A population-level evaluation of barriers and facilitators to referral in Cytoreduction / Hyperthermic Intraperitoneal Chemotherapy using knowledge translation methodology

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Abstract

Introduction: Referral for CS/HIPEC is variable, and barriers encountered by referring physicians are unknown. Identification of such barriers is useful for the creation of tailored knowledge translation (KT) strategies.

Methods: Interviews of 20 medical oncologists and surgeons in the New York (NY) area were completed to identify barrier topics, using the Pathman framework of uptake of innovations (awareness, agreement, adoption, adherence) at the various levels of the individual, practice group, and organization. Barriers were used to structure a survey for evaluation of prevalence at the population level of medical oncologists and surgeons in NY State.

Results: Barrier topics of awareness included training at a CS/HIPEC center, and availability of multidisciplinary cancer conferences. Agreement barriers centered mainly on quality of published literature, and the paradigm shift of carcinomatosis as a systemic to locoregional disease process. Adoption barriers included knowledge of outcomes of a CS/HIPEC surgeon, and concerns with morbidity/mortality rates. Adherence barriers included the lack of reflection of CS/HIPEC in current CPGs, financial/resource and logistic concerns of referrals, and lack of quality measures for the procedure. For the survey, 119 responded (12% response rate), including 42 medical oncologist and 77 surgeons. The majority were aware of CS/HIPEC (n=113, 95%). Medical oncologists were less likely than surgeons to agree with CS/HIPEC related to published evidence (76% vs 92 %, p = 0.02). Surgeons were more likely to be aware of where to refer patients for the procedure, and were less likely to have concerns regarding morbidity/mortality, compared with medical oncologists (p = 0.05, p = 0.04). Representation of CS/HIPEC in CPGs and quality measures/outcomes data was felt to result in adherence to a regular referral practice.

Discussion: This prospective study of stakeholders for CS/HIPEC is the first to evaluate and characterize barriers to referral for this complex and controversial surgical innovation, with prevalence at the population level.
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Acronyms:
CCR: Complete cytoreduction
CIHR: Canadian Institutes of Health Research
CPG: Clinical practice guidelines
CRS: Colorectal cancer
CS: Cytoreductive surgery
DFS: Disease-free survival
5-FU: 5-fluorouracil
HIPEC: Hyperthermic intraperitoneal chemotherapy
KT: Knowledge Translation
KTA: Knowledge-to-Action
OS: Overall survival
PCI: Peritoneal carcinomatosis index
PFS: Progression-free survival
PM: Peritoneal metastases
Chapter 1: Cytoreduction and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) in New York State

1.1: Uptake of innovations in surgery

Modern surgical practice is regularly challenged with the advent of novel techniques or treatments that may improve patient outcomes, cost-effectiveness of treatment, or efficiency. A commonly cited framework for innovation diffusion in medicine is Rogers’ Diffusion of Innovations model (Rogers, 1995). This model describes how innovators and early adopters slowly take up innovations, and then are more rapidly taken up once approximately 20% of the target group has adopted the innovation.

Rogers states that several factors influence the rate of diffusion of innovations. Regarding the innovation itself, the perception of the innovation, including the perceived benefit of the change, and the compatibility of the change due to the innovation with the values, beliefs, and past history of the treatment or problem are relevant. The complexity of the innovation can directly affect diffusion, as more complex innovations spread less quickly. The trialability – if a proposed innovation can be tested out on a small scale without implementation, and the observability – if potential adopters can see others try the new innovation first, are also important features of an innovation that aids in diffusion. Regarding the clinicians who will adopt or fail to adopt the innovation, particular characteristics will identify these individuals as innovators, early adopters (local opinion leaders, well connected individuals, and are watched closely), early majority, late majority (will adopt a new innovation when it appears to be the “standard of care”), and laggards (traditionalists). Finally, a third group of factors that influence
diffusion of innovation are those “contextual” factors within an organization or group that support or impede the process of diffusion such as resources, support for failure, or security (Berwick, 2003)(Greenhalgh, Robert, MacFarlane, Bate, & Kyriakidou, 2004).

The process of uptake of innovations can be different in surgery practice as compared with medical practice, which is felt to make Rogers Diffusion theory difficult to apply to clinical practice. Medical practice, in particular with the administration of a new medication, often involves a trial to evaluate the efficacy of a novel treatment, such as a Phase I trial, with subsequent larger trials in appropriate patients to evaluate response before the treatment is adopted as standard of care. In surgery, the novel technique or treatment is taken up by an innovator or early adopter, and a small case series is published or presented to a larger group of stakeholders (surgeons/colleagues, administrators, industry representatives). Only occasionally are randomized trials designed and completed prior to initiation and uptake by other individuals (Greenhalgh et al., 2004).

Simunovic and colleagues evaluated the uptake of a surgical innovation using data from the Quality Initiative in Rectal Cancer (QIRC) Trial. In the experimental arm of this trial surgeons were encouraged to engage in any or all of five knowledge translation interventions including workshops, intraoperative demonstrations, opinion leaders, postoperative questionnaires, and audit/feedback. For the intraoperative demonstrations participating surgeons would invite a study team surgeon to their operating room to demonstrate new methods of rectal cancer surgery. Such an invitation was a marked departure from usual surgical practice and was considered a proxy for the uptake of an innovation. At the first opportunity to do so, participating surgeons
requested intraoperative demonstrations – or adoption of this innovation - in 34% of cases. This is a much higher rate of adoption than the slow initial rate predicted by Rogers. As well, unlike Rogers’ theory, characteristics of participating surgeons did not predict for uptake of requests for operative demonstrations, such as surgeon resource levels or positive attitudes. Simunovic and colleagues concluded that surgeons may be primed for the uptake of innovations, though more research is required in this area.

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1.1:i. Pathman 4 A’s of practice change

At the individual physician level, the dissemination and implementation (or uptake) of an intervention is described by the Pathman model. This model summarizes the cognitive and behavioural steps physicians take when undergoing practice change. This was initially described for physicians providing pediatric immunizations (Pathman, Konrad, Freed, Freeman, & Koch, 1996). With regard to the uptake of a treatment or innovation Pathman suggests that clinicians sequentially move through four steps including awareness, agreement, adoption, and adherence. Physicians could “stop” at any of the four steps at any point in time and thus not progress to adherence. Factors preventing full adherence would equate to a “barrier”. Factors encouraging full adherence would equate to a ‘facilitator’. This model provides a framework to understand how clinicians adopt innovations, and to assist with the identification of factors influencing progress through the steps, and the potential development of interventions to address such factors.

The Pathman model implies that movement through the four A’s is a linear process. However, this may not always be the case. In a study of Hepatitis B
immunization patterns, more physicians adopted the immunization (77.7 %) than agreed with the concept of it (70.3 %). This was postulated by the authors to represent the non-linear nature of the model in some clinical situations. For example a clinician may adopt a practice due to pressure from superiors or practice group, despite not agreeing with the concept (Pathman et al., 1996).

1.2: Cytoreduction and Hyperthermic Intraperitoneal Chemotherapy (CS/HIPEC), an example of a complex and controversial surgical innovation

1.2:i. Clinical basis of procedure and indications for use

Peritoneal metastases (PM) or carcinomatosis may be a part of the disease process in cancers of gastrointestinal origin (e.g., appendiceal adenocarcinoma and pseudomyxoma and colorectal cancer), gynecologic origin (e.g., ovarian cancer), or cancers originating from the peritoneum itself (e.g., mesothelioma and primary peritoneal carcinomatosis). The presence of PM signifies advanced cancer and in most cases stage IV disease (Edge et al., 2010). The prognostic significance of PM is bleak and is thought to represent an incurable presentation with poor life expectancy. In adenocarcinomas of gastrointestinal origin, life expectancy with PM was historically in the range of 6 months (Chu, Lang, Thompson, Osteen, & Westbrook, 1989; Spiegle et al., 2013)(Sadeghi et al., 2000).

