Nurse-led smoking cessation service utilising motivational interviewing and nicotine replacement therapy (NRT) versus standard of care counselling in Crohn's Disease patients.

Investigators:

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Background:

It has been well established within the literature that smoking has an adverse impact on patients with IBD, particularly Crohn's disease (CD)[1]. Smoking increases the risk of disease flares, post-operative reoccurrence and most recently, has been demonstrated as an independent risk factor for Loss of response to anti-TNAα medication[1,2]. The recent PANTS study published in the Lancet demonstrated that patients who smoked had lower drug levels than that of their non-smoking counterparts[2]. Considering this evidence, it is essential to ensure IBD patients quit smoking to improve their disease outcomes, improve their quality of life and ensure optimal use of medication.

Even with this established knowledge, there has been little done to stop or reduce smoking in the IBD clinic. To date, there has been no prospective, nurse-led smoking cessation service reported. In 2001, Cosnes[3] et al published a smoking cessation intervention study within their IBD cohort. Their primary endpoint was the rate of IBD flare ups and the time to flare up[3]. The authors found the physician played a role in assisting a patient to quit smoking, however in this study, the specialised physician could be visited weekly. Most major IBD centres have access to IBD nursing services, whose role is largely to support patient education and managing helplines to prevent adverse outcomes. The IBD nurse has the most contact with IBD patients thus, the IBD nurse is well placed to assist smoking cessation interventions.

Study Rationale

It is clear from the literature that there is a need for smoking cessation in patients with Crohn's diseases. To date there is no published evidence of the IBD nurse conducting a smoking cessation program and the impact this can have to disease control, quality of life and drug utilisation.

Significance

If it is confirmed that the IBD nurse can assist in smoking cessation in Crohn's disease patients, then the intervention has the potential to be implemented in IBD centres across Australia. This study will set the scene for a potential larger randomised controlled study, involving IBD nurses from across Australia.

Hypothesis:

A nurse-led, smoking cessation service utilising motivational interviewing and NRT is a more effective intervention to reduce or stop smoking in the IBD patient than standard physician counselling.

Aim:

To perform a pilot study to evaluate the efficacy of a nurse-led intervention service to reduce or stop a patient with Crohn's Disease from smoking.

Assessment of Efficacy:

Primary Endpoint:

1. Cessation of smoking at week 12 as reported by patient confirmed on the Readiness to Quit Ladder.

Secondary Endpoint:

1. Reduction in smoking at week 12 as reported by patient confirmed on the Readiness to Quit Ladder.

Exploratory Endpoints:

1. Reduction or cessation in smoking correlates to improvement in C-Reactive Protein (CRP) and Faecal Calprotectin
2. Reduction or cessation in smoking correlates to improvement of CDAI score at week 12
3. Reduction or cessation in smoking correlates to change in drug trough levels from baseline to week 12
4. Improvement in patient quality of life related to reduction or cessation in smoking as measured by SIBQ and SF-36
5. Change in microbiome from baseline to week 12 visit

Study Design:

Prospective, head to head, randomised, pilot study.

Participants:

Participants will be recruited from the IBD patient cohort at Fiona Stanley Hospital. Participants will be invited to participate by their treating clinician after being identified as suitable for the study. Formal consent will occur prior to any study activities occurring. 30 participants with a diagnosis of Crohn's Disease will be sought to participate within this pilot study.

Inclusion Criteria:

1. 18 years of age or older
2. Diagnosis of Crohn's Disease
3. Current smokers who are wanting to quit (a readiness to quite ladder[4] rating of 6 or higher)

Exclusion Criteria:

1. Under 18 years of age.
2. No formal Crohn's Disease diagnosis
3. Unwilling to quit (as measured on the readiness to quit ladder[4] of 5 or less).

Intervention:

Participants randomised to the intervention arm of this pilot study will undergo a motivational interview at baseline, week 6 and at week 12. Motivational interviewing techniques employed will be based on the Royal Australian College of General Practitioners guidelines[5]. Participants will have follow up phone calls on a fortnightly basis until study completion. These participants will be prescribed NRT by their treating Gastroenterologist based upon their results from the Fagerstrom assessment[6,7] at the commencement of the study.

Control:

Participants randomised to the control arm will undergo standard physician counselling regarding smoking cessation. Participants will be seen at week 6 and again at week 12 to assess smoking status, quality of life and disease activity. Participants within the control arm will not undergo motivational interviewing nor will they receive fortnightly phone calls or NRT.

