

**Title**

Efficacy of a lacto-ovo vegetarian diet in ulcerative colitis: a randomised controlled trial

**Study name**

LOVUC

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## **Abstract**

Measured dietary changes can be an important adjunct therapy in Inflammatory Bowel Disease (IBD), not only to achieve remission, but also potentially improve the durability of response and remission. With the burden of the disease, and reported effect on quality of life, the majority of patients with IBD are changing their diets, which may impact on nutrition-related health problems and unnecessary financial burden. A Westernised diet, low in dietary fibre and high in sugar, animal fats and proteins is associated with increased prevalence of IBD. With evidence linking red meat intake with increased risk of IBD, a plant-based diet with dietary fibre is potentially protective as it could reduce disease risk through anti-inflammatory and immune-modulating effects.

A plant-based diet, high in dietary fibre, has been associated with greater diversity and a shift in the composition of the gut microbiota compared to omnivores and less oxidative stress. This could potentially be of benefit in patients with IBD where dysbiotic microbiota has been speculated as an aetiologic factor in the pathogenesis of disease. However, there remains a lack of randomised controlled trials to evaluate the efficacy of diet and its subsequent gut microbiota to enhance the understanding of the role diet plays in the management of ulcerative colitis (UC).

Using a single site, randomised, open-label study, in patients with mild to moderate UC, the effectiveness of a lacto-ovo vegetarian diet will be reviewed as an adjunct to medication therapy. We hypothesise that a lacto-ovo vegetarian diet will reduce disease-related gastrointestinal symptom and inflammation, while improving the quality of life compared to a standard omnivorous diet. Subsequently, a lacto-ovo vegetarian diet will also have a direct effect on the gut microbiota, changing the composition and promoting greater diversity.

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## **1.0 Study Hypothesis, Aims and Objectives**

### **1.1 Study Aim:**

To determine whether a lacto-ovo vegetarian diet is effective in improving gastrointestinal symptoms, quality-of-life, intestinal inflammation and gut microbiota composition in mild-to-moderate UC compared to a standard omnivorous diet.

### **1.2 Study Hypothesis**

Primary Research Hypothesis: Subjects with mild-to-moderate UC who consume a lacto-ovo vegetarian diet will demonstrate a clinical response at 8 weeks (Partial MAYO score, improved stool frequency and rectal bleeding).

Secondary Research Hypotheses: Subjects with mild-to-moderate ulcerative colitis who consume a lacto-ovo vegetarian diet will demonstrate:

- I. Improvements in clinical remission (MAYO score, FCP, CRP, ESR)
- II. Improvements in remission rate
- III. Improved quality-of-life and food-related quality-of-life scores
- IV. Mucosal healing
- V. Increased diversity and favourable composition changes of the gut microbiome
- VI. Increased levels of beneficial metabolites and metabolic profile

## 2.0 Experimental Design and Methods

### 2.1 Study Design

As there are no previous clinical dietary trials reviewing the efficacy of a lacto-ovo vegetarian diet on UC outcomes this study will consist of two phases. Phase one will be a pilot study to establish efficacy of a lacto-ovo vegetarian diet in patients with mild to moderate UC. Phase two will be a randomised controlled clinical trial to compare outcomes of the intervention diet to a control group. Methodology will remain the same for both phases with the exception being randomisation in Phase 2 with a control group arm.

Phase 1: Open labelled, single centre trial (10 patients)

Phase 2: Open labelled, single centre, single blinded, randomised controlled clinical trial (n=30).

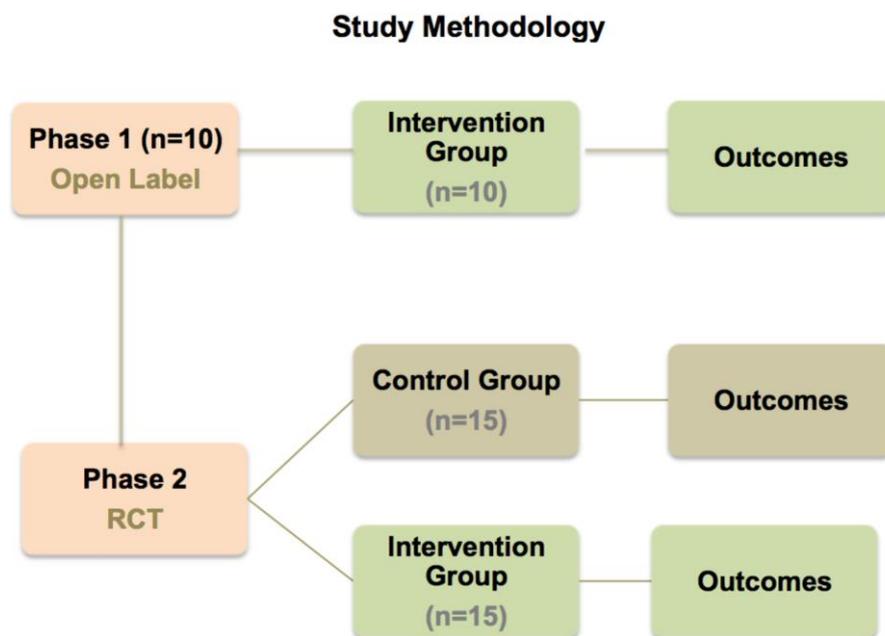


Figure 1 Study methodology

Rational for Trial Design: Due to the nature of this type of dietary intervention it is not possible to blind the participant, but the assessing doctor will be blinded to the patient's

diet during phase two. The lacto-ovo vegetarian diet will be used as an adjunct therapy to current medication treatment as an alternative to escalating medication therapy.

Patients may be contacted one year post their eight week study inclusion to assess which diet they are following, number of flares, time in remission and to assess their quality of life using the IBD-Q.

## **2.2 Recruitment of Participants**

Recruitment of patients will occur at St John of God Subiaco Hospital, Subiaco through an IBD outpatient clinic. Patients from other IBD outpatient clinics can be referred to the study and will be managed through the participating centre for the trial.

## **2.3 Eligibility Criteria**

### Inclusion Criteria

- I. Is able to provide informed consent.
- II. Is over the age of 18 years.
- III. Has a diagnosis of ulcerative colitis for over a 3-month duration that was confirmed by a specialist gastroenterologist with a MAYO score up to 9.
- IV. Medications:
  - a) Oral 5-Aminosalicylates: If taking an oral 5-Aminosalicylates the patient has used them continuously for 4 weeks and has been on a stable dose for 2 weeks prior to the screening visit.
  - b) Oral Corticosteroids: If taking oral corticosteroids the patient has used them continuously for 4 weeks and has been on a stable dose for 2 weeks prior to the screening visit at a dose of  $\leq 30$ mg.

