A feasibility study:

Improving management of comorbidity in patients with colorectal cancer

# Dr C Jackson

# A/Prof Diana Sarfati

Protocol version 1.1

24/08/2015

## Project Title:

# Improving management of comorbidity in patients with colorectal cancer – a feasibility study

## Short title: C3 Comorbidity CRC Pilot Study

## Investigators

Dr Christopher Jackson

Associate Professor Diana Sarfati

Professor John McCall

Associate Professor Katrina Sharples

Dr Stephen Chalcroft

Dr Marie McLaughlin

Dr Stephanie Farrand

Ms Tracy Steiner

Table of Contents

Investigators 2

1. Lay summary 4

2. Background 4

3. Purpose of the current proposal 7

4. Participants 7

4.1 Inclusion criteria 7

4.2 Exclusion criteria 7

5. Study procedures 8

5.1 Patient identification 8

5.2 Screening tool 8

5.3 Medicines reconciliation: 8

5.4 Interaction check: 8

5.5 Comprehensive Medical Assessment 8

6 Outcome Measures 9

7 Statistical Analyses 9

8 Risks/Harms to participants: 9

9 Funding 10

10 Screening tool 10

11 Quality of life assessment 14

12 Eligibility check list 15

## Lay summary

Patients who are diagnosed with colorectal cancer often have other health problems as well as their cancer. These concurrent medical conditions (comorbidity) can impact on the treatment that is recommended for them, and on their recovery from their cancer. In addition, people with a lot of additional health problems may find cancer treatment more difficult to tolerate.

International research has examined the impact of Comprehensive Geriatric Assessment on patients who are receiving chemotherapy. Studies have shown that people undergoing this assessment have fewer serious side effects from the chemotherapy.

We are proposing a large, multi-centre study looking at the impact of a slightly broader intervention aimed at managing comorbidity in patients with colorectal cancer who are undergoing surgery, chemotherapy, or both.

Prior to embarking on such a large study we need to test the appropriateness and acceptability of our screening tools and “road test” our comprehensive medical (geriatric) assessment.

This current application is a pilot study where we aim to test these tools.

## Background

Comorbidity among cancer patients is common. Data from New Zealand indicate that approximately half of all cancer patients have at least one other chronic condition recorded, and a third have two or more. The most common chronic conditions recorded are cardiovascular illness, metabolic illness, diabetes and chronic respiratory disease.(1, 2)

Comorbidity is even more common for Māori and Pacific patients. For example, while 10% of European patients with colon cancer had a Charlson score of 3+ (indicating a high level of comorbidity), 17% of Māori and Pacific patients were in this category.(3)

The coexistence of cancer and other chronic conditions has substantial implications on treatment decisions and treatment outcomes for both cancer and chronic disease. (4-10) However most studies of cancer therapies and treatment guidelines ignore the complex interrelationships between cancer and comorbidity in favour of a “single disease” approach to management.(8)

Previous work led by Sarfati has shown that 70% of patients presenting with colon cancer in New Zealand have at least one comorbid condition identified from their hospital notes and a quarter have three or more. Work from this team in New Zealand and others internationally has consistently found that comorbidity has an adverse impact on cancer outcomes, and that comorbidity substantially reduces the likelihood that an individual will receive treatment despite evidence that the treatment would have been beneficial for at least some of these patients.(4, 7, 11) For example, Sarfati et al found that among patients with colon cancer, those with comorbidity had substantially poorer survival than those without comorbidity. Only 19% of these patients with comorbidity (defined as a Charlson score of 3+) were offered adjuvant chemotherapy compared with 84% of patients without comorbidity. This is despite the fact that within the group who had comorbidity, those who received chemotherapy had 60% lower mortality than those who did not. More recent work from the PIPER study (led by Findlay and Jackson) shows that a substantial proportion of patients with colorectal cancer who are potentially eligible for adjuvant or palliative chemotherapy are still not receiving it. Comorbidity is likely to be an important driver for this.

A number of international studies have confirmed both that cancer patients with comorbidity are less likely to receive definitive treatment and that where such treatment is given, outcomes are significantly better.(9, 12-17) For example, Gross et al used propensity scores to adjust for background likelihood of receiving adjuvant chemotherapy for 5330 older patients with stage III colorectal cancer.(16) They found lower likelihood of receipt of chemotherapy among patients with comorbidity, but clear and consistent survival advantages for those who were treated compared with those who were not. The risk of hospitalisation after treatment was not altered by receipt of adjuvant chemotherapy regardless of comorbidity. Both physical and mental comorbidity appear to be important. Depression at the time of cancer diagnosis, in particular, has been found to be associated with lower likelihood of treatment and poorer survival in a number of studies.(18-21)

Comprehensive geriatric assessments (CGA) are used increasingly in geriatric oncology to provide data on patient functional status, comorbidity, polypharmacy, existence of geriatric syndromes, nutritional status, social support and psychological status.(21-25) There are a large number of studies that show that incorporating such an assessment to the care of older people with cancer can be useful to *predict* complications of care, estimate mortality or survival and to assist in treatment decision making for older people.(20-27) Few studies have assessed the extent to which CGA or similar broad-based medical review at the time of cancer diagnosis actually alter cancer outcomes. However, those that have assessed this question have, without exception, found that such interventions have a positive impact.