Cytoreductive surgery (CS) was initially described for ovarian cancer; this involves the “debulking” or removing of all visible tumor by peritoneal stripping and visceral organ resection, until only microscopic (sub-centimeter) sized disease remains. It was initially hypothesized that CS would decrease the overall tumor burden, and would
make it more likely that systemic chemotherapy could destroy or better control any remaining PM, thus improving patient outcomes.

CS in the abdomen is now considered for other cancers including appendiceal neoplasms, pseudomyxoma peritonei, primary peritoneal carcinomatosis and peritoneal mesothelioma, and colorectal cancer (Look, Chang, & Sugarbaker, 2004; Meigs, 1934; Piver et al., 1988; Sugarbaker, 1995). In the early 1990s, individual investigators further hypothesized that adding heated intraperitoneal chemotherapy (HIPEC) to CS would more effectively eradicate both macroscopic and microscopic PM versus CS and systemic chemotherapy, and improve disease free survival (DFS) and OS for patients with PM (Spratt, Adcock, Muskovin, Sherrill, & McKeown, 1980; Sugarbaker, 2006). These early innovators believed that for patients with various types of PM a surgical procedure – CS/HIPEC - could be used to achieve cure or at least prolong survival.

CS/HIPEC is a complex resource-intensive procedure requiring strong support from anesthesia, intensive care, interventional radiology, pharmacy, and other ancillary departments. The uptake of CS/HIPEC initially began with individual surgeons and small practice groups, generally within academic centers that had high volumes of other major surgeries such that the infrastructure required already existed. CS/HIPEC procedures were – and still are - highly dependent on referrals from other physicians since the number of patients appropriate for the procedure was and is relatively small, compared to the number of patients diagnosed with the various cancers that may include PM. As numbers of CS/HIPEC surgeries grow, continued reliance on referrals by other physicians, namely medical oncologists, general and colorectal surgeons has become clearer. Since CS/HIPEC is only done at select centers with appropriate infrastructure,
and appropriate patients must be referred in to these centers for the procedure, it may be postulated that the referral process is the key rate-limiting step in the uptake of this surgical innovation at an individual hospital or region level.

As with many innovations in surgery, initiation of such practices did not begin with high-level clinical trial evidence but rather with reports of success in small series of patients. The support for and practice of CS/HIPEC has grown from a few scattered surgeons and practice groups to the availability of this procedure at numerous large academic and cancer centers in the US, Canada and Europe (Esquivel, Elias, Baratti, Kusamura, & Deraco, 2008). A search of PubMed using the keyword HIPEC for citations of reports over the last 5 years yielded 531 hits, indicating that the popularity and use of the procedure continues to grow. This uptake has occurred despite controversies in appropriate indications and overall efficacy of CS/HIPEC.

1.2:ii. Evidentiary base for use of CS/HIPEC in colorectal cancer (CRC)

The greatest amount of evidence – including a single randomized trial - related to the evaluation of CS/HIPEC is in the setting of colorectal cancer. For colorectal cancer, only patients with isolated PM (e.g., no evidence of lung or liver metastases) are generally deemed candidates for this procedure. A recent pooled analysis of patients with Stage IV CRC from the North Central Cancer Treatment Group Phase III trials N9741 and N9841, found that 17.4 % of patients had evidence of PM, whereas only 2.1 % had PM as the only site of Stage IV disease (Franko et al., 2012). Other studies have demonstrated that approximately 8 % of patients synchronous PM at the time of primary surgery, and 25 % of patients developing recurrent disease have PM as the sole site of recurrence (Sadeghi et al., 2000). Thus only a small percentage of patients with PM
secondary to CRC are candidates for CS/HIPEC. This indicates that only a proportion of patients with PM, whether synchronous or as a feature of recurrence (anywhere between 8 and 25% of patients with CRC), have PM alone and clearly appropriate selection of patients for this procedure is important.

Taking the example of CRC, the approach to many patients with PM has classically been administration of intravenous chemotherapy, similar to the recommendation for initial treatment of other stage IV sites of metastasis. Current best systemic chemotherapy treatment including 5-FU and oxaliplatin/irinotecan-based regimens can lengthen median overall survival (OS) to 20 months, compared with the traditionally cited 6 month range (Colucci et al., 2005; Goldberg, 2006; Sanoff et al., 2008).

As CRC is the third most common primary cancer site, the evaluation of CS/HIPEC in this group has been the most robust (Siegel, Naishadham, & Jemal, 2013). The evidence base for CS/HIPEC in patients with CRC includes several single-center controlled observational studies and observational series of patients without a control group (Zerhouni & McCart, 2012). These studies had relatively low numbers of participating patients, and variability in terms of technique of CS/HIPEC, with some receiving mitomycin-C intraperitoneal chemotherapy versus oxaliplatin intraperitoneal chemotherapy, and some receiving early post-operative intraperitoneal chemotherapy (EPIC) via surgically placed peritoneal catheters in addition to HIPEC. Of the four multi-institutional studies available to date, numbers of patients were still relatively low, and variability in technique persisted among sites (Cavaliere et al., 2011; T. Chua et al., 2011; Glehen et al., 2004; Quenet et al., 2011).
Two systematic reviews of the available literature exist, one including patients with a variety of primary tumor histologies (n=2787) with only a proportion with CRC (n=352), and the second including only patients with CRC (n=1152) (T. Chua, Yan, Saxena, & Morris, 2009; Yan, Black, Savady, & Sugarbaker, 2006). This second study indicated a 5-year OS of 25-45%, which is significantly higher than survival of patients with metastatic disease treated with systemic chemotherapy alone.

There exists only one randomized controlled trial that evaluated survival in patients with isolated CRC PM. In this Dutch trial, between 1998 and 2001, 105 patients were randomized to systemic chemotherapy (5-FU/leucovorin based) versus CS/HIPEC followed by systemic chemotherapy. A significant benefit in median OS was seen in the CS/HIPEC group; 21.6 months compared with 12.6 months (Verwaal et al., 2003). A recent update of this study, at a median follow up of 8 years with all patients having a minimum of 6 years of follow up, indicated a persistent survival benefit in patients undergoing CS/HIPEC (Verwaal, Bruin, Boot, van Slooten, & van Tinteren, 2008).

1.2:iii. Criticisms of Current Available Evidence and Problems with Generalizability and Application to patients

Although weaknesses of the available literature may be obvious related to study design (retrospective or non-randomized cohort series, only one randomized trial) there are several other issues germane to PM CS/HIPEC studies that make it difficult to interpret and apply relevant evidence.

Selection of patients for inclusion into clinical trials based on performance status

Performance status is a scale used both clinically and in research that assesses a patient’s disease progress and how the disease may affect activities of daily living, which
in turn may assist in determining prognosis and appropriate treatment options. The Eastern Cooperative Oncology Group (ECOG) Performance Status is a standardized way of reporting such functioning (Oken et al., 1982). An ECOG Performance Status of 0 or 1 is considered good and greater than 2 considered limited. In the single CS/HIPEC RCT, 85% if patients had an ECOG Performance Status of 0 or 1, thus highlighting that many of these patients were in good physical shape to be able to tolerate treatment. Critics in the oncology community argue that such patients would be able to tolerate CS/HIPEC well, but conversely, would be able to tolerate any treatment, including standard systemic chemotherapy, well (Dancey et al., 1997). They also argue that such good performance patients being selected for this trial make results difficult to apply to the general population of patients with PM from CRC.