- c) Oral Azathioprine/6MP, Methotrexate or tacrolimus: If taking one of these medications the patient has used them for a minimum of 12 weeks and has been on a stable dose for 4 weeks prior to screening.
  - d) Biologic therapy with infliximab, adalimumab or vedolizumab: If taking one of these medications the patient has used them for a minimum of 12 weeks
  - e) Rectal Preparations; 5-Aminosalicylates, corticosteroids or tacrolimus: If taking one of these medications the patient has used them continuously for 4 weeks and has been on a stable dose for 2 weeks prior to the screening visit.
- V. Willing to participate in the study and comply with the proceedings by signing a written informed consent.
  - VI. Free of any clinically significant disease, other than ulcerative colitis, that would interfere with the study's evaluations.
  - VII. Subjects can read and understand English and is able to adhere to the study methodology and visit schedules.

#### Exclusion Criteria

- I. Has Crohn's disease.
- II. Has been on antibiotics within the last four weeks.
- III. Has a known food allergy to nuts, soy, eggs or dairy.
- IV. Is pregnant or breast feeding.
- V. Following a vegetarian, vegan or low FODMAP diet.
- VI. Has known dementia and the inability to understand the trial requirements.

#### **2.4 Interventions**

Intervention group (Phase one, Group B of Phase 2): Lacto-ovo vegetarian diet for eight weeks. Subjects will be given education and literature on the diet, food lists and recipes to

assist with following the diet. Pending funding, participants will be provided with a lacto-ovo vegetarian food box delivery service with fresh ingredients and recipes to cover three to four dinners per week.

Control group (Phase two only, Group A) Regular omnivore diet

The control group will not be made aware of the specific intervention diet. The treating gastroenterologist will also be blinded to which group the participants have been allocated to reduce bias.

## **2.5 Education and Resources**

Participants in the intervention group will be educated on following a lacto-ovo vegetarian diet by the chief investigator (an accredited practising dietitian) in a one on one session before the commencement of the study. Patients on the intervention diet will be provided with a lacto-ovo vegetarian diet sheet (Appendix A) and a recipe book as part of their resources. All participants in both groups will complete a 3-day weighed food record inclusive of one weekend day (Appendix B) at the commencement and completion of the study. Participants will be counselled on how to complete the record correctly and provided with all equipment (recording sheets, measuring cups, spoons and weighing scales).

## **2.6 Adherence**

Participants in the intervention group will be asked seven questions (less than five minutes) each fortnight to assess their compliance with the lacto-ovo vegetarian diet (Appendix C). This will be completed via a phone call at weeks two, four and six. Additional email, phone call or one on one support will be provided at the participant's request.

## **2.7 Methods**

### Ulcerative colitis assessment

All patients will have a definite diagnosis of UC in accordance with previously established international criteria based on clinical, endoscopic, histological and radiological features (Albenberg, Lewis, & Wu, 2012; Lennard-Jones, 1989). The Montreal Classification (a modification of Vienna classification) (Silverberg et al., 2005) will be used to define the extent of the disease. All subjects will be evaluated at baseline and 8 weeks for a MAYO score and at 2 and 4 weeks for a partial MAYO score (Appendix D). A clinical response is defined as a decrease from baseline in the total Mayo score of at least 3 points and at least 30 percent, with an accompanying decrease in the subscore for rectal bleeding of at least 1 point or an absolute subscore for rectal bleeding of 0 or 1. A clinical remission is defined as a total Mayo score of 2 points or lower, with no individual subscore exceeding 1 point. A flexi-sigmoidoscopy will be performed at baseline and week 8. Mucosal healing is defined as an absolute endoscopy subscore of 0 or 1.

### Clinical data

Serology inflammatory markers of UC, including C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) and EUC, FBC and LFT will be measured at baseline, week 2, 4 and 8. Vitamin D and iron studies will be taken at baseline and week 8. A stool measure of faecal calprotectin (FCP) will be taken at baseline, week 4 and week 8. Week 2 has been excluded, as it is considered too soon to achieve a clinical response. All samples will be analysed through Australian Clinical Labs.

### Gut microbiome characterisation

Faecal sample collection and standing operating procedures are outlined in Appendix E. Faecal processing, subsampling for all planned analysis, is carried out in a biological safety cabinet after the samples are thawed at 4°C (fridge). Sample processing occurs on ice to keep samples cool and all samples are homogenised prior to subsampling.

To extract microbial DNA, samples are lysed using both mechanical and enzymatic breakdown of the bacterial cell membranes and the DNA is extracted using the QIAamp PowerFecal DNA kit (Qiagen). Microbiome signatures are generated using the Illumina MiSeq platform using barcoded primer, V4 (515-806) and the V6-V8 (917-1392), that target two different hypervariable region of the 16S rDNA gene to increase specificity of bacterial classification and ensuring no bacteria are missed due to the selection of primers. Alternatively, we may choose to analyse the mycobiome using ITS2 primers pending satisfactory analysis of the V4 region. Quality control samples are included in the analysis from sample collection to sequence analysis and all samples are individually screened for PCR efficiency prior to building sequence libraries. For building the sequence libraries, a PCR-free ligation protocol is deployed and sample barcodes are never reused in our laboratory. Samples will be sequenced to a depth of minimum 30,000 reads, which is sufficient to identify microbes to a genus/species level.

Sequence data/output is demultiplexed and initial sequence quality control assessments is performed and chimeras are removed. The amplicon data will be analysed using a combination of bioinformatics and statistical software packages. GHAP, an in-house amplicon clustering and classification pipeline built around tools from USearch (Edgar, 2013) and RDP (Cole et al., 2014), combined with locally-written tools for demultiplexing will be used for classification of reads into OTU's and their phylogenetic linkage.

### Quality of Life

Quality of life will be measured using the Inflammatory Bowel Disease Questionnaire (IBDQ) (Irvine et al., 1994) at baseline, weeks 2, 4 and 8 (Appendix F). The IBDQ is widely accepted as a valid and reliable health related quality of life (QoL) questionnaire in patients with inflammatory bowel diseases. Normal QoL is defined as an absolute score of 170 points and a quality of life response is a change of 16 points on the IBDQ. Food-

Related QoL will be measured using the FR-QoL-29 (Hughes et al., 2016) (Appendix G). The FR-QoL-29 shows good reliability and validity across a range of IBD characteristics and will be measured at baseline, weeks 2, 4 and 8. QoL will also be assessed using Short Form 36 (SF-36) (Appendix H). This generic health status measure includes groups of questions which can separately assess physical status and psychosocial status and takes into account disability and dependency, social factors, level of pain and general well-being. It has been validated in the Australian social context (Rand Health, 1994) and will be measured at baseline and week 8.