Two small studies, one of elderly patients with hepatocellular carcinoma in Indonesia (n=87)(28) and one based in the Veterans Administration system in the U.S. (n=99)(29) found that incorporating geriatric-led care into the care of cancer patients resulted in improvements in functional status and quality of life. A larger randomised controlled trial (n= 375) evaluated an intervention that primarily focused on providing specialised post-surgical care to elderly patients who had undergone cancer surgery. The intervention involved comprehensive clinical assessment (including assessment of physical, emotional and functional) status and referrals to specialist medical care as required by advanced practice nurses.(30) This trial found that those in the intervention arm had substantially improved survival (HR=2.04; 1.33-3.12 after adjustment for stage of disease and surgical hospitalisation length of stay).

More recently, Temel et al (2010) carried out an RCT designed to assess the impact of early versus late referral to palliative care for patients with metastatic non-small cell lung cancer.(31) The intervention included review by a palliative care physician and advanced practice nurse with follow-up at monthly intervals (or as required). The intervention involved assessment of physical and psychosocial symptoms, and active coordination of care of the patient. The intervention group performed better in terms of quality of life over a variety of measures, had lower depression rates at 12 weeks, but also unexpectedly, had significantly better survival than the control group (11.9 months compared with 8.9 months; p=0.02).

Finally, a recent cohort study recruited older cancer patients prior to the start of chemotherapy.(32) Outcomes among those who underwent review and care plan development by a geriatrician (n=65) were compared with those who received usual care (n=70) within a single London hospital. The intervention was developed specifically for the study, and the non-intervention and intervention aspects were delivered sequentially. Patients who underwent the intervention were first screened to identify low and higher risk patients on the basis of presence of comorbidity, recent hospital admission, suboptimal functional status or reduced quality of life. Seventy percent of the intervention arm underwent full geriatric-led review, but 7 of the remaining 19 patients also had some intervention from the geriatric team. Those in the intervention group experienced lower treatment toxicity, more treatment completions and fewer treatment modifications compared with the control group. There was only six months of follow up time, during which 15% of the intervention group died compared with 20% of the control group, a difference that was not statistically significant although the study was not powered to detect a difference in survival.

Whilst in combination, this body of research provides a strong rationale for comprehensive medical review at diagnosis for at least some cancer patients, there are substantial gaps in the evidence base which we seek to address. None of the studies provide evidence from adequately powered prospective intervention trials. To date, all studies have been limited to elderly patients. This is important because a substantial proportion of patients under the age of 70 years experience significant comorbidity. For example, one in five patients aged 51-60 years and nearly one in three patients aged 61-70 years with colon cancer had at least one of the 17 conditions included in the Charlson comorbidity index.(3) No studies have included these higher risk younger patients. This is particularly important given that Māori and Pacific people tend to experience more severe comorbidity at a younger age than European people.

## Purpose of the current proposal

As part of an HRC Programme Grant Application (in progress) we propose a multi-centre prospective controlled intervention study assessing the impact of a comprehensive medical assessment (led by Geriatricians), comprehensive medication review, and personalised medical plan in patients with colorectal cancer.

Prior to embarking on an ambitious multi-centre intervention study, several questions regarding feasibility must be addressed. The current proposal is a feasibility study that will be conducted prior to embarking on the larger multicentre study.

We propose a pilot study to assess the appropriateness and effectiveness of the screening tools aimed to identify patients with comorbidity, and the acceptability of a comprehensive medical assessment in patients diagnosed with colorectal cancer.

## Participants

### Inclusion criteria

EITHER:

* All patients with newly diagnosed colorectal adenocarcinoma who have undergone or who are planned to undergo major resection

OR

* Metastatic relapse of colorectal adenocarcinoma, as judged by histological confirmation of relapse or as confirmed by a specialist multi-disciplinary team meeting (MDTM)

OR

* Undifferentiated carcinoma (grade 4) with clinical features consistent with colorectal cancer (and confirmed by a MDTM) will be permitted

### Exclusion criteria

* Histological or cytological diagnosis of cancer type other than adenocarcinoma
* Adenocarcinoma or colon or rectum with polypectomy or local excision as only treatment
* Treatment acuity such that intervention not able to be administered without potentially compromising patient outcome (e.g. acute or sub-acute bowel obstruction, incipient perforation, major GI haemorrhage)
  + Note that these patients may be able to be enrolled post-operatively
* Unable to give informed consent
* Not able to comply with follow up
* Locally recurrent rectal cancer without metastatic relapse
* Life expectancy less than three months from diagnosis.