**Disease burden defined by Peritoneal Carcinomatosis Index (PCI)**

The extent and location of PM affects prognosis, similar to number and location of liver metastases in CRC (Fong, Fortner, Sun, Brennan, & Blumgart, 1999), and can also affect the ability to completely cytoreduce a patient for optimal outcome as compared with leaving gross visible disease. The Peritoneal Carcinomatosis Index (PCI) is a scale that considers the size of tumor implants and anatomic location within 13 set regions of the peritoneal cavity, to determine a PCI score between 0 and 39 (Jacquet & Sugarbaker, 1996). The abdominal cavity is divided into 9 regions, created by a 3x3 grid, and the remainder of the regions is composed of 4 regions of the small bowel (divided proximally to distally). Within each region, the size of the largest tumor implant is estimated, and given a score of 0-3 (0 = no tumor, 1 = less than 5 mm, 2 = greater than 5 mm but less than 5 cm, 3 = greater than 5 cm). A number of different cut-off values have been
considered when defining “low-volume” carcinomatosis based on the PCI score, including PCI \( \leq 10 \) (Pestieau & Sugarbaker, 2000), \( \leq 13 \) (Carmignani, Ortega-Perez, & Sugarbaker, 2004), or \( \leq 20 \) (Gomes da Silva & Sugarbaker, 2006). A criticism of the currently available literature includes that patients with lower PCI scores are generally a large proportion of those in trials, making results less applicable to an average group of patients.

In the largest series of CRC PM treated with CS/HIPEC, a PCI score of \( \leq 20 \) was found to be highly predictive of improved median survival in univariate analysis, and a score of \( < 20 \) is now widely accepted as the threshold above which CS / HIPEC should not be performed (Gomes da Silva & Sugarbaker, 2006). Although originally described as a result calculated from intra-operative exploration, the PCI score can be estimated from pre-operative CT scans. However, in a study comparing pre-operative determination of the PCI score, with subsequent operative exploration for the purposes of CS / HIPEC, pre-operative CT scans were shown to significantly underestimate the PCI score. This adds complexity to determination of appropriateness of a patient for CS/HIPEC, since this is a factor that is not well characterized prior to surgery. Clinicians have difficulty in determining PCI as part of a treatment algorithm, and thus have difficulty in applying available published evidence.

*Variability in systemic and intraperitoneal chemotherapy regimens within and between trials*

Among studies in the area of CS/HIPEC for PM in colorectal cancer there is variation in the timing of systemic chemotherapy, with some patients receiving chemotherapy after CS/HIPEC and some before. Patients with PM may develop other sites of metastases
such as liver or lung metastases, which then precludes the use of CS/HIPEC for the PM. Patients receiving systemic chemotherapy prior to CS/HIPEC are thus given a chance to “declare” tumor biology and progression. Patients in studies of CS/HIPEC that use such a regimen – in contrast to studies where patients would receive systemic chemotherapy following CS/HIPEC – would have a better tumor biology and better outcomes.

The single RCT in the area of colorectal cancer with CS/HIPEC for PM is criticized for utilizing only a 5-FU/leucovorin systemic chemotherapy regimen. This is considered less effective compared with more modern regimens and is not a fair control group for comparison (Verwaal et al., 2003). In the control group of the trial (systemic chemotherapy alone) median OS was 12 months, which is significantly less than median survival of 20 months that current studies cite for OS among patients presenting with Stage IV disease and treated with current systemic chemotherapy regimens.

The type of chemotherapy used for the HIPEC portion of CS/HIPEC also varies among studies. Although Mitomycin-C is the most frequently used intraperitoneal chemotherapy agents, other agents such as Oxaliplatin or Cisplatin have also been used (Zerhouni & McCart, 2012). In a recent publication involving the same patient cohort in the RCT, OS and RFS were compared in patients receiving Mitomycin C versus Oxaliplatin. There was no difference noted in either of these measures, however the follow up for patients treated with Oxaliplatin was significantly shorter (2.8 years vs. 5.1 years) (Hompes et al., 2013). Although these initial results may indicate no difference in which agent is used, the use of different agents in various clinical trials make comparison and interpretation challenging.

Post-operative morbidity and mortality associated with CS/HIPEC
CS/HIPEC involves an exploratory surgery with peritoneal stripping and possible visceral resections (bowel resections, splenectomy) followed by the addition of heated intraperitoneal chemotherapy. Major complications often occur secondary to the major surgical cytoreduction, and the exposure of abdominal cavity contents, including bowel anastomoses, to chemotherapy. The Dutch CS/HIPEC trial cited a mortality rate of 8%, and a rate of anastomotic leak or gastrointestinal fistula of 15%; both of these numbers are very high compared with accepted values for elective major abdominal/colorectal surgeries (Verwaal et al., 2003). Patients that undergo CS/HIPEC and have major complications that preclude the use of future systemic chemotherapy.

**Issues with prospective trial design**

Although evidence to support CS/HIPEC in CRC and other cancers is available, further “higher level” studies in North America have been attempted to obtain meaningful results for clinicians. Recently, a study organized through ACOSOG, with Stojadinovic as the principal investigator, attempted to compare systemic chemotherapy alone versus CS/HIPEC in patients with limited PM from colon cancer in a randomized fashion. Unfortunately, this ACOSOG-Z6091 study had poor accrual and was closed, despite voiced support from surgeons within the American College Surgical Oncology group (National Cancer Institute, 2011).

Regarding the contributory effects of CS versus HIPEC on outcomes, a randomized multicenter French trial, Prodigé 7, is currently underway, having randomized CRC PM patients to one of two arms – CS alone or CS/HIPEC. This study has completed accrual of patients and final analyses are awaited (Elias, D. 2014). Evidence from this trial will likely have a major influence on how CS/HIPEC is utilized.
Overall given these two randomized clinical trial efforts, it is clear that questions still exist regarding proving effectiveness and utility of CS/HIPEC in CRC patients.

**CS/HIPEC in Clinical Practice Guidelines**

Although many societies endorse systemic therapy for patients with CRC PM, only the National Comprehensive Cancer Network (NCCN) makes mention of CS/HIPEC as a treatment option. In the most recent version of the Colon Cancer Guidelines (03/2014), the NCCN continues to consider CS/HIPEC “investigational” and does not endorse the use of this technique outside of a clinical trial. This section of the guidelines does end by recommending future randomized clinical trials to further evaluate CS/HIPEC (National Comprehensive Cancer Network, NCCN., 3.2014).

**Conclusions**

Given the above mentioned issues with quality and generalizability of available published studies, CS/HIPEC continues to be applied as a treatment option for patients, with variable uptake. A barrier and facilitator analysis of CS/HIPEC uptake will likely provide important observations relevant to the uptake of other resource-intense and controversial therapies in oncology.

**1.3: A proposed study of CS/HIPEC referrals in New York State**

**1.3: i. RPCI and New York State as optimal site for KT study in CS/HIPEC**

Roswell Park Cancer Institute (RPCI) is a stand-alone cancer center that provides multidisciplinary cancer care. It is a publicly-funded institute, and those employed at RPCI are considered state employees. Patients can receive care at RPCI through referrals from primary care physicians, surgeons, or other specialists, or can self-refer for a treatment opinion. Many physicians refer to RPCI regularly, and pre-existing referral
networks and relationships exist. The majority of patients seeking and receiving care at RPCI are from the Western New York area, with smaller numbers from Upstate New York, Ohio, Pennsylvania, and Canada. For Fiscal Year 2013, RPCI had 31,000 patients under active care (Roswell Park Cancer Institute, 2014). RPCI is the only National Cancer Institute (NCI)-designated cancer center in Western New York.

Regarding CS/HIPEC, RPCI has had a well-established program since 2003. Other CS/HIPEC programs within the state include the Mount Sinai Hospital and Memorial Sloan Kettering in New York City. Out of state, but in the nearby vicinity, the University of Pittsburgh Medical Center also offers CS/HIPEC. However, RPCI covers a large area of potential patients for referral for this procedure. Due to insurance coverage, patients in the geographical area of Western New York are generally recommended to undergo care at RPCI. Seeking treatment at other out-of-area centers results in the need for patients to pay out of pocket, thus deterring such activity.