### 3-day weighed food record

The 3-day food record will be entered into FoodWorks Professional version 9.0 (Xyris Software, 2012) by a nutritionist or dietitian with advanced competency training for analysis.

## **2.8 Study Protocol**

All subjects who grant consent to participate in the study will attend the IBD clinic for visits at baseline, weeks 2, 4 and 8. Required investigations or questionnaires for each patient shall be conducted as per Table 1.

Table 1 Schedule of Intervention

	Screen Day -3 to -7	Baseline	Week 2	Week 4	Week 6	Week 8
Written consent	X					
Patient demographics	X					
Sigmoidoscopy		X				X
Mayo score		X				X
Randomisation to control or intervention diet (Phase 2)		X				
Partial mayo score			X	X		
Clinic review		X	X	X		X
Dietitian appointment		X				X
Dietitian phone call review			X	X	X	X
Stool collection FCP	X					X
Stool culture and microscopy	X					X
Stool collection SCFA & microbiome	X					X
Stool collection metabolome	X					X
FBC, ESR, CRP EUC	X		X	X		X
Iron studies	X					X
IBDQ		X	X	X		X
FR-QoL		X	X	X		X
SF-36 QoL		X				X
3-day weighed food record	X					X

The investigator is responsible for adherence to the protocol and accurate recording of the data:

- I. Screening visit: All eligible patients will be provided with an information letter (Appendix I) and are required to sign an informed consent form (Appendix J). Patient demographics will be recorded. Stool culture and microscopy are performed to exclude infection. A full Mayo score will be calculated to confirm the presence of active UC (Mayo score of 6-9). Baseline full blood count, ESR, CRP and iron studies will be measured. A stool sample will be taken to measure faecal calprotectin.
- II. Within 7 days prior to baseline an appointment with the dietitian will be arranged for the 3-day weighed food record to be explained and education on the intervention diet for those in the intervention group.

- III. Within 7 days prior to baseline a stool sample will be collected to assess the gut microbiome composition, SCFA and metabolome (pending funding). Equipment and education will be provided at the dietitian appointment.
- IV. Within 7 days prior to baseline a flexible sigmoidoscopy will be performed, biopsies and photos will be taken.
- V. At baseline a Full Mayo score will be calculated at clinic review. The Inflammatory Bowel Disease Questionnaire (IBDQ), Food Related Quality of Life (Fr-QoL) and SF-36 questionnaires will also be administered and the corresponding data are then used to calculate the IBDQ and QoL scores.
- VI. At weeks 2 and 4: A partial Mayo score will be calculated, routine FBC, ESR, CRP, U&E, checked. IBDQ and Fr-QoL completed. Faecal calprotectin remeasured at week 4. In the RCT patients will be given an option to increase the dose of their other medications if they are still symptomatic at Week 4 and those who opt in are regarded as flares.
- VII. Participants in the intervention group will receive a phone call from the dietitian at weeks 2, 4 and 6 to assess compliancy to the diet.
- VIII. At week 8: A flexible sigmoidoscopy will be undertaken  $\pm$  3 days of the week 8 visit and a full Mayo score calculated. Biopsies and photos will be taken and stored at Fremantle Pathology. Routine FBC, U&E, ESR, CRP and iron levels checked.
- IX. At week 8 the gut microbiota composition, SCFA and metabolome will be remeasured using a stool sample collection (pending funding).
- X. At week 8 a 3-day weighed food record will be repeated.
- XI. At week 8 patients in the control group will be advised of the intervention diet.

## **2.9 Randomisation**

Following establishment of eligibility, participants will be randomly assigned in a 1:1 ratio either to receive the control or intervention group using block randomisation. After

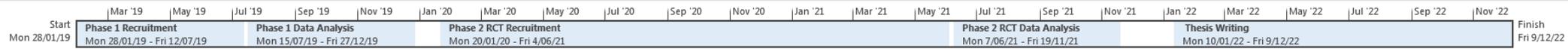
randomisation, participants will be made aware which group they have been allocated too. The control group will remain on their current medication and omnivorous diet. The intervention group will remain on their current medication and follow a lacto-ovo vegetarian diet.

## **2.10 Study Timetable**

Estimated start of the study is January 2019 with estimated completion of the study (date the last subject will complete the study) is July 2021. A Gantt chart is presented in Figure 2

Phase 1: January 2019 to December 2019

Phase 2: January 2020 to July 2021

**Phase 1 Recruitment**

Start: 28/01/19 ID: 1  
 Finish: 12/07/19 Dur: 6 mons  
 Res:

**Phase 1 Data Analysis**

Start: 15/07/19 ID: 2  
 Finish: 27/12/19 Dur: 6 mons  
 Res:

**Phase 2 RCT Recruitment**

Start: 20/01/20 ID: 3  
 Finish: 4/06/21 Dur: 18 mons  
 Res:

**Phase 2 RCT Data Analysis**

Start: 7/06/21 ID: 4  
 Finish: 19/11/21 Dur: 6 mons  
 Res:

**Thesis Writing**

Start: 10/01/22 ID: 5  
 Finish: 9/12/22 Dur: 12 mons  
 Res:

**Candidacy (Feb-Sept 2018)**

- Literature review
- Research proposal
- Ethics application (SJGSH, ECU)
- Grant application

**Phase 1 (Jan – Dec 2019)**

- Recruitment (Jan – July 2019)
- Data analysis (Aug – Oct 2019)
- Grant application Oct – Nov 2019
- Write up and publication (Nov – Jan 2019)

**Phase 2 (Jan 2020 – December 2021)**

- Recruitment (Jan 2020 – June 2021) –note will commence earlier pending funding
- Data analysis (July 2021- Dec 2021)

**Thesis Writing (Jan – Dec 2022)**

- Publications

Figure 2 Gantt Chart

## 2.11 Sample size calculation

Phase two of the study has been designed as a randomised controlled clinical trial. In patients with mild to moderate ulcerative colitis there has been no dietary studies of this design using a lacto-ovo vegetarian diet on which to base the sample size calculations. A study by Konijeti et al. (2017), which utilised an autoimmune dietary protocol, demonstrated significant clinical improvements (corresponding to large effect sizes) in partial MAYO score, stool frequency and rectal bleeding for patients with UC (n=6). Based upon the improvements observed in this study and using G\*Power (Faul, Erdfelder, Lang, & Buchner, 2007), a minimum sample size of 8 in each group (n=16) was deemed necessary in a mixed model design with 4 time points to detect a large effect ( $f=0.4$ ) in the primary outcome at 80% power and 5% level of significance.

