model performance will be assessed using optimism-adjusted internal validation. Internal validation will be performed using bootstrap resampling or repeated k-fold cross-validation. The primary model-performance measure will be root mean squared error, RMSE, between predicted VO_2peak and CPET-derived VO_2peak, expressed in $ml \cdot kg^{-1} \cdot min^{-1}$.

Secondary model-performance measures for the primary VO_2peak prediction model will include:

- Mean absolute error, MAE
- Mean prediction error / bias
- Coefficient of determination, R^2
- Calibration intercept
- Calibration slope
- Bland–Altman mean difference and limits of agreement
- Proportion of predictions within pre-specified clinically acceptable error margins, for example ±2 and ±3 $ml \cdot kg^{-1} \cdot min^{-1}$

Model calibration will be assessed by comparing predicted and observed CPET-derived VO_2peak values. Agreement between predicted VO_2peak and CPET-derived VO_2peak will be further evaluated using Bland–Altman plots. Scatter plots of predicted versus observed VO_2peak will be presented with the line of identity and fitted regression line.

In accordance with local institutional practice, CPET may be performed prior to neoadjuvant chemotherapy, T1, following completion of neoadjuvant chemotherapy, T2, or at both timepoints. For the primary prediction model, the index CPET will be the valid pre-operative CPET performed closest to surgery. For participants with CPET at both T1 and T2, data from both tests will be retained for secondary longitudinal and trajectory analyses. A sensitivity analysis restricted to participants with T2-only CPET will be performed where sample size permits.

Secondary outcomes and analyses

Prediction of CPET-derived anaerobic threshold using wearable-derived measures

A key secondary analysis will repeat the primary prediction-modelling approach using CPET-derived anaerobic threshold, AT, as the reference standard outcome instead of VO_2peak. AT will be expressed in $ml \cdot kg^{-1} \cdot min^{-1}$, where available.

The same pre-operative wearable monitoring period, candidate wearable-derived predictors, additional covariates, model-development approach, and internal validation strategy described for the primary VO_2peak model will be used for the AT prediction model. The index CPET for this analysis will be defined in the same way as for the primary analysis, namely the valid CPET performed closest to surgery and before the operation.

Model performance for the AT prediction model will be assessed using:

- RMSE between predicted AT and CPET-derived AT
- MAE
- Mean prediction error / bias
- R^2
- Calibration intercept
- Calibration slope
- Bland–Altman mean difference and limits of agreement
- Proportion of predictions within pre-specified clinically acceptable error margins

This analysis will evaluate whether wearable-derived physiological and activity parameters can also estimate submaximal aerobic fitness, as represented by CPET-derived AT, which may be particularly relevant in patients unable to achieve maximal exercise performance.

Association between wearable-derived measures and CPET-derived variables

Correlation analyses will be performed as secondary exploratory analyses to describe associations between individual wearable-derived metrics and CPET-derived variables, including VO_2peak, anaerobic threshold, and VE/VCO_2 slope.

Pearson or Spearman rank correlation coefficients, with 95% confidence intervals, will be calculated depending on the distribution of each variable and the presence of outliers. These analyses will be considered exploratory and hypothesis-generating, rather than the primary powered analysis.

Wearable-derived features included in the correlation analyses may include:

- Daily step count
- Minutes active / average acceleration
- MVPA minutes
- Sedentary time
- Resting heart rate
- Heart rate variability, including RMSSD and SDNN
- Heart rate reserve, defined as $HR_{max} – HR_{min}$
- Heart rate change relative to activity and recovery
- Wearable-derived chronotropic response or chronotropic index, where derivable
- Sleep metrics, where derivable

Where participants have CPET at both T1 and T2, both assessments may be included in longitudinal exploratory analyses using appropriate repeated-measures methods. Cross-sectional correlation analyses will use the index CPET unless otherwise specified.

Trajectory of wearable-derived measures

The longitudinal profile of wearable-derived metrics across all study timepoints, T1 to T2 to T3 to T4, will be characterised using linear mixed-effects models with random intercepts for participants. Random slopes for time will be considered where model convergence and data structure permit. Models will adjust for key covariates where appropriate, including age, sex, cancer stage, neoadjuvant treatment received, and baseline functional status.

Time-series plots will be generated to illustrate individual and population-level trajectories. These analyses will describe changes in physiological function, activity, rest, and recovery across neoadjuvant treatment, surgery, and post-operative recovery.

Agreement between wearable-derived estimated VO_2peak and CPET-derived VO_2peak using published algorithms

Where feasible, VO_2peak will also be estimated from raw wearable data using previously published algorithms.[1] Agreement between published algorithm-derived VO_2peak and CPET-derived VO_2peak will be assessed using Bland–Altman plots, Pearson or Spearman correlation coefficients with 95% confidence intervals, RMSE, MAE, and prediction bias.