Given the geographical location of RPCI, the pre-existing referral networks, and insurance coverage limitations, a study of referrals for CS/HIPEC in Western New York should provide important insights on the uptake of a complex surgical innovation at the population-level.

1.3: ii. Identification of stakeholders

There are several stakeholders in the process of referral for CS/HIPEC. The majority of patients with PM, regardless of primary site, have had consultation with and/or treatment by a surgeon and medical oncologist. The patient’s primary care physician is can also be a stakeholder and help coordinate care providers. CS/HIPEC
requires prior authorization and approval from insurance companies in the US due to the fact that the procedure can be costly; thus payors are also stakeholders.

With the availability of electronic information via the internet patients are increasingly aware of treatment options and ramifications of treatments. In fact, there are several websites devoted to providing resources to patients with peritoneal surface malignancies and their families, including “PMP Pals” and “HIPEC Treatment” (HIPEC, 2014; PMP Pals., 2014).

1.3: iii. NY state incidence of CRC and peritoneal disease vs referrals for CS/HIPEC

By evaluating the number of incident cases of CRC in Western New York from 2006-2010 compared with numbers of patients referred for CS/HIPEC to RPCI in a similar time frame (2008-2013) it is evident that not all patients with PM from CRC are referred to RPCI for consideration of CS/HIPEC. Counties with larger populations, such as Erie and Monroe counties, have high numbers of CRC in the time frame, 362 and 264 cases respectively. Given that an estimated 10 % or patients may be candidates for CS/HIPEC (within the range of 8-25 % cited earlier), this would equate to 36 and 26 patients respectively that may referred. From RPCI data, approximately one third of patients undergoing CS/HIPEC do so for PM secondary to CRC (Haslinger et al., 2013). In a similar time frame, Erie County provided an estimated 13 referrals and Monroe County 3 referrals for CS/HIPEC (Figure 1) (New York State Department of Health, 2013). This gap or discrepancy indicates referrals for CS/HIPEC are not consistent, which may be related to a number of factors. Barriers and facilitators to referral may exist to explain this gap. The central concepts of knowledge translation (KT) science,
discussed in the next chapter, will be used to inform this proposed study assessing barriers and facilitators to referral for CS/HIPEC for CRC in Western New York State.
Chapter 2: Introduction to Knowledge Translation

2.1: Quality Health Care and Knowledge Translation

Quality health care encompasses a variety of dimensions and can be measured in different manners. The Donabedian Quality of Care model divides quality of care into three dimensions: structure – the characteristics of the setting where healthcare is delivered; process – direct interactions or steps experienced by patients moving through the system; and, outcomes – the impact of the combined effects of structure and process on healthcare delivery (Donabedian, 1966; Donabedian, 1988). Administration of high quality healthcare is a continuous challenge, given the rate at which new research studies and trials are published, and the often high-stakes outcomes. The transfer of knowledge obtained from research studies into medical practice is generally thought of as a very slow process that often times lacks direction or structure. Although there are several possible reasons for this delay, the ultimate result is less than optimal patient care related to the inefficient use of treatments or resources. This has been well described by Graham and colleagues as the knowledge-to-action (KTA) gap (Graham et al., 2006).

Knowledge translation (KT) research is also known as implementation science, dissemination and diffusion research, and research utilization (Straus, Glasziou, Richardson, & Haynes, 2010). The Canadian Institutes of Health Research (CIHR) defines KT as “a dynamic and iterative process that includes synthesis, dissemination, exchange and ethically-sound application of knowledge to improve the health of Canadians, provide more effective health services and products and strengthen the healthcare system” (Canadian Institutes of Health Research, CIHR, 2013). Gaps in the
structure, process, or outcome of the Donabedian health system model can be evaluated and addressed using KT research approaches.

KT is an important research area since failure to apply evidence to clinical decision-making can occur in a variety of settings, and can potentially affect outcomes. The overall purpose of KT is to improve the healthcare of individual patients and the healthcare system (Graham & Tetroe, 2007). How practice changes is a complex process, and research evidence is only one factor influencing clinical decision-making. Important components of this practice-change process, also termed determinants of KT, include knowledge management (related to access to evidence, appraisal skills, application), financial limitations, organization and local standards of the health care or practice team, individual clinician attitudes, values or skills, and patient values and desires (Straus et al., 2010). Additional complexity results from the fact that determinants of KT may be specific to a particular clinical problem or clinical setting termed the context, and may not be generalizable to another setting (Cabana et al., 1999). Simply ensuring the transfer of knowledge or guidelines to a clinician does not guarantee optimal decision making, as this process is clearly more complex. Given the complexity of KT, it is well accepted that to better understand various factors at work, a framework is necessary.

2.2: The Knowledge-to-Action cycle

The complexity of clinical decision making was recognized, as evidenced by several different frameworks that were developed to assist in the overall process. Graham and colleagues evaluated and summarized 31 different frameworks or processes of KT, and noted these to have common elements, leading to one of the most cited and utilized frameworks in KT science, the Knowledge-to-Action (KTA) cycle. The KTA cycle is
divided into two general concepts: knowledge creation and action. Although these are considered two separate concepts, phases or steps between the two are dynamic and may influence one another (Graham et al., 2006; Graham & Tetroe, 2007).

Central to the KTA cycle, the funnel of knowledge creation is a process by which information is filtered through three stages, including inquiry, synthesis, and tool or product creation. As information is “funneled” through this process, it results in more useable information, and often creates practice guidelines or algorithms for target users, that may include clinicians, administrators, or policy-makers. In surgery specifically, case studies or series are funneled through this step, ultimately producing algorithms, standards documents, or clinical practice guidelines. Although guidelines for the treatment of CRC cancer exist, there is little representation of CS/HIPEC as a treatment option within them (National Comprehensive Cancer Network, NCCN., 3.2014).

Evaluating the KTA cycle in more detail, knowledge inquiry is an amalgamation of the large number of primary research studies of various quality and methodological rigor. Knowledge synthesis involves taking the large volume of studies and using specific methods of appraisal and synthesis to provide more tangible or specific answers to questions, generally in systematic review or meta-analysis type of study. Knowledge tool production consist of clinical practice guidelines or decision aids, that are generally aimed at being end-user friendly with the appropriate amount of detail. These three steps and the overall knowledge creation funnel can be tailored to specific questions that is meant to be addressed by the process, and also tailored to the particular end-users.
Once this distillation has occurred, the “action” portion of the cycle relates to the various activities that are required for application of knowledge. There are seven action phases: initially a problem is identified that requires attention, and the relevant knowledge that needs to be implemented to remedy this problem is identified (including primary research findings, clinical practice guidelines) and are adapted to the particular context. Subsequently, identification of barriers and facilitators to knowledge application follows, after which selection, tailoring, and implementing of an intervention to promote the use of the identified knowledge occurs, with the monitoring and evaluation of the intervention and its ability to be sustained ensuing (Graham et al., 2006). Each of the phases of action can be influence by the phase that comes before it, and there may be feedback between action phases.

2.3: Barriers and Facilitators to Knowledge Use

The focus of this thesis is the evaluation of barriers and facilitators to KT. As mentioned above, with regard to the closing of identified quality gaps through the KTA cycle, researchers suggest that there are usually barriers - factors that impede - and facilitators - factors that enhance or assist with - optimal clinical management. It is postulated that the identification of such barriers and facilitators can be used to design and evaluate intervention strategies. Evaluation of barriers and facilitators can occur before a strategy is selected, such that a chosen intervention can be designed or “tailored” to target a group of clinicians in a particular setting, or during or after the implementation process to assist in comprehending why a particular intervention was successful or not (Wensing, Laurant, Hulscher, & Grol, 1999). We suggest that a barrier and facilitator evaluation is perhaps the most important step in the KTA cycle. Surprisingly there has
been limited research on optimal methods to perform barrier and facilitator evaluations in
different clinical scenarios. In the next chapter we will review related research on this
topic, and introduce a “tailoring grid” as a potential effective method of barrier and
facilitator evaluation.
Chapter 3: Assessing Barriers and Facilitators (B/F) to Knowledge Use

As the starting point for the KTA cycle, one of the most cited models for the process of KT, an analysis of barriers and facilitators to knowledge use is recommended prior to the planning of KT interventions (Graham et al., 2006). Yet there is little empirical data on how such analyses should ideally occur. We present below examples available in the literature.