A study by Gibson et al. (2014) demonstrated a 16-point shift in IBDQ score (corresponding to a medium Cohen's effect size  $d = 0.55$ ) to be clinically relevant in 29 patients with mild to moderate UC. Using a medium effect size ( $f=0.25$ ), we have conservatively estimated a minimum sample size of 15 patients in each group (n=30) at the same power and significance level. This includes an attrition rate of 20%.

Therefore, this study will aim to recruit a total of 30 patients in Phase two to get statistical power in of both the primary and secondary outcome measures. The primary and secondary outcome measures achieved in Phase one will be used to strengthen the sample size calculation prior to commencing Phase two.

## 2.12 Statistical analysis

Statistical analyses will be performed using SPSS 20 (SPSS Inc., Chicago, IL, USA). Normally distributed data are described as mean  $\pm$  standard deviation (SD), and median and interquartile range (IQR) are presented for non-normal data. Normality is verified using the Kolmogorov-Smirnov test. An independent samples t-test (normal distribution) or a Mann-Whitney U test (non-normal distribution) will be used to assess the difference between the two groups in the primary and secondary outcome measures.

Analysis of the overall primary endpoint will be examined using a logistic regression approach to determine the impact of the intervention diet on clinical response at 8 weeks. Odds ratio (OR) and 95% confidence interval will be presented. Continuous measurements taken repeatedly over the study (Mayo, Partial Mayo, FCP, CRP, ESR, IBDQ, FR-QoL-29 and SF-36) will be analysed with a linear mixed model approach. Effects of time, treatment and the time by treatment interaction will be tested and reported.

For multivariate analysis of the microbiome data, Primer7 and Permaplava+ (PRIMER-E, Plymouth) is used. Principal Coordinates Analysis (PCoA) is deployed initially to visualise the multivariate data, and distance-based linear models (DISTLM) and distance-based redundancy analysis (dbRDA) are used for more in-depth analysis and to integrate microbiome findings with other metadata (like metabolites and diet information) that might help explain their relationships.

For all analyses, the impact of potentially confounding demographic variables such as age and sex will be investigated. The level of significance in the study will be  $P < 0.05$ .

An un-blinded statistical analysis will be performed when 10 patients have been recruited to each arm of the RCT (n=20). If statistical significance is achieved the study will be closed for safety and efficacy of the patients.

### **3.0 Ethics and Dissemination**

#### **3.1 *Ethical considerations***

Before study initiation, the protocol will be submitted for review and approval to the Ethics committee(s). Documentation must be signed by the chairperson or designee of the Ethics committee(s) to indicate approval of the protocol and informed consent.

#### **3.2 *Informed consent***

Participants will have the study explained by the chief investigator or nominee. They will receive a full explanation in lay terms, of the aims of the study as well as the discomfort, risks and benefits of participation. The participants will be given time to consider their participation and discuss with their family, friends and/or health care team. The study is for research purposes and any therapeutic benefit to the individual is unknown. The participant must give consent by signing and dating the consent form. Consent should be obtained before any protocol-required procedures are performed including any procedure not part of normal patient.

#### **3.3 *Subject discontinuation criteria***

Subjects will be discontinued from the study if they want to revoke their consent or at the discretion of the principal investigator, based on the side effects, disease progression or poor compliance. Withdrawal from the study will be without prejudice to their future care.

### **3.4 Data management and confidentiality**

Confidentiality will be maintained at all times. Participant confidentiality is strictly held in trust by the research team. All hard copies including consent forms, questionnaires and other sensitive data will be stored in an area of limited access. All electronic data, including identifiable data sets, will be password protected and stored on a network drive at St John of God Subiaco Hospital which only the chief investigator of the study will have access. Electronic data will be stored as Excel and SPSS datasets. Data will be kept for 15 years following completion of the trial.

### **3.5 Adverse events**

A previous study using a SVD had no adverse effects (Chiba et al., 2018). Known adverse events relate to the underlying clinical condition: Expected symptoms of ulcerative proctitis may include faecal urgency, rectal bleeding and diarrhoea. These are not recorded as adverse events unless there is a clear temporal relationship to the study intervention diet or unless these symptoms become worse compared to baseline or subject is hospitalised as a result of these symptoms.

#### 4.0 References

- Albenberg, L. G., Lewis, J. D., & Wu, G. D. (2012). Food and the gut microbiota in IBD: a critical connection. *Current opinion in gastroenterology*, 28(4).
- Chiba, M., Nakane, K., Tsuji, T., Tsuda, S., Ishii, H., Ohno, H., . . . Yamada, K. (2018). Relapse prevention in ulcerative colitis by plant-based diet through educational hospitalization: A single-group trial. *The Permanente Journal*, 22.
- Cole, J., Wang, Q., Fish, J., Chai, B., McGarrell, D., Sun, Y., . . . Tiedje, J. (2014). Ribosomal Database Project: data and tools for high throughput rRNA analysis *Nucleic Acids Res* 42 (D1). D633–D642.
- Edgar, R. C. (2013). UPARSE: highly accurate OTU sequences from microbial amplicon reads. *Nature methods*, 10(10), 996.
- Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G\* Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior research methods*, 39(2), 175-191.
- Gibson, P. R., Vaizey, C., Black, C. M., Nicholls, R., Weston, A. R., Bampton, P., . . . Andrews, J. M. (2014). Relationship between disease severity and quality of life and assessment of health care utilization and cost for ulcerative colitis in Australia: a cross-sectional, observational study. *Journal of Crohn's and Colitis*, 8(7), 598-606.
- Hughes, L. D., King, L., Morgan, M., Ayis, S., Direkze, N., Lomer, M. C., . . . Whelan, K. (2016). Food-related Quality of Life in Inflammatory Bowel Disease: Development and Validation of a Questionnaire. *J Crohns Colitis*, 10(2), 194-201. doi:10.1093/ecco-jcc/jjv192
- Irvine, E. J., Feagan, B., Rochon, J., Archambault, A., Fedorak, R. N., Groll, A., . . . McDonald, J. W. (1994). Quality of life: a valid and reliable measure of therapeutic efficacy in the treatment of inflammatory bowel disease. *Gastroenterology*, 106(2), 287-296.
- Konijeti, G. G., Kim, N., Lewis, J. D., Groven, S., Chandrasekaran, A., Grandhe, S., . . . Wang, X. (2017). Efficacy of the Autoimmune Protocol Diet for inflammatory bowel disease. *Inflammatory bowel diseases*, 23(11), 2054-2060.
- Lennard-Jones, J. (1989). Classification of inflammatory bowel disease. *Scandinavian journal of gastroenterology*, 24(sup170), 2-6.
- Rand Health. (1994). 36 Item Short Form Survey Instrument. Retrieved from [https://www.rand.org/health/surveys\\_tools/mos/36-item-short-form/survey-instrument.html](https://www.rand.org/health/surveys_tools/mos/36-item-short-form/survey-instrument.html)
- Silverberg, M. S., Satsangi, J., Ahmad, T., Arnott, I. D., Bernstein, C. N., Brant, S. R., . . . Geboes, K. (2005). Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. *Canadian Journal of Gastroenterology and Hepatology*, 19(Suppl A), 5A-36A.