Where appropriate, equivalence testing may be performed using a pre-specified equivalence margin. This analysis will be exploratory because existing wearable-derived VO_2peak algorithms were developed outside this surgical oncology population and may not have been trained using the same device configuration, monitoring duration, or clinical context.

Patient-reported outcomes

The association between wearable-derived metrics and patient-reported outcome measures, including EQ-5D-5L and SF-36 domain scores and summary indices, will be assessed using Spearman rank correlation

coefficients. Longitudinal changes in patient-reported outcome scores across timepoints will be assessed using linear mixed-effects models.

Associations between changes in wearable-derived measures and changes in patient-reported outcomes may also be explored to assess whether objective physiological recovery corresponds with patient-reported symptoms, functional recovery, and quality of life.

Usability, acceptability, and data completeness

Device wear-time adherence, data completeness, signal quality, and participant-reported acceptability will be described using summary statistics. Continuous variables will be summarised using mean and standard deviation or median and interquartile range, depending on distribution. Categorical variables will be summarised using frequencies and percentages.

Acceptability questionnaire responses will be summarised descriptively. Reasons for non-wear, withdrawal, incomplete monitoring, failed data capture, or missing CPET data will be reported where available.

Exploratory Outcomes

- Post-operative 30-day and 90-day morbidity: the association between wearable-derived metrics and post-operative 30- and 90-day morbidity will be quantified using odds ratios (ORs) with 95% confidence intervals derived from logistic regression analysis.
- Hospital length of stay and critical care utilisation: the association between wearable-derived metrics and length of stay outcomes will be quantified using incidence rate ratios (IRRs) with 95% confidence intervals derived from negative binomial or Poisson regression analysis.
- Hospital readmission: the association between wearable-derived metrics and unplanned readmission will be quantified using odds ratios (ORs) with 95% confidence intervals derived from logistic regression analysis.
- All-cause mortality and survival: overall survival will be described using Kaplan-Meier methodology. The association between wearable-derived metrics and survival will be quantified using hazard ratios (HRs) with 95% confidence intervals derived from Cox proportional hazards regression.
- Regression models will adjust for prespecified clinically relevant covariates where sample size permits, including age, sex, body mass index, cancer site, clinical stage, neoadjuvant treatment and comorbidity burden. Exploratory postoperative outcome models will be limited in complexity according to the number of observed events and interpreted as hypothesis-generating.

Wearable data quality and signal processing

All raw wearable data will undergo pre-specified quality control procedures prior to analysis, including automated checks for non-wear periods, signal artefact, and data corruption. Wear-time will be calculated and reported for all participants. A minimum wear-time threshold of 72 hours with full diurnal coverage will be applied, consistent with UK Biobank accelerometry processing standards,[15] below which device data will be considered insufficient for inclusion in the primary analysis. A data-driven approach will be adopted to review and if necessary, adjusting this threshold prior to final analysis, with any deviation from the pre-

specified threshold documented. The proportion of expected monitoring time yielding analysable data will be reported for all participants and timepoints.

Physiological and activity metrics will be derived from raw device data using in-house validated algorithms developed by the OxWearables group, Nuffield Department of Population Health, University of Oxford.[12]

11.2. Sample Size Determination

The study will aim to recruit up to 200 participants. The primary analysis is the development and internal validation of a prediction model estimating CPET-derived VO_2peak from wearable-derived physiological and activity parameters. CPET-derived VO_2peak, expressed in $ml \cdot kg^{-1} \cdot min^{-1}$, will be treated as the reference standard outcome.

As this is a prediction-model development study, the sample size is based on the anticipated precision and stability of model performance estimates rather than a conventional hypothesis test of association. The primary model-performance measure will be root mean squared error, RMSE, between wearable-predicted VO_2peak and CPET-derived VO_2peak. Secondary model-performance measures will include mean absolute error, coefficient of determination, calibration intercept and slope, prediction bias, Bland–Altman limits of agreement, and the proportion of predictions within pre-specified clinically acceptable error margins.

A recruitment target of up to 200 participants is considered appropriate to support development and internal validation of a multivariable prediction model while limiting overfitting. Assuming approximately 8–12 candidate predictor parameters are included in the primary model, and assuming moderate anticipated model performance, for example an optimism-adjusted R^2 of approximately 0.4–0.5, a sample size of approximately 100–150 participants with valid paired wearable and CPET-derived VO_2peak data would be expected to provide adequate model stability for internal validation. This would also allow estimation of model prediction error with reasonable precision. For example, if the observed RMSE is approximately 3.0 $ml \cdot kg^{-1} \cdot min^{-1}$, a sample of 100–150 participants would estimate this error with an approximate 95% confidence interval half-width of around 0.34–0.42 $ml \cdot kg^{-1} \cdot min^{-1}$.

