Project Title: Does an ileostomy impact the long term health status of the patient.

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Background to the project:
Inflammatory bowel disease (IBD) which is associated with low bone mineral density is divided into 2 major disease entities: Crohn's disease and ulcerative colitis. Medical therapy is directed at controlling symptoms and reducing the underlying inflammatory process. Studies have reported that 60% of patients with CD and 15%–30% of patients with UC require surgical intervention for the management of their disease (Peyrin-Biroulet 2004, Targownik 2012). Gupta and colleagues (2014) recently highlighted a 29.4% prevalence of low bone mineral density (BMD) in a cohort of US patients with IBD and ileostomy who were > 5 years postoperative. Possible risk factors for bone loss in patients with IBD and ileostomy are considered to include malabsorption secondary to bowel resection, malnutrition and more aggressive disease and inflammation which led to bowel resection in the first place (Gupta 2013). These factors also contribute to reduced intestinal absorption of nutrients and vitamins including B & D and calcium (Vavricka et al 2012) subsequently leading to potential health complications including low BMI and low lean body mass (Ng et al 2013). Although the study by Gupta and colleagues did not assess vitamin D status directly, it has been reported that IBD patients who have surgical intervention to create ileal pouches also have low levels of vitamin D (Khanna et al 2013). Bile acid (BA) malabsorption which is common to IBD is caused by impaired conjugated BA reabsorption and a consequence, numerous pathological sequelae may occur, including the malfunction of lipid digestion (Vitek 2014). Further, bacterial overgrowth can lead to deconjugation of bile salts, leading to formation of free bile acids, again inducing dietary fat malabsorption, which in turn can lead to vitamin D deficiency (Naysmith et al 1989; Salemans et al 1993). Given the paucity of data in the area of ileostomy patients BMD, vitamin D status and calcium intake, we will establish baseline observations within the NI population.

Objectives of the research project:
Almost 13,000 individuals undergo an ileostomy procedure in the UK each year and subsequently have a lifetime of additional healthcare needs, among which may include low BMD and impaired vitamin D and calcium status. The improvement of the long-term health of patients with an ileostomy is an area of need recently identified by Gupta and colleagues (2014). To address this, we need to determine the bone mineral density of an N. Ireland ileostomist patient group and determine intake levels of calcium and vitamin D status.
1) To conduct an observational study to collect a blood sample, ileal fluid sample, Food frequency questionnaire data and DEXA scan from a 100 individuals who have undergone an ileostomy.

2) To for the first time, establish baseline data on the BMD and other clinical parameters for a cohort of ileostomy patients in N. Ireland.

3) To establish baseline data for vitamin D concentration for a cohort of ileostomy patients in N. Ireland, correlated with validated FFQ for dietary assessment.

4) To establish vitamin D levels present in ileal fluid and determine if it correlates with validated FFQ for dietary assessment.

Methods to be used:

The sample size required for this baseline observation study was estimated from previous studies (Gupta et al 2014). A likely dropout rate of 50% is predicted based on previous studies (Mc Dougall et al, 2014). In order to account for a 50% dropout rate, an estimated total sample size of 200 subjects is required.

Objective 1: To conduct an observational study to collect a blood sample, FFQ data and DEXA scan from a 100 individuals who have undergone an ileostomy.
Mr Roger Lawther (Consultant Colorectal Surgeon) and his team via Altnagelvin Area Hospital will recruit individuals with an ileostomy (>5 yrs post-operative, as a result of previous IBD) and obtain relevant clinical data. The participants will visit CTRIC for the purposes of collecting anthropometric data, a blood sample, ileal fluid sample, and to conduct an FFQ interview using a validated tool developed to capture information on vitamin D and calcium intake (UCC, 2008) and information on stoma care and quality of life. Additional clinical variables that could act as confounders will be collected from medical notes.

Objective 2: To establish baseline data on BMD for a cohort of ileostomy patients in N. Ireland.
All participants (N=100) following provision of blood samples and dietary information at CTRIC will be invited to undertake a full DEXA scan at the Ulster, Coleraine (Hisu), assessment will be conducted as described in Slevin et al 2014. In brief, all participants will undergo a whole body Dual Energy X-ray Absorptiometry (DXA scan) DXA scan (maximum of 3) for segmental assessment of body composition e.g. skeletal muscle and trunk fat mass and will have two specific sites scanned; AP spine (maximum of 3) and femur (maximum of 3) to provide a one-off assessment of bone mineral density (BMD).

Objective 3: To establish baseline data for vitamin D concentration for a cohort of ileostomy patients in N. Ireland, correlated with validated FFQ for dietary assessment.
Blood samples collected at CTRIC as part of objective 1 will be analysed for general clinical chemistry (e.g. serum adjusted calcium, lipid profiles, plasma glucose) and will be measured on the ILab auto-analyser. Plasma vitamin D concentration will analyzed by LC-MS according to the method described in Laird et al 2014. Dietary data collected using a validated FFQ for vitamin D (Weir et al. 2016) will be collated and correlated with the results of the blood analysis.

Objective 4: To establish baseline data for vitamin D concentration in ileal fluid does it correlate with with dietary intake.

Ileal fluid samples collected at CTRIC as part of objective 1 will be analyzed for vitamin D content using a modification of the LC-MS according to the method described in Laird et al 2014 and used in objective 3. In conjunction with the plasma measures and dietary intake, the amount of unabsorbed vitamin D derived as a result of food consumption can be determined and related to dietary intake.

Skills required of applicant (200 words Max):
The PhD student will conduct an observational study in collaboration with the WHSCT, including data collection, maintaining study records, biological sampling. The student will undertake data entry/collation, sample analysis in the laboratory (Vitamin D, Calcium, blood profiles), DEXA scans and data analysis for the above study. Excellent organization and communication skills are essential. Previous experience of laboratory techniques would be beneficial but is not essential.
References: