

The OSCAR Study

ObeSity related Colorectal Adenoma Risk

Protocol Version 1.1

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Signatures Page

The OSCAR study, final version 1.1, dated 24/10/2017 has been written and approved by the following:

Professor Colin Rees

Date:

Chief Investigator

Principal Investigator Declaration

I confirm I have read and understood this protocol and I agree to conduct the study in accordance with the protocol.

Name of Principal Investigator : _____

Name of Centre : _____

Signature : _____

Date : _____

Project Investigators

Chief Investigator

Professor Colin Rees
Consultant Gastroenterologist
South Tyneside District Hospital
South Shields, England

Co-Investigators

Professor Mark Hull
Professor of Molecular Gastroenterology
University of Leeds
Leeds, England

Dr Stuart McPherson
Consultant Hepatologist
Freeman Hospital
Newcastle, England

Professor Steven Rushton
Professor of Biological Modelling
School of Biology
Newcastle University, England

Professor John Saxton
Head of Department of Sport, Exercise and Rehabilitation
Faculty of Health and Life Sciences
Northumbria University, Newcastle, England

Dr Laura Neilson
Clinical Research Fellow
South Tyneside District Hospital
South Shields, England

Northern Region Endoscopy Group

Sponsor

South Tyneside NHS Foundation Trust

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Norgine Pharmaceuticals

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1. Background

Colorectal cancer (CRC) is the second most common cancer affecting both men and women in England.¹ The adenoma-carcinoma sequence is established as the mechanism by which adenomatous polyps develop into CRC.^{2,3} Detection and removal of adenomas is important in reducing CRC risk. A study which undertook single screening flexible sigmoidoscopy and adenoma clearance in patients aged 55-64, with high risk features referred for colonoscopy, reduced CRC incidence by 23% and mortality by 31%.⁴ Several clinical risk and protective factors for sporadic colorectal neoplasia (including CRC and colorectal adenomas) are recognised. Age, gender and family history of CRC are non-modifiable risk factors for the detection of advanced colorectal neoplasia.⁵ Cigarette smoking and excess body weight (EBW) are modifiable risk factors.^{5,6}

Obesity is increasingly prevalent in the UK, with 24.4% of men and 25.2% of women classed as obese in England.⁷ In addition to type II diabetes mellitus and increased cardiovascular risk, obesity is independently linked with increased colorectal neoplasia and recurrence of colorectal adenomas.⁸⁻¹¹ One large European study found that up to 94% of obese individuals had non-alcoholic fatty liver disease (NAFLD), compared with 67% of overweight and 25% of normal weight patients.¹² NAFLD is defined as fatty infiltration of the liver affecting more than 5% of hepatocytes, in the absence of alcohol excess or the consumption of steatogenic drugs. NAFLD encompasses various stages of fatty liver disease ranging from steatosis to steatohepatitis (fat + hepatocellular injury +/- fibrosis) through to cirrhosis and hepatocellular carcinoma.¹³⁻¹⁵ Obesity and type II diabetes are major risk factors for the progressive form of fatty liver, non-alcoholic steatohepatitis (NASH).^{15,16} At present there is no gold standard tool in screening for patients at risk of fatty liver disease, apart from identifying risk factors as mentioned above. The fatty liver index (FLI) is one such tool which incorporates height, weight, waist circumference, serum gamma-glutamyl transferase (GGT) and serum triglycerides, and if identified at high risk these patients be considered for further assessment for fatty liver with blood tests and ultrasonography.¹⁷ Approximately 40% of patients with NAFLD develop progressive fibrosis that can result in cirrhosis, putting patients at risk of hepatocellular carcinoma, liver failure and portal hypertension related complications.¹⁸⁻²¹ The development of advanced fibrosis (stage 3-4) in patients with NAFLD is clinically important as it is associated with a >3 fold increase risk of mortality (all-cause and liver-related) compared with a reference population.²² Non-invasive fibrosis scores, such as the FIB-4 score (comprising age, Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) and platelet count), are reliable in diagnosing or excluding advanced fibrosis in patients with NASH and are

now widely used to identify patients with advanced fibrosis who need specialist assessment.²³ A recent study has reported that IgA is an independent predictor of advanced fibrosis.²⁴ Transient elastography, more commonly known as Fibroscan is a non-invasive imaging based technique which measures liver stiffness, and it correlates well with the degree of liver fibrosis. It is commonly used in a wide range of liver conditions including NAFLD. However its use is of limited use in patients above the age of 50, who have central obesity, those who have a body mass index (BMI) of greater than 35 or type 2 diabetes as the results may be invalid.¹³