Allowing for approximately 20–25% attrition due to incomplete wearable wear time, inadequate data quality, device failure, withdrawal, progression to metastatic disease, clinical deterioration, inability to complete CPET, or unavailable paired CPET and wearable data, recruitment of up to 200 participants is expected to yield approximately 150–160 participants with valid paired data for the primary VO_2peak prediction analysis. This sample size will also provide a sufficient basis for internal validation using bootstrap resampling or repeated k-fold cross-validation, and for estimating optimism-corrected model performance.

The study will also include a key secondary prediction analysis in which the primary modelling approach is repeated using CPET-derived anaerobic threshold, AT, as the reference standard outcome instead of VO_2peak. The available sample size for the AT model may be smaller than for the VO_2peak model if AT is not identifiable or valid in all CPET assessments. Therefore, the number of candidate predictor parameters in the AT model may be reduced according to the available sample size and data completeness to minimise overfitting.

In addition to prediction modelling, the study is designed to assess the consistency and comparative performance of wearable-derived measures across clinically important participant subgroups, where numbers permit. These may include comparisons by sex, age group, treatment pathway, study centre, and baseline fitness category, including very low fitness defined by CPET-derived VO_2peak below 10 $ml \cdot kg^{-1} \cdot min^{-1}$. These subgroup analyses will be considered exploratory and interpreted cautiously, as the study is not powered to detect definitive subgroup differences in model performance.

Recruitment of up to 200 participants is therefore justified to support the primary VO_2peak prediction model, the secondary AT prediction model, internal validation, assessment of model calibration and agreement, and planned secondary analyses examining CPET variables, wearable-derived chronotropic response features, physical activity metrics, patient-reported outcomes, and peri-operative recovery trajectories. This sample size will improve the precision and generalisability of estimates while allowing for incomplete paired data, expected attrition, and unequal distribution across subgroups.

A 6-month run-in period will be used to activate 4–6 centres and optimise recruitment procedures. The pilot site recruited approximately 20 participants in 4 months. Assuming a conservative recruitment rate of 3–5 participants per centre per month, 4–6 centres would be expected to recruit 150–200 participants within the planned recruitment window.

11.3. Analysis populations

The all-enrolled population will comprise all participants who provide written informed consent. This population will be used to describe recruitment, retention, withdrawal, device return, protocol adherence, and overall study feasibility.

The primary VO_2peak prediction-model population will include participants with a valid index CPET-derived VO_2peak measurement and valid wearable-derived physiological and activity data from the pre-operative monitoring period closest to the index CPET. The index CPET will be defined as the valid CPET performed closest to surgery and before the operation. This population will be used for development and internal validation of the primary model predicting CPET-derived VO_2peak from wearable-derived parameters.

Participants included in the primary VO_2peak prediction-model population must have sufficient wearable data to derive the pre-specified candidate predictor features required for the primary model. These may include physical activity, sedentary behaviour, acceleration-derived movement, heart rate, heart rate variability, chronotropic response, physiological recovery, sleep metrics where derivable, and data-quality variables. Participants with valid CPET-derived VO_2peak but incomplete wearable features may be included in sensitivity analyses or imputed analyses where appropriate, depending on the extent and mechanism of missingness.

The secondary AT prediction-model population will include participants with a valid CPET-derived anaerobic threshold measurement and valid wearable-derived physiological and activity data from the corresponding pre-operative monitoring period closest to the index CPET. This population will be used to repeat the primary prediction-modelling approach using CPET-derived AT as the reference standard outcome instead of VO_2peak. Participants without a valid or identifiable AT will be excluded from the AT prediction-model analysis.

The extended CPET–wearable physiological analysis population will include participants with valid index CPET data and at least one valid wearable-derived physiological or activity metric from the corresponding pre-operative monitoring period. This population will be used for secondary exploratory analyses examining associations between individual wearable-derived features and CPET-derived variables, including VO_2peak, anaerobic threshold, VE/VCO_2 slope, heart rate response, oxygen pulse, and other CPET parameters where available.

The longitudinal CPET–wearable analysis population will include participants with valid wearable-derived data and CPET data at more than one peri-operative timepoint, where available. This population will be used for secondary analyses examining changes in wearable-derived measures and CPET-derived fitness across the treatment pathway, including changes between pre-neoadjuvant chemotherapy and post-neoadjuvant chemotherapy assessments where both are available.

The longitudinal wearable trajectory population will include participants with valid wearable-derived data at two or more study timepoints. This population will be used to model changes in wearable-derived physiological and activity measures across the peri-operative pathway, including T1, T2, T3, and T4, as applicable.

The PROM analysis population will include participants with at least one completed patient-reported outcome measure. Longitudinal PROM analyses will include participants with PROM data at two or more timepoints. This population will be used to assess associations between wearable-derived measures and patient-reported symptoms, functional status, health-related quality of life, and recovery.