Schedule:

The study will be conducted over 12 weeks in which patients randomised to either the intervention or standard physician counselling (randomised 1:1 ratio). Below is a schematic of events for patients randomised to the intervention. A follow up phone call will occur at 30 days post the week 12 visit measuring adverse events, concomitant medications and a smoking status check, examining sustained smoking cessation or reduction.

	Baseline	W2	W4	W6	W8	W10	W12	30 days post W12
Consent	X							
Demographics	X							
Fagerstrom	X			X			X	
Readiness to Quit Ladder	X			X			X	X
SIBDQ	X			X			X	
SF-36	x			X			x	
CDAI Score	x			X			x	
CRP	x						x	
Faecal Calprotectin	x						x	
Stool Collection for exploratory outcome	x						x	
Motivational Interview	X			X*			X	
Follow-up Phone Call		X*	X*		X*	X*		
Smoking Status Check	x	x	x	x	x	x	X	X
Adverse Events				x			X	X
Concomitant Medication	x			x			X	X
Dispensing of NRT	x			x				

* = For participants randomised to intervention arm.

Ethical Considerations:

Informed Consent:

Informed consent will be documented on a Patient Information and Consent Form and will also be documented in a patient's clinical medical record. Participants will initially have a discussion with the research team about the study where the study information will be provided. Potential participants will then be encouraged to take this information and discuss the study with family, friends and their

GP. A screening appointment will be made where a participant can then ask any questions and decide whether they would like to proceed with the study or not.

Assessment of Safety:

Adverse events are assessed at each face to face visit and will also be discussed at the phone visits. Any safety events will be monitored by a Consultant Gastroenterologist throughout the study to ensure participant safety is maintained.

Nicotine replacement therapy has associated side effects such as headaches, skin irritation, nausea and palpitations. If these arise they will be assessed by a Gastroenterologist or medical physician to ensure patient safety is maintained.

Actual and Potential Risks to Participants:

The main risk associated with this study is the use of over the counter nicotine replacement therapy, advised based on the Fagerstrom assessment. The main risks are localised skin irritation, dizziness, headaches, nausea and palpitations. If any of these occur then the patient will be withdrawn from the study.

Participant Withdrawal:

Participants will be withdrawn from this study if there are safety concerns identified. An independent Gastroenterologist will assess all safety events and will discuss with the investigators if significant safety concerns are realised. Participants have the right to withdraw from the study which is explained during the informed consent process. If a participant requests to withdraw then then the investigators will inform the patient that any current data collected may be used in data analysis however, no further information will be collected from them.

Monitoring and Audit:

This study will be subject to potential monitoring and audit from the South Metropolitan Research Support and Development Unit as the primary sponsor for the study, the HREC committee approving the study or other regulatory bodies. The investigators will allow access to these regulatory bodies and will ensure that all information is available.

Biospecimen Collection:

Stool samples will be collected at baseline and at week 12 and will be stored in the Harry Perkins Institute of Medical Research Building in a Fiona Stanley Hospital freezer for future analysis of sRNA sequencing measuring microbiome composition. These samples will be analysed within 1 year of study completion.

Expected benefits to the participant and community:

Potential benefits extend beyond improvement in disease outcomes, such as prevention of other co-morbidities which can be life-limiting. Potential benefits that are being measured in this study include a reduction in disease related complications, disease progression and improvement in patient quality of life.

Record Storage and Retention:

Security will be implemented in a layered approach consisting of physical and logical security. Physical security consists of secure premises with 24/7 CCTV that is recorded and retained. The storage and computer infrastructure is housed within a secure area in the Harry Perkins Institute of Medical Research Building at Fiona Stanley Hospital (staff require security clearance). Firewalls, antivirus software and regular security updates and data backup and recovery systems are operable.

All paper records will be stored within the IBD research unit office which is secure and only accessible by the research team. Data may be held on the RedCap data management system which is hosted by the South Metropolitan Health Service.

All records will be retained for a period of 15 years as stipulated by the NHMRC and will retained in accordance with the *"Management of Data and Information in Research"* guideline. All records will then be disposed of according to *the "Management of Data and Information in Research"* guideline and in accordance with local policy.

Adverse Event Protocol:

Reporting of AE/SAE/SADE/SUSAR/USADE to the HREC and RGO will be carried out in accordance with the requirements of the National Statement , the AHEC position statement "Monitoring and Reporting of Safety for Clinical Trials Involving Therapeutic Products" 2009 and the TGA's "Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95)" 2000.