As part of the KTA cycle, a barrier and facilitator analysis should ultimately be used to tailor a KT intervention for the particular population or group, specific to the problem or question that needs to be addressed. The idea of tailoring involves the prospective identification of barriers or facilitators to practice change, with the subsequent development of a KT intervention to overcome identified barriers or leverage identified facilitators. This should inform the subsequent selection and design of KT interventions.

Bosch and colleagues performed a qualitative analysis of 22 different studies reporting a barrier analysis in educational or organizational improvement KT intervention. Various methods were used in the individual studies to identify barriers, including face-to-face interviews, workshops with small and large group discussions, and focus groups with key stakeholders, daily practice assessments or shadowing of professionals, or surveys. This study found that although the barriers were assessed prior to development of the intervention, the choice of the specific intervention was not always directly reflective of the barrier in question. For example there was often a mismatch between the level of the identified barrier (e.g., individual, practice group, or organization
level) and the type of intervention that was selected for use (Bosch, van der Weijden, Wensing, & Grol, 2007).

A recent Effective Practice and Organization of Care Group (EPOC) review included a meta-regression of studies of tailored interventions to identified barriers versus control groups that either received no intervention, or a non-tailored intervention. The results of the 12-study quantitative analysis indicated that those studies that involved an intervention specifically tailored to a prospectively identified barrier were more likely to improve or change practice. However, it was again also clear that the optimal method used to identify barriers for subsequent tailoring could not be determined, and this area was felt to deserve further research effort (Baker et al., 2013).

3.1: i. Prior work in B/F analysis; strengths and weaknesses

There are some cited examples of methods of evaluation of barriers and facilitators to knowledge use in health care. The “Clinical Practice Guidelines Framework for Improvement” by Cabana and colleagues, was the result of an extensive review of barriers physicians face related to a specific context, namely adherence to clinical practice guidelines (Cabana et al., 1999). The authors classified the identified barriers into those related to knowledge, attitudes, or physician behavior. Knowledge-related barriers included lack of familiarity and awareness, involving volume of information present, time needed to remain informed, and accessibility of guidelines. Attitude-related barriers include lack of agreement with specific guidelines due to interpretation of evidence, application to the specific patient, cost-benefit assessment; a lack of agreement with guidelines in general, such as issues with autonomy or “cook-book” practice; a lack of motivation or inertia of previous practice, and lack of belief that expected outcome
will occur. There are also several behavior barriers, such as external barriers (patient factors), guideline barriers (characteristics, presence of multiple different guidelines), and environmental barriers (time, resources, reimbursement). More recently, Legare and colleagues used the Cabana classification framework, and extended this to both barriers and facilitators of implementing shared decision making in clinical practice (Legare et al., 2006).

There are a number of examples in the literature of tools used to identify barriers and facilitators to practice change. The “Attitudes Regarding Practice Guideline” tool by Larson uses a 6-point Likert scale, divided into two sections – attitude statements about clinical practice guidelines in general, and then a section specific to hand-hygiene guidelines (Larson, 2004). The author felt that this tool was useful but required further testing as a tool to measure barriers to adherence to general clinical practice guidelines. A further instrument that was designed to assess barriers and facilitators to knowledge specific to nursing practice and utilization of research, the BARRIERS Scale was developed related to four characteristics: nurse, setting, research, and presentation; all related to the theory of diffusion of innovation (Funk, Champagne, Wiese, & Tornquist, 1991).

Although the various instruments and comprehensive review methods discussed above were designed to identify and assess barriers and facilitators to knowledge use, it is clear that each was developed related to a specific clinical setting, problem or context. Legare argues that these tools must be adapted and tested in a variety of clinical settings to test applicability (Legare, 2009).
3.1:ii. Grol framework

Grol and colleagues used the example of hand-hygiene in the prevention of infections in hospitals to evaluate barriers and facilitators to uptake of guidelines in clinical practice. This study involved a survey of 120 physicians and nurses at hospitals and nursing homes, in an attempt to identify barriers and facilitators to compliance with hand-hygiene guidelines. The authors conclude that “problems” or barriers could be identified at various levels, including the individual professional (involving attitudes, behaviors, and routines), the team or unit (involving social influence, leadership) and the hospital or health center (involving organizational structure, and resources) (Grol, 1997). From this work, Grol and Grimshaw concluded that for a thorough analysis of obstacles or barriers to practice change, it is important to consider the impact of effects from these various levels, and that such information can be used to tailor appropriate KT strategies (Grol & Grimshaw, 2003). They also concluded that many identified barriers work at various levels, so complete characterization and evaluation would mean a comprehensive review of the effects at various levels.

3.2: Qualitative Research Methodologies in B/F Analysis

Qualitative research involves collection of information through a variety of measures, including in-depth study, focus groups, interviews of personal experiences, and observational evaluation with data collection occurring face-to-face with subjects (Denkin & Lincoln, 1994). Results include a very detailed description of a situation or phenomenon rather than numerical or statistical calculations.
The positive aspects of using qualitative research techniques include the ability to convey complexity or richness of information. It also includes well-studied and evaluated techniques and methods. The negative aspect of qualitative research stems from the complexity and need to fully understand various topics; as such projects are time-consuming and labour intensive (Patton, 2002; Taylor, 2005).

Qualitative research methods may be appropriate for a barrier and facilitator analysis given the need to directly interact with stakeholders in some manner. Prior studies evaluating barriers and facilitators in various clinical settings have used methods such as interviews and focus groups, often supplemented with surveys (Cabana et al., 1999).

3.3: Theoretical Domains Framework

The Theoretical Domains Framework (TDF) is a more recent development for describing behavioural change research, and has been applied across a variety of different clinical situations. Behaviour change of health care professionals is felt to be a critical step in using evidence based studies in practice. In guideline development and implementation studies, only a fraction of such studies used behavioural theories to inform final constructs, making it difficult to understand the processes important to successful behavior change. To directly address this, the TDF was developed by health service researchers and psychologists, with an aim of simplifying behaviour change theories and making them more useable. The framework, consisting of 14 domains, has been used by several research teams in various clinical areas to explain implementation problems. Most of this research has utilized labour-intensive methods such as focus groups and interviews {{187 Cane, J. 2012}}
The TDF was validated and refined in a study resulting in the various framework domains, namely knowledge, skills, professional role/identity, capability, optimism, consequences, reinforcement, intentions, goals, memory, resources, social influences, emotion, and behavioural regulation {{187 Cane, J. 2012}}.

The TDF was used clinically to investigate possible determinants of behaviour change associated with the ordering of routine testing for patients undergoing low-risk surgical procedures. An interview guide based on the TDF was developed regarding pre-operative testing practices. Seven of the 12 domains in the TDF were identified as likely contributing to change in physician behaviour regarding pre-operative testing. Overall these factors in turn identified potential beliefs at the individual, team, and organization levels for which KT interventions could be designed to reduce unnecessary routine ordering of tests {{188 Patey, A.M. 2012}}.

Overall the TDF appears to provide a good framework from which to design structured questionnaires for evaluating stakeholders. However, the completeness of identification of factors using this framework has yet to be determined.