The surgical outcome population will include participants who undergo the planned index oesophago-gastric cancer operation and have postoperative clinical outcome data available. This population will be used for exploratory analyses of postoperative morbidity, hospital length of stay, critical care utilisation, readmission, mortality, and survival.

The published wearable-estimated VO_2peak algorithm analysis population will include participants with sufficient wearable data to generate an estimated VO_2peak using a previously published algorithm and a valid CPET-derived VO_2peak from the index CPET. This population will be used for exploratory agreement analyses comparing published algorithm-derived VO_2peak estimates with CPET-derived VO_2peak. This analysis will be considered separate from the primary internally developed VO_2peak prediction model.

11.4. Decision points

A planned internal feasibility review will be conducted when approximately 50% of participants have completed the pre-operative assessment. This review will assess recruitment rate, site activation, device return, wearable wear-time adherence, accelerometry and ECG data completeness, CPET availability and questionnaire completion. The review will not involve formal hypothesis testing and will not be used to change the primary analysis. Operational changes may be made to improve recruitment, device logistics, participant instructions or data completeness.

11.5. Stopping rules

There are no formal efficacy or futility stopping rules for this observational study. In the event of unanticipated safety concerns identified at the interim analysis or at any other point during the study, the Chief Investigator will determine whether continuation of the study is appropriate.

11.6. The Level of Statistical Significance

A two-sided significance level of $p<0.05$ will be used for all analyses unless otherwise specified. Given the exploratory nature of several secondary and exploratory analyses, results will be interpreted in the context of effect sizes and confidence intervals rather than solely on the basis of statistical significance.

11.7. Procedure for Accounting for Missing, Unused, and Spurious Data.

Where possible, complete data entry on REDCap will be strongly encouraged to minimise missing data. Patterns and proportions of missing data will be tabulated for all variables. For participants with less than 20% item-level missingness on demographic measures, multiple imputation by chained equations (MICE) will be applied with a minimum of 20 imputations, combined using Rubin's rules. Sensitivity analyses will include complete-case analysis. Wearable data will undergo pre-specified quality control as described in section 11.1, with documented handling of missing or artefact-corrupted data epochs. Appropriate imputation methods will be implemented where there is missing wearable data. Pre-defined spurious measures which are deemed a priori to be unphysiological (e.g. HR <30 or >230) will be excluded. Participants failing to meet the minimum wear-time threshold will be excluded from the primary analysis population but retained in the all-enrolled population for feasibility analyses.

11.8. Procedures for Reporting any Deviation(s) from the Original Statistical Plan

Any deviations from the pre-specified statistical plan will be documented, dated, and justified in the final study report. Post-hoc analyses will be clearly labelled as such in all publications.

11.9. Health Economics Analysis

No formal health economics analysis is planned as part of this study. This section is not applicable.

12. DATA MANAGEMENT

The plan for the data management of the study are outlined below. There is not a separate Data Management document in use for the study.

12.1. Source Data

Source documents are where data are first recorded and from which participants' eCRF data are obtained. These include but are not limited to hospital medical records, clinical letters and correspondence, CPET reports, wearable device data files, completed questionnaires, and signed informed consent forms.

eCRF entries will be considered source data where the eCRF is the site of original recording and no other written or electronic record exists. All source documents will be stored safely in confidential conditions.

On all study-specific documents, other than the signed consent form, participants will be referred to by their unique study participant number only and not by name.

Wearable device data will be stored locally on the device until return to the research team. Raw data files will be downloaded via USB connection onto a secure encrypted drive hosted on the University of Oxford network. Data files will then be processed using in-house validated algorithms developed by the OxWearables group as described in section 11.1.

12.2. Access to Data

Direct access will be granted to authorised representatives from the Sponsor and host institutions for monitoring and audit of the study to ensure compliance with regulations. Access to participant data will be restricted to members of the research team at participating sites with delegated responsibility from the site Principal Investigator, and members of the central study team at the University of Oxford where necessary for their role.

Research staff who are not part of a potential participant's direct healthcare team will not have access to personally identifiable data until the individual has provided informed consent to participate in the study.

Neither wearable device manufacturer will have access to any study data at any point.

12.3. Data Recording and Record Keeping

All participant data will be recorded onto the REDCap electronic data capture platform, hosted and maintained by the Surgical Intervention Trials Unit, Nuffield Department of Surgical Sciences, University of Oxford. REDCap is a validated, Good Clinical Practice-compliant electronic data capture system. Participants will be identified by a unique pseudonymised study number in the database. Names and other personally identifiable information will be held in the same system but access to this data will be restricted to authorised individuals as described in section 12.2.