## **5.0 Appendices**

### **Appendix A Healthy guidelines for vegetarian eating**

Refer to supporting attachment: **Healthy Guidelines for Vegetarian Eating**

**EDITH COWAN UNIVERSITY**  
**Nutrition & Dietetics Program**

### **Guide to Completing a Food Record**

1. Try not to change your eating habits. This is difficult because the measuring becomes intrusive and you end up eating items that you know you can measure with ease. If you are distracted by measuring, it is better to consume your normal choices and then, later, weigh a similar-weighted food item.
2. Record ALL that you eat: a mouthful of water at the water fountain; a bite of somebody's apple; a taste of wine; a nibble of a chip; multi-vitamin pills and any other drugs etc., etc.
3. Record as soon as possible after eating. The longer you leave it the less likely you are to be accurate.
4. If it is a commercial food item, write down the brand name and keep any nutrition information which is on the label.
5. Weigh and/or measure food with absolute accuracy. Use a small set of digital scales and standard cups and measuring spoons. Use a measuring jug for liquid measures. As suggested in Point 1, if it is not possible to weigh/measure at the time of eating, weigh a similar amount of the item later. Or, later, weigh a similar amount of a like-weighted food. Use your Conversion Tables to assist you in the estimation of like-weighted foods.
6. Record as neatly as possible so that unnecessary errors do not occur.
7. If what you eat has been prepared by someone else, try to obtain a list of the ingredients and estimate the proportion which you ate.



*I am calling to see how you are progressing with your vegetarian diet as part of the diet in ulcerative colitis research study. Would it be ok if we talked about it?*

Yes       No

**If participant agrees proceed.**

1. *Following a vegetarian diet can be challenging (shows empathy). On a scale of 0 to 10, with 10 being the highest, how motivated are you to continue on the vegetarian diet?*

Score:    /10

2. *Why did you choose 6 instead of 7? What would help you to move from 6 to 7?*
3. *How many times in the last two weeks have you consumed red meat, processed meat, poultry or fish?*
4. *What have been the barriers of being on a vegetarian diet?*
5. *What have been the benefits of being on a vegetarian diet?*
6. *Did you have any questions you would like to discuss with me?*

**Thank the participant for their time and advise of next contact date**

At week 6 phone call remind participant to complete 3 day weighed food record and stool collection

## Appendix D MAYO Score

<b>Mayo Score for assessment of Ulcerative colitis severity</b>	
	<b>Subtotal</b>
<p><b>Stool frequency</b></p> <p>0 = Normal no. of stools for this patient            1 = 1-2 stools more than Normal            2 = 3-4 stools more than Normal            3 = 5 or more stools more than Normal</p> <p>Each patient served as his or her own control to establish the degree of abnormality of the stool frequency.</p>	
<p><b>Rectal bleeding</b></p> <p>0 = No blood seen            1 = Streaks of blood with stool less than half the time            2 = Obvious blood with stool most of the time            3 = Blood alone passed</p>	
<p><b>Findings of flexible Sigmoidoscopy</b></p> <p>0 = Normal or inactive disease            1 = Mild disease (erythema, decreased vascular pattern, mild friability)            2 = Moderate disease (marked erythema, absent vascular pattern, friability, erosions)            3 = Severe disease (spontaneous bleeding, ulceration)</p>	
<p><b>Physician's global assessment*"</b></p> <p>0 = Normal (there are No symptoms of colitis, the patient feels well, and the flexible sigmoidoscopic score is 0) (stool frequency = 0, rectal bleeding = 0, patients functional assessment = 0, sigmoidoscopy findings = 0)</p> <p>1 = Mild disease (mild symptoms and sigmoidoscopy findings that were mildly abnormal) (subscores should be mostly 1's: stool frequency = 0 or 1; rectal bleeding = 0 or 1; patients functional assessment = 0 or 1; sigmoidoscopy findings = 0 or 1)</p> <p>2 = Moderate disease (more serious abnormalities and sigmoidoscopic and symptom scores of 1 to 2) (the subscores should be mostly 2's: stool frequency = 1 or 2; rectal bleeding = 1 or 2; patients functional assessment = 1 or 2; sigmoidoscopy findings = 1 or 2)</p> <p>3 = Severe disease (sigmoidoscopic and symptom scores are 2 to 3 and the patient probably requires corticosteroid therapy and possibly hospitalisation) (subscores should be mostly 3's: stool frequency = 2 or 3; rectal bleeding = 2 or 3; patients functional assessment = 2 or 3; sigmoidoscopy findings = 2 or 3)</p>	
<b>TOTAL</b>	

## **Appendix E – SOP Human faecal sample collection, handling and aliquoting**

Refer to supporting attachment: **Standing Operating Procedure : Human Faecal Sample Collection, Handling and Aliquoting (Samples Collected from Internal and External Agencies/Institutions)**

## Appendix F Inflammatory Bowel Disease Questionnaire (IBDQ)

This questionnaire is designed to find out how you have been feeling during the last 2 weeks. You will be asked about symptoms you have been having as a result of your inflammatory bowel disease, the way you have been feeling in general, and how your mood has been. Please circle the number next for each question. Please **Do Not** leave any question blank

**1. How frequent have your bowel movements been during the last two weeks? Please indicate how frequent your bowel movements have been during the last two weeks by picking one of the options from:**