Additionally patients with NAFLD are at higher risk of developing cardiovascular disease and the two are strongly associated.²⁵ The Qrisk 2 score is a validated tool in risk stratifying patients for cardiovascular disease.²⁶ It is a score comprising of the past medical history, family history, smoking status, blood pressure, weight and height.

A 2011 Hong Kong study demonstrated a high prevalence of colorectal adenomas and advanced neoplasia in patients with NAFLD. Adenomas were found more commonly in the right colon.²⁷ A subsequent systematic review and meta-analysis investigating the link between NAFLD and colorectal neoplasia in screening patients found a significant association; however, this association was more prominent in the Asian population.²⁸ These studies have not been repeated in a Western population, specifically the UK. Previous studies diagnosed NAFLD using ultrasound or liver biopsy, but have not determined whether there is an association between colonic adenomas and liver enzymes and / or non- invasive markers of fibrosis, such as the FIB4 or NAFLD fibrosis score.^{27,29–32} The advantage of using liver enzymes and non-invasive fibrosis scores to identify patients with NAFLD is that they can be readily assessed on large numbers of patients and could potentially be included in risk models to predict colonic adenomas. This negates the necessity for liver biopsy- an expensive, invasive procedure with significant risk.

Approximately 400,000 colonoscopies are performed each year within the NHS for the investigation of gastrointestinal symptoms, including altered bowel habit, rectal bleeding and iron deficiency anaemia.³³ Adenoma detection rate (ADR), defined as the number of procedures in which at least one adenoma is detected, is a widely accepted quality measure.³⁴ A recent colonoscopy audit demonstrated an average polyp detection rate of 32.1%; however, ADR is variable between colonoscopists.³⁵ A recent study estimated mean ADR of 15.9%.³⁶ Patients found to have adenomas receive surveillance procedures, however these are currently based entirely upon number and size of adenomas with no patient factors considered.³⁷ The NHS Bowel Cancer Screening Programme (BCSP)

invites all individuals aged 60-74 to undertake biennial faecal occult blood testing (FOBT). Screening is currently population based and non-targeted. Patients with a positive FOBT are invited for colonoscopy. The national Bowelscope screening programme is currently being rolled out in England and Wales, with the Lead applicants unit the first nationally to deliver this programme. All individuals aged 55 are invited for a single flexible sigmoidoscopy and adenoma clearance. Those deemed to be high risk undergo completion colonoscopy.

The mean ADR per colonoscopist within the FOBT BCSP is 46.5%, which is much higher than the symptomatic population due to the targeted nature of the programme.³⁸ The BCSP has demonstrated a significant stage shift in CRC diagnosed.³⁹ At present, the FOBT based screening programme is not providing protection against right sided CRC.^{40,41} A trial within the Scottish screening programme demonstrated that screening was an effective environment for interventions to alter patient behaviour.⁴²

In summary, although a study in an Asian population suggested an association between NAFLD and colorectal neoplasia, this has not been repeated in a Western population. It is important that the association is explored in a Western population but using non-invasive markers of liver disease and a wider range of colorectal neoplasia risk factors. This will allow development of a model to predict colorectal adenoma risk guiding screening and surveillance.

2. Study Objectives

To measure the extent to which individuals with obesity and abnormal liver function are at increased risk of developing colorectal adenomas and CRC. This study aims to quantify that risk by developing a model of obesity-related and other known CRC risk factors. In addition the model will be refined using non-invasive measures of liver disease.