Clinical data will be entered into the REDCap eCRF by trained site research staff. Automated range and logic checks will be applied to eCRF entries to identify implausible or inconsistent data. Data queries will be raised and resolved in accordance with the study monitoring plan.

The study will comply with the General Data Protection Regulation (GDPR) and Data Protection Act 2018. The University of Oxford will act as data controller for the study. Personal data will be de-identified as soon as practicable. All study documents will be stored securely and will only be accessible to authorised study staff and personnel.

Identifiable data including consent forms will be stored in locked cabinets with restricted access at participating sites and at the Nuffield Department of Surgical Sciences, University of Oxford. Electronic data will be stored on password-protected encrypted network drives with restricted access.

Research data will be retained for a minimum of 10 years following the end of the study in accordance with the University of Oxford's research data management policy and sponsor requirements. Personal identifiable data will be retained only for as long as necessary and in accordance with GDPR requirements. Participants will be informed of data retention arrangements in the Participant Information Sheet.

13. QUALITY ASSURANCE PROCEDURES

The study will be monitored and audited in accordance with the current approved protocol, Good Clinical Practice (GCP), relevant regulations, and standard operating procedures. Quality assurance procedures have been designed proportionate to the observational, non-interventional nature of the study and the associated risk profile.

13.1. Risk assessment

A risk assessment and monitoring plan will be prepared before the study opens and will be reviewed as necessary over the course of the study to reflect significant changes to the protocol or outcomes of monitoring activities. The risk assessment will consider risks to participant safety, data quality, and study integrity, and will inform the nature and frequency of monitoring activities at each participating site.

13.2. Study monitoring

Central monitoring will be conducted by the coordinating centre at the University of Oxford and will include review of recruitment rates and screen failure logs, review of data completeness and query resolution rates in REDCap, review of wearable device wear-time adherence and data quality metrics, and review of protocol deviation logs.

On-site monitoring will be conducted at a frequency determined by the risk assessment and monitoring plan. During on-site visits, monitors will verify that the study is being conducted in accordance with the approved protocol, GCP, and applicable regulatory requirements, and will perform source data verification for a sample of eCRF entries.

13.3. Study Committees

Given the non-interventional, observational nature of POLARIS-OG and its low-risk profile, formal Trial Management Group and Trial Steering Committee structures are not considered necessary or proportionate. The study will be overseen by the central study group chaired by the Chief Investigator, which will include the co-investigator team based at the University of Oxford and representatives from participating sites. This group will meet regularly throughout the study to oversee recruitment, data quality, protocol adherence, and study progress, and will be responsible for escalating any concerns to the Sponsor.

14. PROTOCOL DEVIATIONS

A study related deviation is a departure from the ethically approved study protocol or other study document or process (e.g. consent process or administration of study intervention) or from Good Clinical Practice (GCP) or any applicable regulatory requirements. Any deviations from the protocol will be documented in a protocol deviation form and filed in the study master file.

A standard operating procedure will be in place describing the procedure for identifying non-compliances, escalation to the central team at the University of Oxford, and assessment of whether a non-compliance or deviation may constitute a potential Serious Breach.

15. SERIOUS BREACHES

A “serious breach” is a breach of the protocol or of the conditions or principles of Good Clinical Practice which is likely to affect to a significant degree –

(a) the safety or physical or mental integrity of the trial subjects; or

(b) the scientific value of the research.

In the event that a serious breach is suspected the Sponsor must be contacted within 1 working day. In collaboration with the C.I., the serious breach will be reviewed by the Sponsor and, if appropriate, the Sponsor will report it to the approving REC committee and the relevant NHS host organisation within seven calendar days.

16. ETHICAL AND REGULATORY CONSIDERATIONS

16.1. Declaration of Helsinki

The Investigator will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki.

16.2. Guidelines for Good Clinical Practice

The Investigator will ensure that this study is conducted in accordance with relevant regulations and with Good Clinical Practice.

16.3. Approvals

Following Sponsor approval, the protocol, informed consent form, Participant Information Sheet, and any proposed advertising material will be submitted to an appropriate Research Ethics Committee (REC) and the Health Research Authority (HRA), and host institutions for written approval.

The Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents. No substantial amendments will be implemented prior to receiving the necessary approvals, except where required to eliminate an immediate hazard to participants.

16.4. Other Ethical Considerations

Due to the widespread uptake of wearable devices in everyday life, the risks associated with wearing the study devices are well recognised and very low. There may be some mild discomfort associated with wearing the Bittium Faros 180 chest-worn device for a prolonged period, and mild skin irritation may occur at the adhesive site. Participants with metal allergies or sensitivity to medical adhesives are excluded from participation. In the event that a participant experiences discomfort with either device, they will be encouraged to discuss their concerns with the study team and may discontinue device wear without prejudicing their continued participation in other aspects of the study or their clinical care.