3.4: Survey methodology in B/F analysis

Survey methodology has been used frequently in barrier and facilitator analyses reported in the literature. A potential advantage of a survey is that it allows for a sampling of a larger group of individuals, for a more broad evaluation of barriers and facilitators at the population level, as compared with focus groups which usually evaluate the individual clinician. For example, the study by Cabana et al. evaluated why clinicians do not follow CPGs, by a thorough analysis of 76 studies describing 120 surveys designed to determine barriers. While used very frequently to evaluate a variety of
different barriers, most surveys (58%) evaluated only one proposed barrier. The positive aspects of using survey methodology to answer such questions included the ability to sample heterogeneous clinician populations (based on location and type of practice), and different subjects. The final results of this study included that barriers to uptake of CPGs could be identified in a variety of domains, including lack of awareness, familiarity, agreement, self-efficacy, motivation, outcome expectancy, and other external barriers (Cabana, 1999).

3.5: Previous evaluation of B/F through survey methodology to uptake of CS/HIPEC

A recent survey-based study by Spiegle and colleagues aimed to evaluate physician awareness as a possible barrier to referral for CS/HIPEC. This study was initiated in the province of Ontario, where a CS/HIPEC program had not yet been formally organized. Patients in need of this procedure would be referred out of province (to Calgary, Halifax, Montreal) or out of country (to Buffalo). General surgeons and medical oncologists were identified through Ontario’s central medical licensing body, and these clinicians were mailed a 12-item questionnaire including demographic information and awareness of CS/HIPEC, for both pseudomyxoma peritonei (DPAM) and CRC. Survey questions were developed by researchers (mainly surgeons), and no particular framework or input from other clinicians were used. A response rate of 44% resulted from this survey. While many respondents were aware of CS/HIPEC for pseudomyxoma peritonei (86%), only 46% were aware of this treatment for CRC. This awareness did not differ related to specialty (e.g., medical oncology or surgery). The main reasons for non-referral of such patients were patient comorbidities/characteristics, and secondly lack of awareness of programs that offer such treatments. Of the variables
selected for a multivariate regression analysis, practice in a university/academic center made physicians 2.7 times (95 % CI 1.09-6.73) more likely to be aware of CS/HIPEC than community/private practice physicians, and surgeons were 3.65 times (95 % CI 1.27-10.48) more likely to be aware of CS/HIPEC than medical oncologists (Spiegle et al., 2013).

The conclusions of this study include overall physician awareness for CS/HIPEC for CRC was low in Ontario at the time of the survey administration. However, the study was unable to identify specific provider characteristics that might assist in identifying groups of clinicians that should be targeted in interventions aimed to improve referrals, and was the only study aimed at identifying barriers and facilitators available in the published literature. Overall this study was limited due to the methodology undertaken to determine barrier topics to include in the survey, namely consensus of the authors. Also, no framework was used to develop questions posed in the survey (Spiegle et al., 2013).

3.4: A “Tailoring Grid” for B/F Analysis

The use of a “tailoring grid” methodology for one-on-one practitioner interviews was a concept introduced by Simunovic and colleagues for the evaluation of barriers and facilitators to optimal total mesorectal excision (TME) technique for practicing surgeons. This was done within a larger surgical quality improvement project in the Linked Health Integration Network 4 area of Ontario. Within this study, the tailoring grid allowed researchers to determine key barriers to optimal TME technique, including lack of radiology and pathology expertise related to TME techniques and principles (Simunovic et al., 2013).
The tailoring grid methodology also identified the location of key stakeholders on the Pathman 4 A’s continuum (i.e., awareness, agreement, adoption, adherence). For further characterization and description of barriers and facilitators in this construct, the Grol levels of individual clinician, practice group, and organization were used.

We postulate that a tailoring grid can efficiently provide an in-depth assessment of barriers and facilitators to practice change. In addition, given that many interventions have been noted to be unsuccessful because they are not matched with or tailored to the “level” at which they occur, using a framework such as the tailoring grid that allows for organization of each topic or issue with a level including the individual, practice/social group, or organization is exceptionally helpful for future successful intervention design. However, as mentioned, this was trialed in pilot form, and further evaluation of the tailoring grid is necessary.

Regarding comparing the tailoring grid to the TDF, the latter identifies topics mainly related to physician behaviours and how such affect implementation of an intervention. The Tailoring Grid allows for a greater breadth of information to be gleaned from interviews with stakeholders, related to behaviours but also other factors at work.

The tailoring grid interviews act to assess in detail the thoughts and actions of a select group of practitioners, similar to qualitative research methodologies. However, there can be bias associated with this small group, even though random selection of those for participation may occur, individual participants may have specific views on the topic, and may not be a good representation of the views at the population level. To provide a more “macroscopic” population-level view, topics or themes identified in a series of tailoring grid interviews to inform a larger survey of clinicians at the population level can
be informative and could provide a more realistic and accurate view of barriers and facilitators for designing KT interventions.

3.5: Conclusions

The KTA cycle recommends the evaluation of barriers and facilitators to innovation uptake or efforts to change practice prior to embarking on a relevant KT strategy. However, the optimal manner in which a barrier and facilitator analysis should be completed is unknown, and prior scales and methods have not been used in the specific context of a novel surgical innovation. Complex innovations with variable uptake in turn make barrier and facilitator analysis more complex and can provide insight into why some surgical techniques are taken up successfully, and others are not. In addition, new methods for barrier and facilitator analysis in KT strategies are likely needed, and the tailoring grid methodology piloted in the QICC-L4 study has shown promise for this purpose.

CS/HIPEC is a good example of a complex novel innovation with variable uptake related to referral of patients for consideration of the procedure. To understand how a novel surgical innovation becomes popular, a study of barriers and facilitators to referral in the context of advanced cancer patient treatment is useful.

We hypothesize that a “tailoring grid” methodology can be used to identify barriers or facilitators related to referral for CS/HIPEC for CRC. Furthermore, a survey methodology can then be used to quantitate the prevalence of the identified barriers and facilitators at the population level. This study is not designed to answer if more referrals for CS/HIPEC for CRC should or should not occur. However, the variable uptake of
CS/HIPEC for CRC in most jurisdictions offers an excellent opportunity to gain insights on the methodology of barrier and facilitator analysis in surgical KT efforts.
Chapter 4: Study Part I - Using a tailoring grid to identify barriers and facilitators to referral for CS/HIPEC in Western New York State

To determine factors of importance for the evaluation of barriers and facilitators to referral for CS/HIPEC at the population level of clinicians, interviews with subjects that are part of this referral process is critical. The Pathman 4 A’s of awareness, agreement, adoption, and adherence discussed in detail in Chapter 1, steps physicians may proceed through when presented with a novel technique or innovation, are incorporated into a tailoring grid as a tool to organize interviews with these key stakeholders. To further assist in characterizing such barriers and facilitators, Grol’s levels of the individual clinician, practice group, or organization to determine at what level such factors mentioned work. This section presents the methodology associated with the development of the tool, administration of the tailoring grid to participants through interviews, and results.

4.1: Study environment and target group participants

In the New York State area, Western New York consists of 12 counties, with a population of approximately 2.5 million. There are 38 hospitals identified within Western New York State (New York State Department of Health, 2013). Within New York State, there are 6 NCI-designated cancer centers, and Roswell Park Cancer Institute (RPCI) is the only center in the Western New York area, with the remainder of the 5 in the New York City area (National Cancer Institute, 2014). The only other major academic center in the Western New York area is the University of Rochester/Strong Memorial Hospital, offering some major surgical oncology procedures. Out of state, the two other major
academic/cancer centers are located at the Cleveland Clinic and University of Pittsburgh (HIPEC, 2014).

As discussed in previous chapters, given insurance coverage, the majority of referrals for cancer treatment for patients in Western New York are to RPCI. In addition, due to transportation difficulties and expense to families needing to stay in the area as patients receive treatment, many patients in New York State outside of the Western New York area choose to be referred to RPCI, even if New York City centers are closer geographically. This results in a large catchment area with opportunities to evaluate referral practices from a variety of different clinicians.