- 1 Bowel movements as or more frequent than they have ever been
- 2 Extremely frequent
- 3 Very frequent
- 4 Moderate increase in frequency of bowel movements
- 5 Some increase in frequency of bowel movements
- 6 Slight increase in frequency of bowel movements
- 7 Normal, no increase in frequency of bowel movements

**2. How often has the feeling of fatigue or of being tired and worn out been a problem for you during the last 2 weeks? Please indicate how often the feeling of fatigue or tiredness has been a problem for you during the last 2 weeks by picking one of the options from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**3. How often during the last 2 weeks have you felt frustrated, impatient, or restless? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**4. How often during the last 2 weeks have you been unable to attend school or do your work because of your bowel problem? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**5. How much of the time during the last 2 weeks have your bowel movements been loose? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**6. How much energy have you had during the last 2 weeks? Please choose an option from:**

- 1 No energy at all
- 2 Very little energy
- 3 A little energy
- 4 Some energy
- 5 A moderate amount of energy
- 6 A lot of energy
- 7 Full of energy

**7. How often during the last 2 weeks did you feel worried about the possibility of needing to have surgery because of your bowel problem? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**8. How often during the last 2 weeks have you had to delay or cancel a social engagement because of your bowel problem? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**9. How often during the last 2 weeks have you been troubled by cramps in your abdomen? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**10. How often during the last 2 weeks have you felt generally unwell? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**11. How often during the last 2 weeks have you been troubled because of fear of Not finding a washroom? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**12. How much difficulty have you had, as a result of your bowel problems, doing leisure or sport activities you would have liked to have done during the last 2 weeks? Please choose an option from:**

- 1 A great deal of difficulty; activities made impossible
- 2 A lot of difficulty
- 3 A fair bit of difficulty
- 4 Some difficulty
- 5 A little difficulty
- 6 Hardly any difficulty
- 7 No difficulty; the bowel problems did not limit sports or leisure activities

**13. How often during the last 2 weeks have you been troubled by pain in the abdomen? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**14. How often during the last 2 weeks have you had problems getting a good night's sleep, or been troubled by waking up during the night? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**15. How often during the last 2 weeks have you felt depressed or discouraged? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**16. How often during the last 2 weeks have you had to avoid attending events where there was No washroom close at hand? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**17 Overall, in the last 2 weeks, how much of a problem have you had with passing large amounts of gas? Please choose an option from:**

- 1 A major problem
- 2 A big problem
- 3 A significant problem
- 4 Some trouble
- 5 A little trouble
- 6 Hardly any trouble
- 7 No trouble

**18. Overall, in the last 2 weeks, how much a problem have you had maintaining or getting to, the weight you would like to be at? Please choose an option from:**

- 1 A major problem
- 2 A big problem
- 3 A significant problem
- 4 Some trouble
- 5 A little trouble
- 6 Hardly any trouble
- 7 No trouble

**19. Many patients with bowel problems often have worries and anxieties related to their illness. These include worries about getting cancer, worries about never feeling any better, and worries about having a relapse. In general, how often during the last 2 weeks have you felt worried or anxious? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**20. How much of the time during the last 2 weeks have you been troubled by a feeling of abdominal bloating? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**21. How often during the last 2 weeks have you felt relaxed and free of tension? Please choose an option from:**

- 1 None of the time
- 2 A little of the time
- 3 Some of the time
- 4 A good bit of the time
- 5 Most of the time
- 6 Almost all of the time
- 7 All of the time

**22. How much of the time during the last 2 weeks have you had a problem with rectal bleeding with your bowel movements? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**23. How much of the time during the last 2 weeks have you felt embarrassed as a result of your bowel problem? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**24. How much of the time during the last 2 weeks have you been troubled by a feeling of having to go to the bathroom even though your bowels were empty? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**25. How much of the time during the last 2 weeks have you felt tearful or upset? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**26. How much of the time during the last 2 weeks have you been troubled by accidental soiling of your underpants? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**27. How much of the time during the last 2 weeks have you felt angry as a result of your bowel problem? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**28. To what extent has your bowel problem limited sexual activity during the last 2 weeks? Please choose an option from:**

- 1 No sex as a result of bowel disease
- 2 Major limitation as a result of bowel disease
- 3 Moderate limitation as a result of bowel disease
- 4 Some limitation as a result of bowel disease
- 5 A little limitation as a result of bowel disease
- 6 Hardly any limitation as a result of bowel disease
- 7 No limitation as a result of bowel disease

**29. How much of the time during the last 2 weeks have you been troubled by nausea or feeling sick to your stomach? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**30. How much of the time during the last 2 weeks have you felt irritable? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**31. How often during the past 2 weeks have you felt a lack of understanding from others? Please choose an option from:**

- 1 All of the time
- 2 Most of the time
- 3 A good bit of the time
- 4 Some of the time
- 5 A little of the time
- 6 Hardly any of the time
- 7 None of the time

**32. How satisfied, happy, or pleased have you been with your personal life during the past 2 weeks? Please choose one of the following options from:**

- 1 Very dissatisfied, unhappy most of the time
- 2 Generally dissatisfied, unhappy
- 3 Somewhat dissatisfied, unhappy
- 4 Generally satisfied, pleased
- 5 Satisfied most of the time, happy
- 6 Very satisfied most of the time, happy
- 7 Extremely satisfied, could not have been more happy or pleased

## Appendix G Food Related Quality of Life Questionnaire

This questionnaire is designed to find out how you have been feeling during the last 2 weeks in relation to food. Please **Do Not** leave any question blank.