2.1 Primary Objectives

1. To explore the link between liver enzymes, NAFLD, obesity and colorectal neoplasia in terms of adenoma burden, site and histological features
2. To assess whether the presence of liver fibrosis, measured using the FIB4 score, affects the risk of colorectal neoplasia

3. To identify which demographics contribute to increased predisposition to colorectal neoplasia

3. Study Design

A multi-centre observational study will identify colorectal neoplasia burden in patients undergoing index screening or diagnostic colonoscopy. Non-invasive markers of liver disease and obesity will be assessed and a multivariate model constructed. The primary outcome is to develop a risk model with emphasis on obesity-related factors, particularly in the population with abnormal liver enzymes, to inform colorectal screening. Secondary outcomes will support this model by identifying demographics which contribute to increased predisposition to colorectal neoplasia, additionally assessing whether the presence/degree of liver fibrosis affects this risk. The link between NAFLD, obesity and colorectal neoplasia in terms of adenoma burden, site and histological features will also be explored.

3.1 Patient Recruitment

Eight Northern Regional Endoscopy Group (NREG- with a strong track record in delivering large endoscopy trials) units and Kettering General Hospital NHS Trust will recruit patients. Sites from NREG include: South Tyneside District Hospital, Freeman Hospital, Northumbria NHS Trust, Sunderland Royal Hospital, James Cook University Hospital, County Durham and Darlington Foundation Trust, Leeds Teaching Hospitals NHS Trust and North Tees University Hospitals.

Approximately 1430 patients undergoing colonoscopy as part of the BCSP or symptomatic service (most commonly patients with iron deficiency anaemia, altered bowel habit, weight loss and rectal bleeding) will be identified from endoscopy lists and recruited by a member of the research team. The final target number of participants will be refined after the first 100 participants have been recruited however this is not expected to vary significantly. Methodology by Peduzzi et al is used to calculate the minimum number of cases required to measure all variables and develop the risk model.⁴³ Sample size $N=10*(k/p)$, where k is the number of covariates to be investigated in the model ($n=15$) and p the smallest of the proportions of positive or negative cases ($=ADR=0.15$). For non-BCSP population, ADR is around 15%; 1000 from this population are required. Minimum ADR within the BCSP is 35%; 430 cases are required to adequately power and build the model. This will allow resolution of small scale effects of covariates on risk prediction. Using Demidenko's method, the sample size needed for logistic regression with 80% power and 5% level of significance is $N=8V/\beta^2$, where β is the natural log of the

odds ratio and V is logistic model variance due to covariates.⁴⁴ This formula can be rearranged to determine the minimum odds ratio that can be detected at a sample size of 2000 with sufficient power. Assuming a moderate standard error in the regression ($se=0.125$), and calculating V from the standard error ($V=(se \cdot \sqrt{N})^2$) the study will have sufficient statistical power to detect an effect with a small effect size with an odds ratio of 1.42. The final sample size will be refined using data from the first 100 participants and observed effect size(s), however, the total number of recruits will not exceed 2000.

All potential participants will be sent or given a patient information leaflet about the study when their colonoscopy paperwork is sent or given to them, allowing adequate time to read the information leaflet (at least 24 hours) before consenting to the study. On attending the endoscopy unit for their procedure, they will be approached by a member of the research team and given the opportunity to discuss the study. Written consent will be obtained from those wishing to participate in the study. Specific consent to inform the participant's General Practitioner (GP) of participation will be obtained. Both non-consenting and consenting patients will receive their colonoscopy according to standard routine practice. Study participants will also undergo a health questionnaire, height and weight measurements and blood tests. In addition, intra-procedure data will be collected by a member of the research team onto a case report form (CRF). Any polyps detected and removed will be followed up, and histological diagnosis recorded post procedure by the research team. No additional follow-up or alteration of subsequent care is required for this study. The study will not affect the timing of out-patient appointments or results. Data will be collated and analysed by the research team. Adverse events will be classified by the chief investigators team.