CPET testing is widely accepted and adopted in routine clinical practice at all participating centres. Its risks are well described and contraindications to CPET will be carefully assessed prior to testing.

This study involves patients with a cancer diagnosis undergoing major surgery, who may be considered a vulnerable population. All participants will be approached sensitively, provided with adequate time to consider participation, and will have the opportunity to discuss the study with the research team, their clinical team, or other independent parties before consenting. Participation in the study will not affect clinical care in any way, and this will be made explicit in the Participant Information Sheet and consent process.

In the event of serious safety concerns arising during the study, the Chief Investigator will determine whether the event warrants withdrawal of a participant or suspension of the study.

16.5. Reporting

The CI shall submit once a year throughout the study, or on request, an Annual Progress report to the REC Committee, HRA (where required) host organisation, Sponsor and funder (where required). In addition, an End of Study notification and final report will be submitted to the same parties.

16.6. Transparency in Research

This study is non-interventional and registration is therefore not applicable.

16.7. Participant Confidentiality

The study will comply with the General Data Protection Regulation (GDPR) and Data Protection Act 2018, which require data to be de-identified as soon as it is practical to do so. The processing of the personal data of participants will be minimised by making use of a unique participant study number only on all study documents and any electronic database(s), with the exception of the baseline CRF, where participant initials may be added. All documents will be stored securely and only accessible by study staff and authorised personnel. The study staff will safeguard the privacy of participants' personal data.

16.8. Expenses and Benefits

There is no financial reimbursement associated with participating in this study. No additional visits beyond routine standard care are required solely for study participation.

17. FINANCE AND INSURANCE

17.1. Funding

This study is funded by Cancer Research UK through the Oxford Cancer Centre, CRUK Oxford Centre, University of Oxford. The funder has had no role in the design of the study and will have no role in data collection, analysis, interpretation, or publication of results.

17.2. Insurance

The University of Oxford has a specialist insurance policy in place which would operate in the event of any participant suffering harm as a result of their involvement in the research (Newline Underwriting Management Ltd, at Lloyd's of London).

17.3. Contractual arrangements

Appropriate contractual arrangements will be put in place with all third parties.

18. PUBLICATION POLICY

The Investigators will be involved in reviewing drafts of all manuscripts, abstracts, press releases, and any other publications arising from the study. Authorship will be determined in accordance with the International Committee of Medical Journal Editors (ICMJE) guidelines and other contributors will be acknowledged appropriately.

Authors will acknowledge that the study was funded by the Oxford Cancer Centre, CRUK Oxford Centre, University of Oxford in all publications and presentations arising from the study.

Findings will be disseminated through peer-reviewed publication, with reporting following relevant observational and prediction-model reporting guidance, including STROBE and, where applicable, TRIPOD/TRIPOD+AI. Results will be presented at relevant national and international meetings including those of the Association of Upper Gastrointestinal Surgery of Great Britain and Ireland (AUGIS).

A plain-language summary of the study findings will be made available to participants and the public following publication. This will be shared to participants who opted to receive a summary on their consent form via the email address provided. De-identified study data will be made available to qualified researchers on reasonable request, subject to a data access agreement and in accordance with the consent provided by participants.

19. DEVELOPMENT OF A NEW PRODUCT/ PROCESS OR THE GENERATION OF INTELLECTUAL PROPERTY

Ownership of IP generated by employees of the University vests in the University. The University will ensure appropriate arrangements are in place as regards any new IP arising from the trial.

19. ARCHIVING

All study documentation will be retained for a minimum of 10 years following the end of the study, in accordance with the University of Oxford's research data management policy and sponsor requirements. This includes but is not limited to the study protocol and amendments, ethical and regulatory approvals, participant consent forms, completed eCRFs, wearable device data files, CPET reports, and correspondence with the Sponsor, REC, and HRA.

All research data will be pseudonymised and stored securely with support from the Surgical Intervention Trials Unit, Nuffield Department of Surgical Sciences, University of Oxford and the Big Data Institute, Nuffield Department of Population Health, University of Oxford. Electronic data will be held on password-protected encrypted network drives with restricted access. Paper documents will be stored in locked cabinets with restricted access at the University of Oxford.

At the end of the retention period, data will be disposed of securely and in accordance with the University of Oxford's data disposal policy. Participants will be informed of archiving arrangements in the Participant Information Sheet.