**There are explicitly no restrictions by:**

* age;
* involvement in other trials;
* ECOG performance status.

## Study procedures

### Patient identification

Potential participants will be identified by clinicians at colonoscopy, MDTM, or after post acute ward rounds. A trial-specific Research Nurse would be notified of potential eligibility.

Potential participants will be approached by the Research Nurse and offered a written Patient Information Sheet [(Patient Information Sheet)](#PIS)

After having time to consider whether they wish to participate in the study, including having time to discuss with family, whanau and/or friends, potential participants may consent to entering the study and offer written [informed consent](#Informed_Consent)

### Screening tool

A [screening tool](#Screening_Tool) to identify comorbidity will be administered by the Research Nurse

### Medicines reconciliation:

* The patient is asked to identify what medications they take
* The notes are reviewed to identify what medications are recorded on the admission note
* The patient’s GP and usual Pharmacy are contacted and reconciliation undertaken, identifying accuracy of current prescription

### Interaction check:

* Medications are entered into the Lexi-Comp online interaction checker ([www.utdol.com](http://www.utdol.com)). A printout of potential interactions is provided to the Study Clinician

### Comprehensive Medical Assessment

* Patients who are identified via the screening tool are invited to attend a Comprehensive Medical Assessment

The individualised comprehensive medical assessment will include:

1. Physician (geriatrician) led medical assessment of comorbidity, with medical optimisation, investigations or further referrals where indicated, and treatment of medical comorbidity.
2. Assessment of mental health status with referral as necessary.
3. Analgesia and pain management review, and assessment of impact on blood pressure, cognition, balance and mood.
4. Specific assessment of ECOG performance status.
5. Review of social circumstances and risk factors such as living alone, social isolation.
6. Referral to occupational therapy, physiotherapy, social worker, dietician and palliative care as appropriate.
7. Follow-up appointment prior at three months from first assessment or when indicated (if shorter).
8. Note that assessment of inpatients is intended to focus on offering advice on management of comorbidity rather than issues pertaining directly to surgical management.

## Outcome Measures

Proportion of patients with colorectal adenocarcinoma who are approached who consent to enter.

Proportion of patients who consent to enter whom complete screening criteria and fulfil criteria to proceed to CMA.

Narrative of comorbid conditions identified at CMA.

Medication review:

* Discrepancy between medications identified at admission and those held by GP and at Pharmacy.
* Potential interactions, graded as “clinically significant” or “potentially significant”.

Completion rate of [QoL tool](#QoL).

Narrative feedback from participants (including clinicians).

## Statistical Analyses

No formal hypothesis testing nor statistical analyses are planned – this is a feasibility study. There are no “gold standards” against which our proposed tools can be validated.

We propose to enrol approximately 30 patients into the screening process to progress up to 20 patients in the Comprehensive Medical Assessment module

## Risks/Harms to participants:

Potential participants who have recently learned they have been diagnosed with a cancer are likely to be distressed.

They may consider that participation in the study influences their care (either favourably or unfavourably).

Participants’ distress may influence their willingness to undertake study procedures.

Participants may conflate participation in the study with their routine care.

There are unlikely to be medical harms from having additional review from a specialist physician.

If additional comorbidity or medical issues are identified as part of the CMA, then these issues will be raised with the responsible clinician whom can determine whether this should impact on their cancer treatment (risk grid).

## Funding

There is no external funding of this pilot study.

Investigators are undertaking this pilot as “time only”.

Research nurse salary is covered by surplus funds from commercial trials led by Dr Jackson.