3.2 Inclusion criteria

1. Aged 18 years and over
2. Able to give informed consent
3. Indications:
 - a. Patients with positive faecal occult blood test (FOBT) referred for index colonoscopy as part of Bowel Cancer Screening Programme
 - b. Colonoscopy conversion from Bowelscope
 - c. Index diagnostic colonoscopy due to new gastrointestinal symptoms (including but not restricted to diarrhoea, change in bowel habit, abdominal pain, PR bleeding, weight

loss), iron deficiency anaemia, family history of CRC, abnormal findings on cross sectional imaging

Recruitment materials will be produced in English; however, if language difficulties emerge in an interested patient, a professional translation service specialising in facilitating phone consultations will be used.

3.3 Exclusion Criteria

1. Absolute contraindication to colonoscopy
2. Unable to give informed consent
3. Known colorectal cancer
4. Known polyposis syndrome
5. Previous total/subtotal colectomy
6. Known colonic stricture which would prevent completion of colonoscopy
7. Attending for therapeutic procedure
8. Attending for assessment of a known lesion
9. Attending for assessment of known inflammatory bowel disease (IBD)
10. Attending for surveillance colonoscopy (polyp surveillance, post colorectal cancer surveillance, IBD surveillance)
11. Colonoscopy within the last 5 years

3.4 Withdrawal Criteria

1. New diagnosis of a polyposis syndrome
2. Incomplete procedure due to any cause such as colonic stricture or obstructing lesion preventing completion of procedure, withdrawal of consent from patient

3.5 Data Collection

On attendance for colonoscopy and following completion of a written consent form, the participant will be asked to complete a health questionnaire. This can be done either by the participant alone or with help from a member of the research team. This questionnaire will include the following details:

1. Age
2. Ethnicity
3. Gender

4. Smoking History- current and previous
5. Alcohol consumption- current and previous
6. Medication history
7. Family history of colorectal cancer
8. Family history of ischaemic heart disease
9. History of liver disease
10. Hypertension history
11. Diabetic history
12. History of chronic kidney disease (stage 4/5, eGFR <30ml/min)
13. History of atrial fibrillation
14. History of rheumatoid arthritis
15. Previous anti-obesity surgery

The clinical notes will be used to confirm the indication for the colonoscopy and to support the health questionnaire where participants are unsure of details. The research nurse will measure blood pressure, weight, height, waist circumference and calculate the body mass index (BMI in kg/m²). This information, including the health questionnaire, will be entered onto the case report form (CRF).

Blood tests will be taken to identify patients with fatty liver defined as:

- Definite if patients have raised ALT levels (above the upper limit of normal) and are overweight or obese (in the absence of excessive alcohol consumption)
- Probable if the ALT >30 IU/ml for males and >19 IU/ml for females and they are overweight or obese (in the absence of excessive alcohol consumption)

We will also determine stage of fibrosis defined by FIB-4 score ((age x AST)/(platelets x $\sqrt{\text{ALT}}$)) as:

- No / mild: FIB-4 score <1.3
- Moderate: FIB-4 score 1.3 – 2.67
- Advanced: FIB-4 score >2.67

We will also determine the patient's Qrisk 2 score and Fatty Liver Index (FLI) Score.

Patients undergoing a colonoscopy usually have an intravenous cannula inserted to allow administration of sedative medication, analgesia and smooth muscle relaxants. Where possible the blood tests will be taken at the time of cannula insertion. To enable this, a size 18G (green) cannula will

be used. Where obtaining bloods from the cannula is not possible (failed attempt or poor venous access), this will be done using separate standard venepuncture methods. Blood samples will be collected in the appropriate containers and sent to the clinical laboratory at the site hospital. The blood tests will be requested and labelled according to individual site-specific usual practice. The samples will not be anonymised, to enable the results to be later checked by a research nurse and entered onto the pseudonymised CRF. The samples will be destroyed in line with individual site Trust policy (usually within 3-7 days). Bloods will include:

1. Bilirubin
2. Alanine aminotransferase (ALT)
3. Alkaline phosphatase (ALP)
4. Aspartate aminotransferase (AST)
5. Gamma-glutamyl transferase (GGT)
6. Immunoglobulin A
7. Full blood count (FBC)
8. HbA1c
9. Fasting blood glucose
10. Lipids: Cholesterol, HDL and Triglycerides
11. Albumin

In the event that haemolysis of LFTs occurs, patients will still be included in the study to allow for analysis of other risk factors and their association with adenomas.

