Research Proposal:  
Early Integrated Supportive Care Study

Primary Investigator: Dr. Philippa Hawley, Palliative Care Specialist, BC Cancer Agency, Vancouver Centre

Study location: BC Cancer Agency, Vancouver Cancer Centre, 600 West 10th Ave, Vancouver, British Columbia, V5Z 4E6

1. Summary

Currently at the BC Cancer Agency oncologists refer a patient to the Pain and Symptom Management/Palliative Care team (PSMPC) based on their practice. Their decisions are made subjectively and without standard guidelines/symptom assessment tools. Patients are sometimes referred quite late in their illness. The PSMPC team sees patients in their own clinic, separate from the oncologists, and do not often collaborate in a patient’s care. Early integration of palliative care into oncological care has been shown to improve quality of life and to prolong survival, to reduce inappropriately aggressive oncological care at end of life, and to reduce costs of care. We are testing an earlier integrated oncology-palliative care model at the time of cancer diagnosis, with the aims of determining whether:

1) the introduction of PSMPC support at the time of diagnosis will lead to better symptom management and quality of life,

2) early integration of palliative care into medical oncology care will reduce aggressiveness of cancer treatment near end of life

3) a fully integrated service delivery model is sustainable.

Our model’s intervention will provide for the early involvement of the PSMPC team in collaboration with the gastrointestinal (GI) oncology team in order to provide patients with support from both subspecialties at a single visit. Patients in need of pain and symptom support will be identified using a validated symptom assessment tool. The GI cancer team was approached for testing this model as their patients are referred more frequently to the PSMPC clinic in the Vancouver Centre than any other tumour site - 23.4% of total referrals. This intervention would be aimed particularly at helping the most unwell patients who find attendance at multiple appointments very difficult.

This study builds on work published in 2010 by Temel et al\textsuperscript{1}, which showed that early palliative care intervention improved the quality of life and survival time of metastatic lung cancer patients at the Massachusetts General Hospital, Boston. A 2014 study conducted by Bakitas et al in mixed cancers has shown similar benefits\textsuperscript{2}. Both these studies were in patients with advanced cancer and a short life expectancy. We propose to move the integration even earlier, to time of referral to oncology, to maximize the potential benefits. If the intervention is shown to benefit patients, we will have evidence to support the implementation of a new standard of cancer patient care.

2. Objectives

A) To test whether the introduction of PSMPC support at a stage of patient care earlier than current practice (referral by the oncologist when deemed necessary) allows for better management of patients’ pain and symptoms from cancer or its treatment, and improves quality of life of patients
B) To test whether early integration of palliative care into medical oncology care reduces aggressiveness of cancer treatment near end of life

C) To test whether a service delivery model in which PSMPC support is introduced at an early stage in patient care is sustainable

3. Intervention
The intervention is earlier PSMPC team involvement in patient care as informed by patients’ self-reported symptom assessment.

   Tool: symptom assessment questionnaire
   Decision: patients with symptom scores ≥4 are identified as needing symptom management
   Specialist involvement: patients in need will meet with a PSMPC team member either at the GI appointment (collaboration with GI team) or at a later date.

4. Assessment tool
Our patient assessment will be conducted using a modified BC Cancer Agency Patient Pain and Symptom Questionnaire, which includes the Edmonton Symptom Assessment Scale (ESAS) and the Canadian Problem Checklist (CPC). Our primary outcome of symptom assessment will be collected using the ESAS, which is a validated, reliable tool for patient symptom intensity. Several past palliative care studies have used the ESAS as an assessment tool, and have shown decreases in symptom scores following similar specialist team interventions.

5. Eligible patients
- diagnosed with a GI cancer (small intestine, colorectal, stomach*, esophageal*, pancreatic*, liver, gallbladder)
- have appointments in GI clinic during study days
- not yet receiving care from the PSMPC team
- can complete symptom assessment questionnaire on their own or with the help of a family member or interpreter

6. Study Design/Randomization
This is a cluster randomized study with the randomization being performed at the level of the oncologists. Controlled randomization allows us to make the intervention and control groups comparable with respect to all factors that could influence the outcome of the intervention.

Cluster randomization - oncologists will be randomized into either the intervention or the control group, and patients will be automatically sorted according to their oncologist’s assigned group. By randomizing at the level of the oncologist and including multiple oncologists in each study arm, we can adjust for differences in schedules and referral patterns to ensure the groups are comparable.

Update 9-Feb-18:
All oncologists will be allocated to the intervention arm for the remainder of the study now that we have the desired sample size for the control group. By recording which oncologist saw which patient this will not be an issue for obtaining study outcomes.

7. Groups
Intervention

- **Assessment questionnaire + early PSMPC involvement**
  - GI cancer patients complete a symptom assessment questionnaire prior to their oncology appointment.
  - The questionnaire is reviewed and discussed with the oncologist.
  - If a patient self-reports at least one symptom score ≥4, the PSMPC team will be from the PSMPC clinic area to meet with the patient in the GI clinic, during or immediately following the oncology appointment.

Control

- **Assessment questionnaire for data collection only, not to be assessed**
  - GI cancer patients will complete a symptom assessment questionnaire prior to their oncology appointment.
  - The questionnaire data will not be shared with the oncologist. Control patients will be made aware that their questionnaire will not be discussed at this appointment, but that they are free to raise pain and symptom/palliative care concerns with the oncology team.
  - Oncologists may refer patients to the PSMPC team if/when they deems necessary.

8. Sample Size

Our total estimated sample size is 176 and assumes a 5%* drop-out rate:
  - Integrated arm = 88
  - Control arm = 88

The sample size calculations were derived using Hemming et al. 9.