## Screening tool

**Baseline data**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ***Colorectal cancer Diagnosis*** | | | | | | | | |
| New primary diagnosis of CRC | |  | Metastatic relapse of known CRC | | | |  | |
| Date of diagnosis | \_ \_ / \_ \_ / \_ \_ | | | | | | | |
| Method of diagnosis  *Please select most relevant option* | Histology confirming adenocarcinoma  Suspicious lesion visualised directly  Suspicious lesion visualised on imaging | | | |  | Clinical picture consistent with CRC  Other (*please specify below)*  *\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_* | |  |
| ***Co-morbidity Assessment*** | | | | | | | | |
| Evidence of co-morbidity  *Please select all options that apply* | Medical record  Self-reported  On regular medication | | |  | | Hospitalised in last 12 months  Any significant functional or QoL limitations on questionnaire | |  |
| *Co-morbidities recorded up to and including date of diagnosis* | | | | | | | | |
| |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | | Any comorbidities documented? | | ASA: | | | | | | | | O 1. Yes O 2. No | | | **Cardiovascular system** | | | | | | | | | | 1. Angina or coronary artery disease (includes CABG) | | O | | | | 1. Hypertension | | | | 3. Previous myocardial infarction | | O | | | | 1. Cardiac arrhythmia (includes supraventricular tachycardia, atrial fibrillation or flutter, heart block) | | | | 5. Valvular disease (includes valvular stenosis,valvular insufficiency/regurgitation, rheumatic heart disease, history of valve surgery) | | O | | | | 6. Congestive heart failure | | | | 7. Peripheral vascular disease (including claudication, skin ulcers) | | O | | | | 8. Previous pulmonary embolism (PE) | | | | 9. Other cardiovascular system disorder (e.g. cardiomyopathy, aneurysms)  ..................................................................................................................................... | | | | | | | | | | **Respiratory** | | | | | | | | | | 1. Asthma | | O | | | | 2. Chronic airways disease (includes emphysema, bronchitis) | | | | 3. Other respiratory conditions ................................................................................................................................. | | | | | | | | | | **Haematological** | | | | | | | | | | 1. Blood loss anaemia (incl iron deficiency) | | O | | | | | | 2. Other anaemia (e.g. megaloblastic, haemolytic) | | 3. Other haematological disorder (e.g. clotting disorders, thalassaemias, myelodysplastic syndrome, myeloproliferative disorders. Do not include haematological malignancies) .............................................................................................................. | | | | | | | | | | **Gastrointestinal** | | | | | | | | | | 1. Ulcer disease (includes GORD, peptic ulcer disease, oesophagitis) | O | | | | | | 2. Inflammatory bowel disease (includes Crohns disease and ulcerative colitis) | | | 3. Liver disease (includes chronic hepatitis, cirrhosis, haemachromatosis, Wilson’s disease. Do not include cancers.) | O | | | | | | 4. Other GI conditions ............................................................ | | | **Neurological** | | | | | | | | | | 1. Previous stroke or TIAs | O | | | | | | 2. Parkinson’s disease | | | 3. Dementia | O | | | | | | 4. Multiple sclerosis | | | 5. Other neurological conditions ........................................................................................................................................................... | | | | | | | | | | **Endocrine**  (1=history noted but not currently active; 2=currently on medication, controlled; 3=currently active and not well controlled) | | | | | | | | | | 1. Diabetes mellitus   1 O 2 O 3 O | | |  | | | |  | | | O 3. Hypothyroidism | | | O | | | | 4. Other endocrine disorder (e.g. hyperthyroidism, hyper/hypoparathyroidism, Addison’s disease, Cushings syndrome hypopituitarism) ........................................... | | | **Other malignancy** | | | | | | | | | | 1. Leukaemia | O | | | | 2. Lymphoma | | | | | 3. Solid tumour | O | | | | 4. Metastatic tumour | | | | | Specify (if available:  ..................................................................... |  | | | | Specifiy (if available:  .................................................................. | | | | | **Mental health disorder**  (1=history noted but not currently active; 2=currently on medication, controlled; 3=currently active and not well controlled) | | | | | | | | | | 1. Substance dependence/abuse | O | | | | 2. Alcohol dependence/abuse | | | | | 1. Major depression   1 O 2 O 3 O | O | | | | 1. Anxiety disorders   1 O 2 O 3 O | | | | | 1. Bipolar disorder | O | | | | 1. Schizophrenia and other psychoses | | | | | 5. Other ................................................................................................................................. | | | | | | | | | | **Other** | | | | | | | | | | 1. Connective tissue disease (incl systemic lupus erythematosus, scleroderma, polymyositis, rheumatoid arthritis) | | | | O | | | | 2. Chronic kidney disease | | 5. osteoarthritis and other non-specific arthritis | | | |  | | | |  | | 6. Other ................................................................................................................................. | | | | | | | | |   *Please list all current medications* | | | | | | | | |

## Quality of life assessment

## QLQ-C30-English

## Eligibility check list

|  |  |  |
| --- | --- | --- |
| Inclusion Criteria  *Any selection of “No” means the patient is ineligible for the study* | Yes | No |
| 1. Known or presumed diagnosis of colorectal cancer (including metastatic relapse) | ❑ | ❑ |
| 1. Evidence of current co-morbidity | ❑ | ❑ |
| 1. Ability to understand and the willingness to sign a written informed consent document. | ❑ | ❑ |

|  |  |  |
| --- | --- | --- |
| Exclusion Criteria  *Any selection of “Yes” means the patient is ineligible for the study* | Yes | No |
| 1. Life expectancy less than 3 months | ❑ | ❑ |
| 1. Colorectal adenocarcinoma treated by polypectomy only | ❑ | ❑ |
| 1. Non-adenocarcinoma histology | ❑ | ❑ |
| 1. Unable or un-willing to comply with follow-up | ❑ | ❑ |