Following colonoscopy to allow completion of the histological dataset, additional information will be collected either at the time of colonoscopy or from hospital reporting systems or from the patient record on the BCSP dataset. These will include:

1. Site and number of cancers diagnosed
2. Number of adenomas
 - a. Site
 - b. Morphology
 - c. Size
 - d. Villous component
 - e. Degree of dysplasia

f. Presence of advanced neoplasia

In a subset of patients attending for colonoscopy in the centres where Fibroscan is available patients will have a liver stiffness measurement by Fibroscan using the M or XL probe as appropriate.

The above data will be entered onto the CRF by a member of the research team. For patients who attend for a diagnostic colonoscopy but are taking warfarin or other anti-coagulation, polypectomy is contraindicated. If polyps are found, a further colonoscopy is usually organised as part of standard care. The polyp details will be recorded at this second colonoscopy to prevent confusion and unnecessary exclusion.

4. Adverse Events

As this is an observational study, there are no expected additional adverse events specifically associated with the study. Intravenous cannula insertion may cause some discomfort and bruising.

5. Assessment and Follow Up

Clinical follow up will be as per routine clinical practice. Where colonoscopy is incomplete, the reason for this will be recorded. Eligible, consented patients will remain in the study for two weeks following discharge from the endoscopy day ward on the day of their procedure. This is to allow time to collect data from the blood and histology reporting systems. No additional visits are required for patients who enter the study. Any follow up appointments post-colonoscopy will be as per routine care for the unit. The timescale for the out-patient appointment and subsequent care will be unaltered by participation in the study.

Checking liver function tests and HbA1c may pick up new diagnoses of fatty liver disease or diabetes. All abnormal blood tests will be communicated to the participant's GP for further action by a member of the research team.

6. Statistics and Data Analysis

Data from the CRFs will be transferred to a secure and encrypted electronic computer database. Statistical analysis will be undertaken by Professor Steven Rushton, Professor of Biological Modelling at Newcastle University.

The relationship between adenoma incidence, NAFLD and blood markers will be investigated using logistic regression whilst adjusting for patient-related demographic variables including age and gender. This will assess the independent contribution of predictors to the odds of adenomas being found. Stepwise removal of non-significant covariates will then be used to identify variables best able to predict adenoma presence. ROC plot and AUC analyses of sensitivity and specificity will be used to characterise the ability of the model to discriminate between patients with and without adenomas and their potential as a predictive tool. These analyses assess the independent contribution of variables to the probability that adenomas will be found, but do not allow for confounding, interaction and associated indirect effects on detection. Structural Equation Modelling (SEM) will be used to investigate impact of indirect and direct effects of the predictors on adenoma incidence. Parsimonious models for logistic regression and SEM will be compared in terms of their ability to predict adenoma presence.

As multiple adenomas may occur, the extent to which adenoma number is related to abnormal liver enzymes using Poisson regression models and SEM will be measured, following the same analytical framework. It is anticipated that the presence of multiple adenomas will be zero-inflated, with some patients having zero and others many. The extent to which zero-inflated models (eg allowing for aggregation) improve the prediction of adenomas will be assessed. Robustness and validation of all models will be validated using bootstrapping. The best model will be developed into a predictive tool.

7. Regulatory Issues

7.1 Ethics approval

Ethical approval will be sought via the NHS Research Ethics Committee (REC) prior to study commencement. As the majority of patients undergoing colonoscopy have an intravenous cannula inserted for sedative medication or smooth muscle relaxants, the necessary blood tests can be obtained from this. To prevent haemolysis, a slightly larger cannula will be used (18G). In some cases,

the larger cannula may cause slightly more discomfort than the smaller cannulae commonly used for this procedure.