In the New York State area, clinicians in medical oncology, general surgery, surgical oncology or colorectal surgery, all considered “stakeholders” in the referral process for CS/HIPEC, were identified based on prior referral practices, or randomly via the internet to ensure appropriate representation of the following key factors: academic vs. private practice, surgery vs. medical oncology, junior (< 5 years in practice) vs. senior. Participant characteristics for this portion of the study can be found in Table 1.

4.2: Development of the tailoring grid study instrument

Using the Pathman and Grol framework, a tailoring grid for the current study was created to evaluate barriers and facilitators to referral for CS/HIPEC. Specific questions for referral practices for each of the Pathman 4 A’s were selected, and listed in rows on the grid. Possible topics for inclusion into questions were identified based on previously documented controversial areas from publications, conferences, or word of mouth from referring or non-referring clinicians. Tailoring grid questions were structured as open-ended to allow for participant comments and expansion on identified topics. For the
columns of the grid, the Grol levels of individual clinician, practice group, and organization were used, to determine where each idea fell within a practice. The finalized version of the tailoring grid used in interviews in this study can be found in Appendix A.

In an initial attempt to evaluate where a clinician was with respect to the 4 A’s, direct questions were posed such as “Are you aware that patients with PM from CRC can be referred for consideration of CS/HIPEC?”, similarly for agreement, adoption and adherence. At each of the 4 A’s, participants were walked through a series of factors that could be perceived as barriers or facilitators to the referral process, and there were encouraged to provide other factors they could identify, for each position.

4.3: Sample size

To ensure identification of all factors that may influence referrals for CS/HIPEC, a sample of 20 subjects for tailoring grid interviews was selected. This was felt to represent a number with good contribution from both stakeholder groups (surgeons and medical oncologists) and to obtain some redundancy in answers. A planned half of subjects were from medical oncology, and half were surgeons including surgical oncology, general surgery, and colorectal surgery. Also, half of subjects were selected as internal (RPCI) physicians, and the remainder was external, from other institutions or from private practice. An attempt at approximately half academic and half private/community practice was also planned.

Potential subjects for the tailoring grid interviews were selected based on specialty (surgery and medical oncology), number of years in practice, and speculated position within the 4 A’s by the PI. Two trainees were selected to be a part of the
interviews as to provide the perspective of individuals who have not yet started formal practice, to clarify factors at work during fellowship or residency training.

4.4: Ethics approval, interview details and structure

Prior to administration of the final tailoring grid to participants, ethics approval was obtained from both Roswell Park Cancer Institute and McMaster University. Letters of approval from both organizations can be found in Appendix B. Participants were selected as per criteria noted above, and approached by email or telephone regarding their willingness to participate. The purpose and structure of the proposed interview was reviewed, and the use of final results for the purposes of this thesis and future publication was noted. The participant information sheet (Appendix C) was emailed, faxed, or provided in-person to the participant prior to the interview for their review. Verbal agreement to participate was obtained from each participant.

Those that agreed to participate remained anonymous and were subsequently identified by a subject number. Interviews occurred either in person or by telephone, at the convenience of the participant. Basic demographic information including fellowship training and location, current and previous positions, description of current position (academic or private practice, proportion of patients with gastrointestinal malignancies seen) were collected at the beginning of the interview.

A blank tailoring grid form was used for each participant. All interviews were completed by the principal investigator (VF). Notes were taken by the interviewer including verbatim quotes and examples provided by participants. Each question was posed in the same fashion and wording to each participant. The final question included an open ended type that evaluated for any “perceived barriers or facilitators to referral for
CS/HIPEC” to catch any unidentified topics. Total interview time was recorded in minutes.

4.5: Analysis

Once all interviews were complete, each subject’s responses were evaluated and classified as being a barrier or facilitator to the referral process for CS/HIPEC. Comparison for each of the 4 A’s across responses for each subject occurred to detect common factors. Those with common ideas were grouped into sub-topics within the tailoring grid framework.

To be considered a relevant response, at least 2 participants, or 10% of the group, needed to endorse the response, to avoid a lengthy list of factors not necessarily relevant to the overall opinion of the group.

4.6: Results

Participants

A total of 39 potential participants were approached either by email or by telephone. For those that did not respond to the first request, a second and third request was sent. No response at that point was considered to represent disinterest in participation. Overall, 20 clinicians agreed to participate. Of the 19 potential participants that did not ultimately agree to participate, 3 were initially interested but difficulties with scheduling and devoting time to the commitment resulted in final refusal. The remainder had messages with inquiries left with secretarial or nursing staff, with no response from the actual potential participant.

A total of 10 surgeons and 10 medical oncologists were included. Two trainees from RPCI (programs affiliated with University of Rochester) were included (one
surgical oncology, one medical oncology). The median number of years in practice was 8.5 (range 1.5 – 30 years). The median proportion of GI cancer patients in each subject’s practice was 55 % (range 10 – 100 %). Academic physicians were more likely to have a practice including a large proportion of patients with gastrointestinal cancers as compared with private practice physicians, who had more heterogeneous practices.

Of the 9 surgeons included in the tailoring grid interviews (excluding one fellow) 6 were academically-based, and 3 were in private practice. Regarding the 9 medical oncologists, excluding one fellow, 4 were in academically-based, 5 were in private practice. One medical oncologist (Subject 2) had both private and academic practices and gave responses to questions based on both experiences.

Interview Details

Twelve interviews occurred in person and the remainder by telephone. Median interview time was 25 minutes (range 10 – 40 minutes). Interviews were lengthier for initial subjects, becoming shorter for the final interviews. Considering the Pathman 4 A’s, one participant was unaware of CS/HIPEC, 9 participants considered themselves aware, one agreed, 3 considered themselves adopters, and 6 considered themselves adherent. Of those participants that were adopters or adherent to referrals for CS/HIPEC, only a minority actually agreed with the concept of referrals for the procedure and indications and evidence for its use. For adopters, only one of three subjects considered themselves in agreement with referrals for the procedure, and for adherent subjects, only two of six subjects considered themselves in agreement.

Interview Results
Results of interviews were collected and common factors were identified. Main subject areas within each of the 4 A’s were identified and classified with respect to the Grol levels of individual practicing physician, practice group or team, and organization as presented below.

**Barriers/Facilitators to Awareness**

The majority of interview participants were aware of the CS/HIPEC procedure. The one participant that was not aware was a trainee in medical oncology in the second year of a three year program at RPCI. The majority of participants became aware of the procedure during training or in early practice, either directly participating in the procedure or having the option to refer for the procedure at their center or nearby.

At the individual level, clinicians that trained at a center that had an active CS/HIPEC program were likely to have become aware at the time of their training related to direct contact with CS/HIPEC surgeons or care of patients that had undergone the procedure, and were more likely to be adopters or adherent with frequent referrals. Regarding those that did not train at a CS/HIPEC center, or whose training predated the procedure, individual self-directed learning from published materials such as journal articles and reviews was important as a facilitator to keep up to date of new techniques. The utility of face-to-face interaction and discussion with colleagues especially from different practice settings at national or international conferences was a strong facilitator of keeping up to date of new techniques, technologies, or treatments. Having a solo practice or lack of attendance at conferences for interaction with colleagues was felt to represent a barrier to awareness of novel procedures.
As part of the interaction with colleagues’ topic area, within a clinician’s own individual practice, exposure to trainees emerged as a facilitator to keeping abreast of newer techniques such as CS/HIPEC. Trainees have exposure to many different clinicians and practices, sometimes at different centers. Educational objectives and preparatory reading of current literature may also contribute to trainees discussing such treatment options during rounds, clinic, or organized journal clubs. This in turn was felt to act as a facilitator for awareness of clinicians acting in a supervisory role for these trainees, and conversely, lack of any exposure to trainees, a barrier.

