POLARiS

Pathway of Low Anterior Resection Syndrome relief after Surgery

Trial Background	Colorectal cancer is the third most common cancer worldwide with 14,000 patients in the UK being diagnosed with rectal cancer per year. Over half of those patients will undergo major resectional surgery. Low Anterior Resection Syndrome (LARS) is a consequence of this surgery and describes a constellation of bowel symptoms including urgency, faecal incontinence, stool clustering and incomplete evacuation. It has a significant adverse impact on Quality of Life (QoL). LARS symptoms are present in up to 75% of the patients in the first year after surgery and may persist in 25%, remaining in up to half of these patients for more than 10 years. There is poor evidence to support the various treatment options currently in use. As disease-free survival is regarded as the most important factor following curative rectal cancer surgery, QoL and potential ways to improve it may be overlooked. Patients are often not aware or not told that bowel function can change significantly following surgery and radiotherapy and may think any adverse effects will be short-term. It is not known when post-operative bowel dysfunction, which may occur after any colonic resection, can be defined as LARS and how the trajectory of LARS changes over time, especially in patients undergoing radiotherapy.
Trial Design	POLARiS is a prospective, international, open-label, multi-arm, phase 3 randomised superiority trial (RCT) within a cohort (TWiCs design), with internal pilot phase, qualitative sub-study, process evaluation, and economic evaluation.
Trial Aim	**Cohort:** To explore the natural history of LARS, identify predictors of major LARS and to screen patients for recruitment to the RCT **RCT:** To evaluate the clinical and cost-effectiveness of Transanal irrigation (TAI) or Sacral neuromodulation (SNM) versus optimised conservative management (OCM) for people with major LARS.
Trial Endpoints	**Primary Endpoint:** The primary endpoint for the POLARiS RCT is LARS score up to 24 months post-randomisation. The LARS score will be collected at baseline and 3-monthly until 24 months post-randomisation **Secondary endpoints:** Secondary endpoints include health-related quality of life (EORTC QLQ-C29 and QLQ-C30) up to 24 months post-randomisation/registration, and safety profile (nature and severity of adverse events) within 24 months post-randomisation.
Trial Population:	Approximately 1500 adult participants from UK hospitals and 500 from Australian hospitals who have undergone a high or low anterior resection for colorectal cancer in the last 10 years will be recruited into the cohort. 600 participants from the UK and 200 participants from Australia, with major LARS symptoms, defined as a LARS score of 30+, will be randomised to the randomised controlled trial element.
Randomisation:	Patients entering the RCT will be randomised between Optimised Conservative Management (OCM), Sacral Neuromodulation (SNM) or Trans-Anal Irrigation (TAI). There are three randomisation options all with equal allocation ratios to allow for the inclusion of patients who may not be eligible for Sacral Neuromodulation (SNM) or Trans-Anal Irrigation (TAI)

Trial Intervention:	**Optimised Conservative Management (OCM):** The OCM package includes practical support and advice as well as describing treatment options such as diet, medications and physiotherapy. **Sacral Neuromodulation (SNM):** Surgical insertion of a small device that sends electrical pulses to the nerves located in the lower back. This is a two-stage procedure starting with a test phase, whereby a temporary device is implanted. Following a good clinical response, implantation of a permanent battery device is offered. **Trans-Anal Irrigation (TAI):** TAI involves instilling warm water into the rectum and colon via the anus to empty out the stool. Patients attend a one-hour education practical session with a nurse and will be provided with a starter pack.
Duration:	Trial recruitment will be over a 27 month period. Participants will be followed up for 24 months post-registration or post-randomisation.
Evaluation of outcome measures	The primary outcome measure for both the cohort study and the RCT is the LARS score. Secondary outcome measures for both the RCT and the cohort study include: • Health-related quality of life and physical, psychological and emotional functioning. • Adverse events Secondary outcome measures (RCT only) Secondary outcome measures collected strictly in the RCT include: • Treatment compliance measures • [Outcome(s) used to assess cost-effectiveness] o Cost to the health service of treatment o Modelled long-term costs of health and social care, and broader societal costs • [Occupational outcomes] o Employment status o Time lost from productive activities

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