### In the past **TWO WEEKS**

1	I have regretted eating and drinking things which have made my IBD symptoms worse	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
2	My enjoyment of a particular food or drink has been affected by the knowledge that it might trigger my IBD symptoms	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
3	My IBD has meant that I have had to leave the table while I am eating to go to the toilet	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
4	I have not been able to predict how long it will take for my body to respond to something I have had to eat or drink due to my IBD	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
5	Certain foods have triggered symptoms of my IBD	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
6	My IBD has meant that I have been nervous that if I eat something I will need to go to the toilet straight away	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
7	I have avoided having food and drink I know does not agree with my IBD	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
8	I have felt relaxed about what I can eat and drink despite my IBD	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
9	I have felt in control of what I eat and drink in relation to my IBD	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
10	I have struggled to eat the way that is best for my IBD because of other commitments during the day	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
11	I have been frustrated about not knowing how food and drink will react with my IBD	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
12	I have had to concentrate on what I have been eating and drinking because of my IBD	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
13	I have been worried that if I eat I will get symptoms of my IBD	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
14	I have felt the way that I eat and drink for my IBD has affected my day to day life	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
15	The way I have had to eat for my IBD has restricted my lifestyle	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)

## In the past **TWO WEEKS**

16	I have had to concentrate on what food I buy because of my IBD	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
17	It has been on my mind how my IBD will be affected by what I eat and drink	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
18	My IBD has prevented me from getting full pleasure from the food and drink I have had	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
19	I have felt that I need to know what is in the food I am eating due to my IBD	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
20	I have felt that I have had to be careful about when I have eaten because of my IBD	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
21	I have had to be more aware of what I am eating due to my IBD	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
22	I have missed being able to eat or drink whatever I want because of my IBD	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
23	I have felt that I would like to be able to eat and drink like everyone else	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
24	I have been happy to eat and drink around people I do not know despite my IBD	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
25	I have felt that I have been eating and drinking normally despite my IBD	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
26	I have found it hard not knowing if a certain food will trigger IBD symptoms	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
27	My IBD has meant I have had to make an effort to get all the nutrients my body needs	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
28	I have felt that I have not known how my IBD will react to food or drink	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)
29	My IBD has meant that I have had to work hard to fit my eating habits in around my activities during the day	Strongly agree (1)	Agree (2)	Neither agree nor disagree (3)	Disagree (4)	Strongly disagree (5)

## Appendix H 36- Item short form survey instrument (SF-36)

RAND > RAND HealthSurveys > RAND > Medical Outcomes > Study36-Item Short Form Survey (SF-36) >

# 36-Item Short Form Survey Instrument (SF-36)

## RAND 36-Item Health Survey 1.0 Questionnaire Items

Choose one option for each questionnaire item.

1. In general, would you say your health is:

- 1 - Excellent
  - 2 - Very good
  - 3 - Good
  - 4 - Fair
  - 5 - Poor
- 

2. **Compared to one year ago**, how would you rate your health in general **now**?

- 1 - Much better now than one year ago
  - 2 - Somewhat better now than one year ago
  - 3 - About the same
  - 4 - Somewhat worse now than one year ago
  - 5 - Much worse now than one year ago
-

The following items are about activities you might do during a typical day. Does **your health now** **limit you** in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
3. <b>Vigorous activities</b> , such as running, lifting heavy objects, participating in strenuous sports	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
4. <b>Moderate activities</b> , such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
5. Lifting or carrying groceries	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
6. Climbing <b>several</b> flights of stairs	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
7. Climbing <b>one</b> flight of stairs	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
8. Bending, kneeling, or stooping	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
9. Walking <b>more than a mile</b>	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
10. Walking <b>several blocks</b>	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
11. Walking <b>one block</b>	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
12. Bathing or dressing yourself	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3

---

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

- |   | Yes                     | No                      |
|---|-------------------------|-------------------------|
| 13. Cut down the <b>amount of time</b> you spent on work or other activities                          | <input type="radio"/> 1 | <input type="radio"/> 2 |
| 14. <b>Accomplished less</b> than you would like  | <input type="radio"/> 1 | <input type="radio"/> 2 |
| 15. Were limited in the <b>kind</b> of work or other activities                                       | <input type="radio"/> 1 | <input type="radio"/> 2 |
| 16. Had <b>difficulty</b> performing the work or other activities (for example, it took extra effort) | <input type="radio"/> 1 | <input type="radio"/> 2 |
- 

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

- |  | Yes                     | No                      |
|--|-------------------------|-------------------------|
| 17. Cut down the <b>amount of time</b> you spent on work or other activities | <input type="radio"/> 1 | <input type="radio"/> 2 |
| 18. <b>Accomplished less</b> than you would like                             | <input type="radio"/> 1 | <input type="radio"/> 2 |
| 19. Didn't do work or other activities as <b>carefully</b> as usual          | <input type="radio"/> 1 | <input type="radio"/> 2 |
- 

20. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

- 1 - Not at all
  - 2 - Slightly
  - 3 - Moderately
  - 4 - Quite a bit
  - 5 - Extremely
-

21. How much **bodily** pain have you had during the **past 4 weeks**?

- 1 - None
  - 2 - Very mild
  - 3 - Mild
  - 4 - Moderate
  - 5 - Severe
  - 6 - Very severe
- 

22. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)?

- 1 - Not at all
  - 2 - A little bit
  - 3 - Moderately
  - 4 - Quite a bit
  - 5 - Extremely
-

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the **past 4 weeks**...

- |   | All of the time         | Most of the time        | A good bit of the time  | Some of the time        | A little of the time    | None of the time        |
|---|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| 23. Did you feel full of pep?   | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3 | <input type="radio"/> 4 | <input type="radio"/> 5 | <input type="radio"/> 6 |
| 24. Have you been a very nervous person?                                | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3 | <input type="radio"/> 4 | <input type="radio"/> 5 | <input type="radio"/> 6 |
| 25. Have you felt so down in the dumps that nothing could cheer you up? | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3 | <input type="radio"/> 4 | <input type="radio"/> 5 | <input type="radio"/> 6 |
| 26. Have you felt calm and peaceful?                                    | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3 | <input type="radio"/> 4 | <input type="radio"/> 5 | <input type="radio"/> 6 |
| 27. Did you have a lot of energy?                                       | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3 | <input type="radio"/> 4 | <input type="radio"/> 5 | <input type="radio"/> 6 |
| 28. Have you felt downhearted and blue?                                 | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3 | <input type="radio"/> 4 | <input type="radio"/> 5 | <input type="radio"/> 6 |
| 29. Did you feel worn out?  | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3 | <input type="radio"/> 4 | <input type="radio"/> 5 | <input type="radio"/> 6 |
| 30. Have you been a happy person?                                       | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3 | <input type="radio"/> 4 | <input type="radio"/> 5 | <input type="radio"/> 6 |
| 31. Did you feel tired?   | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3 | <input type="radio"/> 4 | <input type="radio"/> 5 | <input type="radio"/> 6 |

---

32. During the **past 4 weeks**, how much of the time has **your physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?

- 1 - All of the time
- 2 - Most of the time
- 3 - Some of the time
- 4 - A little of the time
- 5 - None of the time

How TRUE or FALSE is **each** of the following statements for you.