Patients will be informed of the risks associated with standard colonoscopy and consented for the procedures according to standard practice, in addition to a study specific consent form which will be explained by the research team.

The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

7.2 Consent

Consent to enter the study will be sought from each participant only after a full explanation has been given, an information leaflet has been offered and time allowed for consideration. Signed participant consent will be obtained. The right of the participant to refuse to participate without giving reasons will be respected. All participants will be informed of their right to withdraw at any time from the study without giving reasons and without prejudicing further treatment. Potential participants will be assessed by a member of the study team, eligibility will be confirmed and baseline assessments performed.

7.3 Confidentiality

The Caldicott Principles and Data Protection Act will be fully adhered to when dealing with patient identifiable data. The Chief Investigators will preserve the confidentiality of participants taking part in the study. No staff beyond the usual care team will have access to identifiable data. No identifiable participant data will be passed outwith the participating Trusts. The data will be held at the site in accordance with local Trust policies and will be destroyed following the study close in accordance with local Research and Development protocols.

7.4 Sponsor

South Tyneside Foundation Trust will be the sponsor for this trial.

7.5 Funding

This study will be conducted on existing NHS and BCSP lists, at no extra cost to the NHS. Funding for cannulation and blood collection equipment, blood test analysis and clinical trial unit costs will be provided by Norgine Pharmaceuticals.

The chief investigator is a full-time dedicated clinical researcher and will be supported by a research team consisting of a research fellow and research nurses, who will invite, assess and consent participant, in addition to collecting data. No additional NHS resources will be required to conduct this study.

8. Study Management

8.1 Data Protection

Patient data will be held on site at the Trust in accordance with local Trust policies. Patients will be assigned a unique study ID at study entry. All data passed to the trial team will have all patient identifiable data removed, aside from the unique study ID. Patients who withdraw will have all data collected up until the point of withdrawal included in the study. This data will be uploaded onto an electronic CRF and included in the analysis of the study. Data will be submitted either directly onto the electronic CRF or onto paper CRF before input into the electronic CRF.

8.2 Records Retention

The Principal Investigator will retain all study related records (CRFs, source documents, Investigator site file) for fifteen years after the end of the study. All study related records may be archived after the study has closed, the database has been locked and notification has been received from the trial team. The PI will be responsible for ensuring that these archived records are accessible, as required by current legislative regulations. Archiving will occur at each site according to local R+D protocols.

8.3 Protocol Compliance

A representative group of staff who will be part of the research team will attend a site initiation meeting to ensure compliance with the protocol and allow training in study procedures and data collection methods. The PI at each study site will apply for local R+D approval. The PI will sign a copy of the ethically approved protocol to confirm agreement to carry out all study related tasks in accordance with the protocol.

8.4 Responsibilities

All staff involved in the study will undergo GCP training. Day to day delivery will be supported by a research nurse and a research fellow. The responsibilities of the trial team are as outlined below.

Chief Investigator:

1. Protocol development
2. Coordination of trial
3. Education of trial team
4. Ensuring GCP training and governance
5. Support application through approval processes and ethics
6. Data interpretation
7. Contribution to report and papers for publication
8. Ensure uploading of accrual data

Principal Investigators

1. Protocol development
2. Coordination of trial
3. Education of trial team, hosting of trial
4. Ensuring GCP training and governance
5. Support application through approval processes and ethics
6. Data interpretation (including timely assessment of seriousness of adverse events)
7. Contribution to production of report and papers for publication
8. Ensure uploading of accrual data
9. Overall responsibility for conduct and running of the trial at site
10. Ensuring local governance
11. Applying for R&D approval at their site
12. Recruitment and study conduct according to protocol

9. Financing and Insurance

This study will be funded by the Norgine Pharmaceuticals. Standard NHS indemnity arrangements are in place.

10. Dissemination

OSCAR is supported by the British Society of Gastroenterology (BSG) Endoscopy Research Committee (Appendix 2). The study has been reviewed and endorsed by the Bowel Cancer Screening Research Committee (Appendix 3).