The South Metropolitan Health Service Human Research Ethics Committee will be notified by the principle investigator (or their delegate) of anything that might warrant review of the approval of the project including serious and unexpected adverse events in accordance.

The Investigators will capture and report AEs, including SAEs which occur at their site to the South Metropolitan Human Research Ethics Committee and Research Support and Development Unit in accordance with the protocol and TGA Good Clinical Practice guidelines. A WA Health Adverse Event Notification Form will be used for AE/SAE/SADE/SUSAR/USADE reporting, and will be completed (using the RGS and aligned with the PRN) by the PI (or delegate) and sent to the CPI for signing. This will be completed and sent to the HREC and RGO as soon as possible.

Investigators will take prompt steps to deal with any unexpected risks. Investigators will notify the CPI of an AE/SAE/SADE/SUSAR/USADE where there is a material impact on the continued ethical acceptability, or the AE/SAE/SADE/SUSAR/USADE indicates a need for a change to the protocol. The CPI will report to the SMHS HREC within 24 hours any SAE/SUSAR that is required to be reported under local policy and NHMRC guidelines. The report will include information regarding the event and indicates whether it: materially impacts the continued ethical acceptability of the project; or requires, or indicates the need for, a change to the protocol and/or PICF, including changes to safety monitoring as recommended by the investigator.

Publication Plan:

Results derived from this study will be published in reputable journals within the Inflammatory Bowel Disease literature. The results of this study will also be presented at national and international conferences such as the European Crohn's and Colitis Conference or Australian Gastroenterology Week Conference.

Results from this study will be made available to patients through patient advocacy groups such as Crohn's and Colitis Australia.

Timeline:

Project Activity:	**Target Date:**
Preparation and submission of Ethics Application and Governance Application	June 2020
HREC and RGO Approval	August 2020

Patient Screening Commences	August 2020
Last Patient Enrolled	February 2021
Data Analysis Completion	April 2021
Submission for Publication	June 2021

Budget:

Item and brief description	$ Amount sought from Spinnaker	Amount	Total $	Secured From (details of funding partner)
Infliximab Drug Levels	$67.10ea	Est 20 samples	$1342.00	Sought from Janssen
Infliximab Antibody Levels	$81.40ea	Est 6 samples	$488.40	Sought from Janssen
Administration Costs and Study Equipment (printing, stationary etc)	$300.00	1	$300.00	Sought from Janssen
Nicotine Replacement Therapy	$1813.50	30 patients	$1813.50	Sought from Janssen
Clinical Nurse (Level 2.1 with on costs)	$5918.40	120hrs	$5918.40	Sought from Janssen
C-Reactive Protein	Standard of Care			
Faecal Calprotectin	Standard of Care			
Total overall	$9864.10	$0.00	$9864.10	$9000.00 sought

References:

1. Parkes G. C., Whelan K., Lindsay J. O., Smoking in inflammatory bowel disease: Impact on disease course and insights into the aetiology of its effect. Journal of Crohn's and Colitis; 2014(8):717-725.
2. Kennedy N. A., Heap G. H., Green H. D., Hamilton B., Bewshea C., Walker G. J., et al. Predictors of anti-TNF treatment failure in anti-TNF-naive patients with active luminal Crohn's disease: a prospective, multicentre, cohort study. Lancet Gastroenterology Hepatology; 2019(4):341-353
3. Cosnes J., Beaugerie L,. Carbonnel F., Gendre J. Smoking Cessation and the Course of Crohn's Disease:An Intervention Study. Gastroenterology; 2001(120):1093-1099
4. Biener, L., Abrams, D. B. The Contemplation Ladder: Validation of a measure of readiness to consider smoking cessation. Health Psychology, 1991, 10(5), 360-365

5. Smoking Cessation Guidelines For Australian General Practice, The Royal College of General Practitioners. Developed by: Zwar N, Richmond R, Borland R, Sullivan S, Cunningham M, Litt J.

6. Pomerleau C S, Majchrezak MI, Pomerleau OF. Nicotine dependence and the Fagerstrom Tolerance Questionnaire: a brief review. J Substance Abuse, 1989, 1: 471-7.

7. Heatherton TF, Kozlowski LT, Frecker RC, Fagerstrom KO. The Fagerstrom Test for Nicotine Dependence: a revision of the Fagerstrom Tolerance Questionnaire. Br J Addict, 1991, 86:1119-27.