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21. APPENDIX A: STUDY FLOW CHART

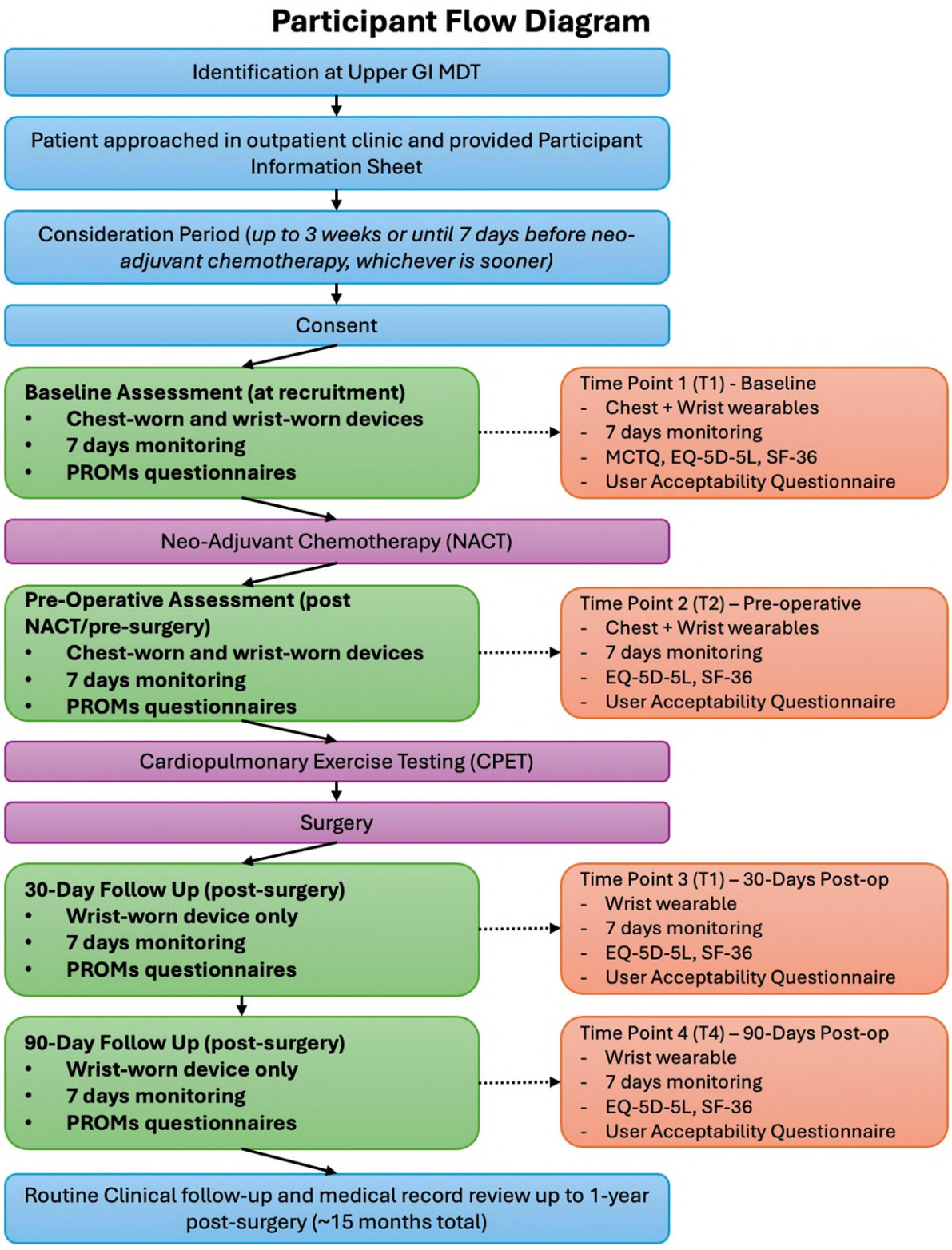


Figure 1. Participant pathway for the prospective multi-centre observational study evaluating wearable-derived physiological and activity measures in patients undergoing treatment for oesophagogastric cancer. The diagram summarises recruitment, longitudinal wearable monitoring, questionnaire completion, clinical data collection, and follow-up through 1-year post-surgery.