Statistical analysis will be undertaken by Professor Steven Rushton, and the results will be written up in the form of a report by the research and academic team. Data from the study will be disseminated to participating patients within the study via the Trust's websites. The results will then be submitted for publication in international peer reviewed journals and presented to the British Society of Gastroenterology Endoscopy Research Committee, BSG guideline groups and the Bowel Cancer Screening Programme. Feedback will be given to regional and national Endoscopy leads, maximising the exposure of findings to colonoscopists. Data will also be disseminated to local networks, and national and international symposia.

11. Publication Policy

The chief investigators will take responsibility to present and publish the outcomes of the study. The results will be disseminated through peer reviewed national/international journals and learned scientific societies.

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**National Cancer Research Institute
Colorectal Clinical Studies Group**



15th May 2015

Dear Professor Rees

Re: ObeSity-related Colorectal Adenoma Risk (OSCAR)

I confirm that the above study was reviewed by the NCRI Colorectal Cancer CSG Screening & Prevention subgroup at its last meeting on 5th February 2015, at which several points were raised, including the use of both screening and symptomatic patient cohorts, which have now all been addressed in the current proposal.

The study fits well with the current CSG strategy to expand the national screening & prevention studies portfolio. The Subgroup recognised the importance of the clinical question that is being addressed.

The NCRI Colorectal CSG is supportive of your proposal and looks forward to supporting it from funding application through to delivery.

Yours sincerely

Professor Mark Hull
Chair, Screening & Prevention Subgroup, Colorectal CSG

Appendix 2- BSG Endorsement



3 St Andrews Place
Regent's Park
London NW1 4LB
T 020 7935 3150
F 020 7487 3734
www.bsg.org.uk

14 May 2015

Dear Colin

Thank you for submitting your Proposal "Obesity-related Colorectal Adenoma Risk (OSCAR)" to the BSG Endoscopy Clinical Research Group (CRG).

This proposal was peer reviewed by members of the CRG and the BSG Research Committee Chairman.

I am pleased to inform you that the CRG formally endorses your proposal and will upload the proposal onto the BSG Endoscopy CRG database.

We wish you success with your funding applications; please keep us informed regarding progress. Please note that any publications (including abstracts) relating to the work should mention the BSG Endoscopy CRG's endorsement.

Best wishes

Julie Solomon
BSG Head of Research & Learning

Appendix 3- BCSP Research Committee Approval



Bowel Cancer Screening Programme Research Committee

John Scholefield
Chair

C/o NHS Cancer Screening Programmes
Fulwood House
Old Fulwood Road
Sheffield
S10 3TH

Tel: 0114 2013040

rachel.athorn@phe.gov.uk

Professor Colin Rees
South Tyneside District Hospital
Harton Lane
South Shields
NE34 0PL

colin.rees@stft.nhs.uk

17th July 2015

Dear Professor Colin Rees,

The Bowel Cancer Screening Programme (BCSP) Research Committee met on 15th July 2015 to discuss your research plans: *ObeSity-related Colorectal Adenoma Risk (OSCAR) Study ID 155*

The Committee gave their support to the project providing they can be assured on the consistency of the laboratory testing.

As a condition of support, the BCSP Research Committee requires you to keep them informed of developments with the project, including any changes of status, any significant adverse events, when completed, and when written up.

Please note that any applications requiring patient identifiable data from the BCSP programme will also require PHE ODR (Office of Data Release) approval.

The BCSP Research Committee requires you to notify them promptly of any incidents that would be recorded on the National Research Ethics Service (NRES) Breaches Register. Undertaking research within the Screening Programme following receipt of this letter of support assumes your agreement to fulfil this obligation. NRES has the potential to share information with the BCSP Research Committee regarding any breaches of ethics related to projects involving the BCSP.

The Committee wishes you well with your project.

Yours sincerely

Rachel Athorn MSc BMedSci
On behalf of the NHS BCSP Research Committee.

Appendix 4- OSCAR study Gaant chart