9. Patient recruitment

We will be recruiting new patients for a period of approximately 4-6 months. Based on the current new patient appointments, we estimate that for each study arm we can approach 17-20 patients a month on study days.
10. Patient following
Each patient will have data collected for four months.
Timeline for collection of symptom assessment data (pink forms): based on existing follow up schedule for patients

- **baseline (at first appt in GI clinic)**
- 4 weeks
- 8 weeks
- 12 weeks
- 16 weeks

*Intervention patients and control patients*
11. Summary of Procedures

PC STUDY FLOW version B (grouped by physician) – intervention group

GI patients in with (a) certain physician(s) are given the GREEN form to complete by (clerk/care aide/nurse/Mara?) (either Tues pm, Thurs am)

Some patients may not complete the form...

Gi patient seen by oncologist on a non-study clinic day (Mon, Wed, Fri)

Patient has at least one symptom score of 4 or higher (incl. max pain): Flagged for further assessment

ONCOLOGIST identifies patient as needing pain/symptom management or palliative care

Patient has all symptom scores 3 or under: no follow up by PSMPC (resource code = PG1)

Identified as not needing pain/symptom management or palliative care at this time

Identified as needing pain/symptom management or palliative care

Patient seen in PSMPC clinic

resource code = PGSAM
activity code = SYMCN

patient seen same day by PSMPC in GI clinic room (w/ GI nurse, onc?)

patient seen same day by PSMPC in Pod 8 (w/ GI nurse)

patient’s needs managed by oncologist and GI nurse

referred to PSMPC for follow up

resource code = PGIFU
GREEN form

no further action

referred to PSMPC for follow up

resource code = PSMP1/2/3/4
activity code = SYMCN SYMFU SYMST

patient’s needs managed by oncologist and GI nurse

All new GI referrals to PSMPC

resource code = PGSAM
activity code = SYMCN
PC STUDY FLOW version B (group by physician) – control group

GI patients in with (a) certain oncologist(s) are given the GREEN form to complete by clerk/care aide/nurse/Mara (Tues pm or Thurs am)

Patient sees oncologist

Identified as not needing pain/symptom management or palliative care at this time

Form is collected by ___: content is not discussed with physician resource code: PGICO

no further action

Identified as needing pain/symptom management or palliative care

referred to PSMPC for follow up

patient's needs managed by oncologist and GI nurse

New GI referrals to PSMPC

resource code = PSMP1/2/3/4
activity code = SYMCN SYMFU SYMST

patient seen in PSMPC clinic

PINK form

Some patients may not complete the form...

GI patient seen by oncologist on a non-study clinic day (Mon, Wed, Fri)

Identified as not needing pain/symptom management or palliative care at this time

no further action
12. Outcome measures

<table>
<thead>
<tr>
<th>Outcome category</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptom assessment</strong></td>
<td>Pain and symptom assessment questionnaire (ESAS)</td>
</tr>
<tr>
<td>(aim: reduce symptoms)</td>
<td>• change in individual symptom scores between visits</td>
</tr>
<tr>
<td></td>
<td>• change in composite score of symptoms</td>
</tr>
<tr>
<td></td>
<td>• proportion with change in individual symptom scores of ≥2 points between first and last visits</td>
</tr>
<tr>
<td><strong>Use of health services</strong></td>
<td># of hospital admissions for non-treatment reasons</td>
</tr>
<tr>
<td>(aim: reduce incidence of non-treatment visits to hospital)</td>
<td># of ER visits</td>
</tr>
<tr>
<td></td>
<td># of referrals to PSMPC</td>
</tr>
<tr>
<td></td>
<td># of PSMPC follow up visits per patient</td>
</tr>
<tr>
<td><strong>Aggressiveness of cancer treatment</strong></td>
<td># of patients being treated with chemotherapy in last 2 - 4 weeks of life</td>
</tr>
<tr>
<td>(aim: provide alternative to cancer treatment when no longer beneficial)</td>
<td># of patients admitted to home hospice in last 3 days - 2 weeks of life</td>
</tr>
<tr>
<td><strong>Details of death</strong></td>
<td>survival time (from first appointment at BC Cancer)</td>
</tr>
<tr>
<td>(aims: improve end of life care, improve survival time)</td>
<td>location of death</td>
</tr>
</tbody>
</table>

Our primary outcome is the total distress score over time for each patient.

13. Estimated time frame

<table>
<thead>
<tr>
<th>Activity</th>
<th>Length of time</th>
<th>Point in timeline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient recruitment and primary data collection</td>
<td>8-10 months</td>
<td>8-10 months</td>
</tr>
<tr>
<td>Survival follow up</td>
<td>12 months</td>
<td>20-22 months</td>
</tr>
<tr>
<td>Primary data analysis</td>
<td>2 months ?</td>
<td>22-24 months</td>
</tr>
<tr>
<td>study write up</td>
<td>4 months</td>
<td>26-28 months (2 years, 2-4 mon.)</td>
</tr>
</tbody>
</table>

14. Statistical Analysis

Our primary outcome is the total distress score over time for each patient. We will compare the individual distress scores within groups and between groups.

The intervention effect is expressed as the difference in mean changes in symptom scores from baseline to last follow-up between the two treatment groups. Our hypothesized effect size is 2 points. Based on previous studies\(^{10,11,12,13}\), this difference is both realistic and clinically meaningful.

The type-1 error level and power of the study are pre-specified as 5% and 80%, respectively\(^{14}\).

The standard deviation is assumed to be the same in each treatment group (4 points), yielding a “medium” standardized effect size of 2 points/4 points = 0.5\(^{15}\).
The Intra-Cluster Correlation (ICC) coefficient, which represents how strongly patients within the same study group (cluster) are related to each other, is assumed to be \(\rho = 0.005^{16}\).

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