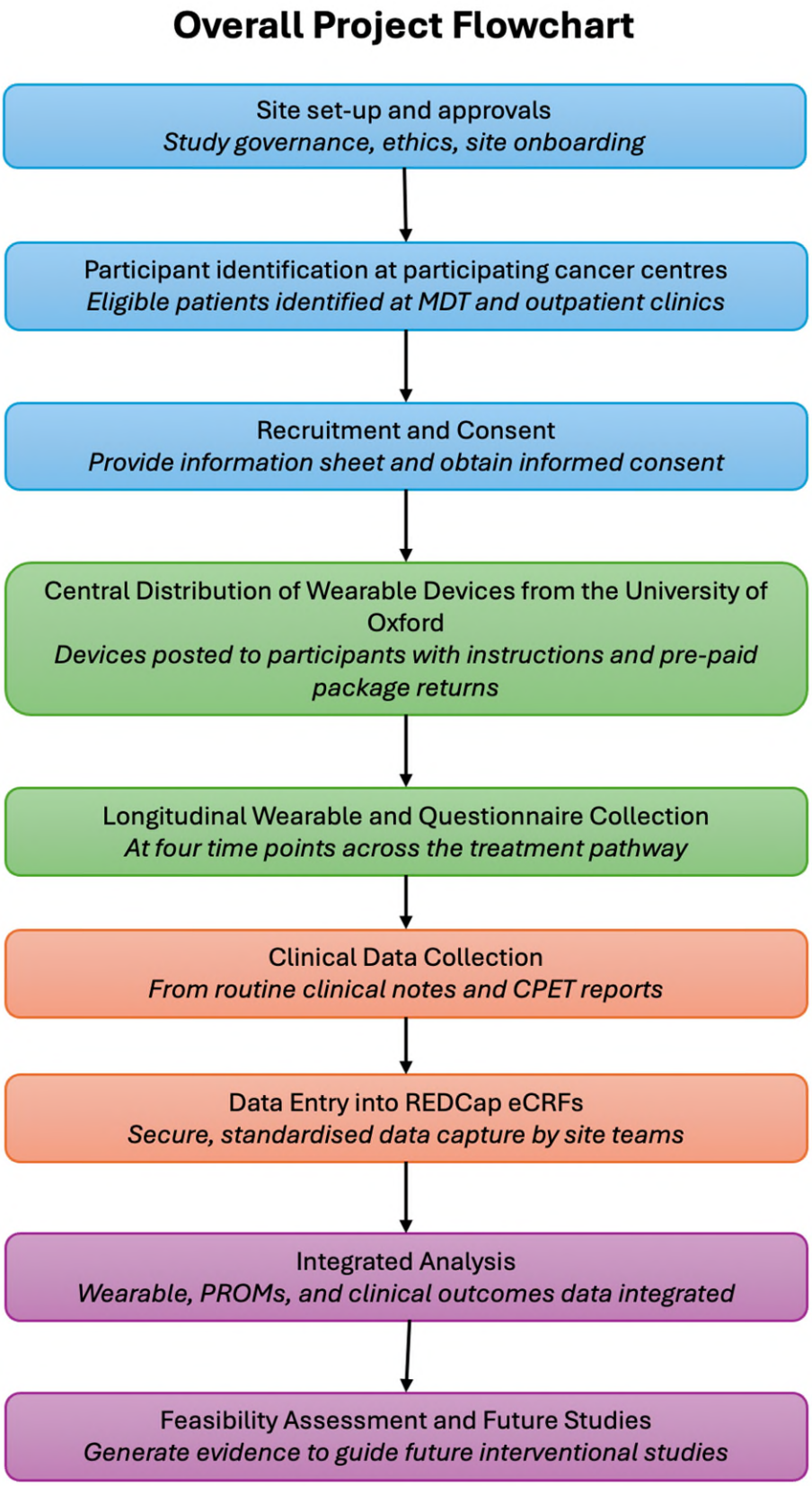


Figure 2: Overall Study Workflow for the prospective multi-centre observational study evaluating wearable derived metrics in patients undergoing treatment for oesphagogastric cancer. CPET = Cardiopulmonary Exercise Test, eCRF = Electronic Case Report Form.

22. APPENDIX B: SCHEDULE OF STUDY PROCEDURES

Procedures	T1 Baseline (pre-neoadjuvant)	T2 Pre-operative (post-neoadjuvant / pre-surgery)	T3 30 days post-surgery	T4 90 days post-surgery	T5 1-year follow-up
Informed consent	✓				
Eligibility confirmation	✓				
Demographics and medical history	✓				
Bittium Faros 180 chest-worn device (7 days)	✓	✓			
Garmin® wrist-worn device (7 days)	✓	✓	✓	✓	
CPET*	✓	✓			
MCTQ	✓				
EQ-5D-5L questionnaire	✓	✓	✓	✓	
SF-36 questionnaire	✓	✓	✓	✓	
Wearable experience questionnaire	✓	✓	✓	✓	
Clinical outcome data collection			✓	✓	
Survival and clinical records review					✓

**CPET may be performed prior to neoadjuvant chemotherapy, following completion of neoadjuvant chemotherapy, or at both timepoints, in accordance with local institutional practice. Where more than one valid CPET is available, the pre-operative CPET closest to surgery will be used as the index CPET for the primary analysis, with all available CPETs retained for secondary longitudinal analyses.*

23. APPENDIX C: AMENDMENT HISTORY

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made

List details of all protocol amendments here whenever a new version of the protocol is produced. This is not necessary prior to initial REC / HRA submission.

Protocol amendments must be submitted to the Sponsor for approval prior to submission to the REC committee and HRA (where required).

24. APPENDIX D: POTENTIAL SITE COLLABORATORS

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