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
33. I seem to get sick a little easier than other people	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5
34. I am as healthy as anybody I know	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5
35. I expect my health to get worse	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5
36. My health is excellent	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5

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## ABOUT

The RAND Corporation is a research organization that develops solutions to public policy challenges to help make communities throughout the world safer and more secure, healthier and more prosperous. RAND is nonprofit, nonpartisan, and committed to the public interest.



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## Appendix I Information Letter to Participants

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ABN 54 361 485 361 CRICOS IPC 00279B

### **Study title:** Role of diet in ulcerative colitis

You are invited to take part in a study examining the effect of dietary patterns in mild to moderate ulcerative colitis. The study will run for 8 weeks and is being undertaken as part of the requirements for a Doctor of Philosophy at Edith Cowan University (ECU).

### **Study aims**

This study will examine the effect of dietary patterns on mild to moderate (MAYO score 6-9) disease activity, inflammation, gut microbiota, symptoms and quality of life. Outcomes will help determine evidence based dietary recommendations in mild to moderate ulcerative colitis.

### **Study details**

Your participation will require you to be randomised to an intervention or control group. The intervention diet details will be provided to the control group after the 8 week trial so it does not change their dietary patterns. Each group will be required to be evaluated by the research gastroenterologist at baseline, weeks 2, 4 and 8 for a MAYO score (full or partial), inflammatory blood markers (ESR and CRP), stool markers (FCP), gut microbiota composition, metabolome analysis and quality of life measures. This study requires a stool sample and 3 day weighed food record prior to commencing the study and at the completion of the study. An appointment with the dietitian will be attended at the beginning and completion of the study. At one year after your eight week trial you may be contacted regarding your disease management and asked to complete an IBD – quality of life questionnaire.

#### What we will ask you to do

- Complete a 3 day- weighed food record at the beginning and end of the study (including one weekend day). You will be given scales, measuring cups, spoons, recording sheets and instructions by the researcher. You do not need to alter the way you eat for this three-day period.
- Complete questionnaires on IBD, quality of life and food related quality of life.
- Complete blood tests at your routine visits to the IBD clinic
- Complete a stool sample at the beginning and end of the study to assess your microbiota composition and metabolome (pending funding).
- Complete an interview with an Accredited Practising Dietitian.

## **Risks and discomforts**

There are no known health risks of the intervention diet. You may experience some inconvenience, anxiety or discomfort associated with attending appointments, disclosing personal information in the questionnaires or completing the weighed food record.

A flexi-sigmoidoscopy poses few risks with rare complications including bleeding from the site the tissue sample was taken or a tear in the colon or rectal wall. In addition risks associated with blood sampling are infrequent and may include local bruising, inflammation of the vein, local thrombosis and possible infection of the sampling site.

## **Potential benefits**

This research may help us to understand the role diet may play in ulcerative colitis activity, inflammation, gut flora, symptoms and quality of life.

## **Consent to participate in the study**

If you choose to participate in the study, you are required to sign the informed consent form.

## **Confidentiality of information**

Access to all data will be limited to the chief researcher and supervisors of the study. A confidentiality agreement has been signed by all members of the research team. Confidentiality will be maintained by de-identifying all data. Hard copies of all data will be stored in a secure, lockable cabinet at St John of God Subiaco Hospital or at the chief researchers home and data will be transferred in a secure manner. Computer files will be stored on the St John of God secure servers and on an external hard drive and all files will be password protected. After five (5) years of the finished project, all electronic data will be deleted and any paper-based records will be destroyed using St John of God Subiaco Hospital's confidential waste. It should be noted there are legal limits to confidentiality. The data and/or samples collected for the purposes of this research may be used in further approved researcher projects. Your name and other identifying information will be removed.

## **Results of the study**

You will receive feedback from your gastroenterologist regarding your inflammatory markers and disease activity as per normal protocol at baseline, weeks 2, 4 and 8. The findings from this study will be used to develop a thesis and may be presented as a journal article and presented at conferences. All data will be deidentified, therefore no individual data will be made available

### **Voluntary participation in the study**

Your decision to participate in this study is entirely voluntary. No explanation or justification is needed if you choose not to participate. A decision to participate will not disadvantage you or involve any penalty.

### **Withdrawing from the study**

You are free to withdraw from the study without further involvement at any time. There will be no consequences of withdrawing from the study. Information or material that has been collected will be used unless you request otherwise.

### **Questions or further information**

If you have any questions or require any further information about the study, please contact:

Chief Investigator: Charlene Grosse – [cgrosse0@our.ecu.edu.au](mailto:cgrosse0@our.ecu.edu.au)

If you have any concerns or complaints about the study and wish to talk to an independent person, you may contact:

#### **Research Ethics Officer**

Edith Cowan University

270 Joondalup Drive JOONDALUP WA 6027

Phone: (08) 6304 2170 Email: [research.ethics@ecu.edu.au](mailto:research.ethics@ecu.edu.au)

This project has been approved by the St John of God Subiaco Hospital Ethics Committee and the ECU Human Research Ethics Committee

## Appendix J Consent Form

JOONDALUP CAMPUS

270 Joondalup Drive, Joondalup  
Western Australia 6027  
☎ 134 328

**Study title:** Role of Diet in Ulcerative Colitis

[www.ecu.edu.au](http://www.ecu.edu.au)

**Research team:**

ABN 54 361 485 361 CRICOS IPC 00279B

Charlene Grosse (chief researcher), Dr Claus Christophersen (co-supervisor), Professor Amanda Devine (co-supervisor), Professor Ian Lawrance (external supervisor), Dr Johnny Lo (co-supervisor).

### Informed Consent

By consenting to participate in the study, I acknowledge the following:

- I have been provided with a copy of the Information Letter to Participants, explaining the research study
- I have read and understood the information provided.
- I have been given the opportunity to ask questions and I have had any questions answered to my satisfaction.
- I am aware that if I have additional questions I can contact the research team.
- I understand that participation in the research project will involve: completing a 3 day weighed food record, 24 hour stool sample, routine blood and stool testing, routine sigmoidoscopy and completing required questionnaires.
- I understand that the information provided will be kept confidential, and that the identity of participants will not be disclosed without consent.
- I understand that the information provided will be used for the purposes of this research project and understand how the information is to be used.
- I understand that I am free to withdraw from further participation at any time, without explanation or penalty.
- I understand that data collected for the purposes of this research project may be used in further approved research projects, and that my name and other identifying information will be removed.
- I freely agree to participate in the study.

**YOUR NAME:** .....

(please provide full name)

**SIGNATURE:** ..... **DATE** ( / / )

(dd/mm/yyyy):