Lastly, the barrier of individual clinician attitude regarding patients with PM and indications for CS/HIPEC emerged. At the individual practicing clinician level, the idea of “futility” of treatment of patient with PM was discussed. Such patients were felt to have infrequent responses to treatment and generally have negative outcomes overall regardless of therapy. The mention of PM, as compared with other forms of Stage IV cancer such as liver metastases, especially in CRC, was felt to be a “lost cause”. This was felt in part to be related to the historical manner in which PM was treated – with systemic therapy and surgery reserved for palliation of symptoms. The paradigm shift to offering an invasive procedure with possible complications to a patient traditionally treated in a palliative fashion was thought to represent a barrier to referrals for current and future patients with PM.

At the level of the individual practicing surgeon, it was felt that a “knowledge gap” existed regarding what options are available for patients where PM is encountered unexpectedly, on exploration in an elective surgical case, or when called to the operating room to assist a colleague from another surgical discipline with a procedure. The
knowledge gap appeared to encompass two extremes of a spectrum. Firstly, surgeons may be directly involved in identification or biopsy of PM at the time of surgery, but failure of knowledge of which patients may be candidates for CS/HIPEC results in lack of consideration of referral or deferring such decisions to a medical oncologist or other practitioner. This “critical time” where a surgeon could intervene to assist in directing a patient for consideration of CS/HIPEC was felt to be missed often due to lack of awareness of candidacy or indications for the procedure, or locations to which to refer. On the other end of the spectrum, surgeons become involved in a case where overly aggressive “debulking” is completed in asymptomatic or minimally symptomatic patients, causing the development of complications related to the procedure precluding further surgery or systemic therapy. A similar knowledge gap exists – on one end of the spectrum minimally aggressive but lacks information for directing patients leading to harm from lack of treatment, the second excessively aggressive leading to complications precluding further treatment.

From the Grol level perspective of practice group, a barrier to referral was identified as lack of regular interaction with colleagues. Individual practicing clinicians in solo practice were less likely to be aware of the procedure, and be aware of advances related to the procedure and indications. As well, interaction with colleagues in a multidisciplinary cancer conference (MCC) setting was felt to also represent a facilitator for dissemination of novel treatment options. For centers that lacked structured MCCs, even informal meetings between colleagues were felt to assist with this communication. In addition to a forum to discuss novel techniques for dissemination, for medical oncologists specifically, MCCs were felt to act as a “net” to catch candidates for referral
for CS/HIPEC if this was not initially part of their treatment plan, or the patient did not have a surgeon they had contact with for a long period of time that might facilitate such a referral. This likely is related to the uniqueness of the CS/HIPEC procedure, including surgical and chemotherapy components, and the fact that stakeholders for this procedure have emerged from a variety of backgrounds. Lack of this organized interaction between multidisciplinary groups was felt to represent a barrier to awareness.

From an organizational perspective, another barrier to awareness was identified as the advertising or marketing of centers offering CS/HIPEC, especially to participants with practices geographically separate from such centers. Given that many centers do not offer the procedure, awareness appeared to be facilitated by communication from the centers that do to keep individual clinicians and practice groups abreast of potential centers to which to direct referral.

**Barriers/Facilitators to Agreement**

Only one clinician, a medical oncologist, personally felt they were best classified as in “agreement” with CS/HIPEC. Also, although almost half the participants (n=9) were adopters or adherent – either have referred or routinely refer for the procedure, only 2 (22%) also agreed with the procedure, indications, and adequacy of published research supporting it.

Specific barriers related to published literature in support of CS/HIPEC were identified at two levels. At the individual clinician level, personal interpretation of published series of patients undergoing CS/HIPEC or trials compared with patients undergoing standard systemic chemotherapy was felt to be difficult. Good quality evidence for this purpose was felt to be lacking. The particular issues stemmed from the
heterogeneity of patients included in such studies (related to site of primary cancer, differences in PCI, different systemic therapy options) and therefore the difficulty in applying these results directly to patients in clinical practice.

The difficulty in applying previously published results to routine patient care, by the individual practicing clinician, also highlighted the issues with the comparison group (those receiving systemic chemotherapy). The only available randomized controlled trial in patients with CRC and PM compared CS/HIPEC with patients receiving 5-FU/leucovorin, which is now considered by medical oncologists to be an outdated regimen, and less effective than current regimens that are available. As a study directly comparing current standard-of-care systemic chemotherapy options to CS/HIPEC in a large group of more homogeneously selected patients is not currently available, many clinicians, especially medical oncologists, are hesitant to refer for or support CS/HIPEC as a good option as effectiveness has not been proven.

Also, similar to issues arising regarding awareness, the concept of PM as a systemic rather than locoregional disease emerged as a barrier to agreement. At the Grol level of practice group (medical oncologists, surgeons), this has required a paradigm shift related to CS/HIPEC as a viable option. Participants felt that treating a systemic disease with a locoregional treatment did not make inherent sense, working against what many disciplines understand to be consistent with cancer biology and behavior. This was noted both in medical oncologists and surgeons. There were no barriers or facilitators to agreement identified at the organizational level.

**Barriers/Facilitators to Adoption**
For clinicians who had adopted a referral practice for CS/HIPEC, the main barrier to referral for CS/HIPEC was lack of information regarding the “profile” of the surgeon offering the procedure, found to be important at several levels. Lack of availability and accessibility of a CS/HIPEC surgeon took precedence, specifically when communication (either by email, phone) regarding candidacy of a patient for the procedure was important. Although not all communications were felt to result in referral or the CS/HIPEC procedure for a particular patient, the idea of a CS/HIPEC surgeon being available to field questions or discuss options was felt to be mutually beneficial. This relationship was felt to be supportive to the referring clinician, and would avoid inappropriate referrals to CS/HIPEC surgeons.

From a practice group perspective, the reputation of the CS/HIPEC surgeon in the community or area in which he or she practices is also important, as word-of-mouth, especially amongst those in private practice and not necessarily affiliated with an academic center, was an important social interaction that resulted in adoption of referral to a specific CS/HIPEC surgeon. This was important to surgeons, but equally as important to medical oncologists who may not be aware of new surgeons in practice in their vicinity. Therefore, lack of knowledge of the reputation of a CS/HIPEC surgeon within the community he or she practices in was considered a barrier to referral.

From the level of the center that offers CS/HIPEC, lack of readily available outcomes at the practice group level and at the individual surgeon level was felt to be an important barrier to referral for the procedure. Outcomes were felt to not be “standardized” as an acceptable level for morbidity or mortality has not been identified. Both identification of these thresholds and an indicator of where the CS/HIPEC surgeon
in the referring physician’s practice area falls were felt to assist with adoption of referrals.

**Barriers/Facilitators to Adherence**

To follow with the idea of the CS/HIPEC procedure being resource intensive, the outcomes of the procedure, including surgical morbidity and mortality and the cost of management of such complications, were felt to not be well defined. From an individual clinician perspective, especially in surgeons, early published reports of CS/HIPEC had high morbidity and mortality rates, and this “bad reputation” has followed the procedure despite progress and improvement in the area. In addition, as referring physicians are invested in the outcome of their patients, related to a longer-term relationship, a CS/HIPEC surgeon or team’s outcomes are important to gauge. Referring physicians relayed wanting to feel comfortable and secure a CS/HIPEC surgeon they choose to refer a patient to have good post-operative outcomes. These issues regarding outcomes of CS/HIPEC were felt to act as barriers directly impacting referrals.

At the group level of practicing clinicians that regularly refer patients for consideration of CS/HIPEC, a barrier emerged related to the lack of well-defined timing for referral within a patient’s treatment planning (including surgery, systemic chemotherapy) given the overall length of some treatments and likelihood that many patients are chronically on therapy over long periods of time administered by many different providers.

The majority of barriers to adherence to referrals for CS/HIPEC were identified at the organizational level. The appropriate timing of referral was felt to be unclear as
CS/HIPEC is not discussed in detail in current clinical practice guidelines (CPGs) of various professional societies.

Related to the lack of reflection of the treatment in current CPGs such as the NCCN Colon Cancer guidelines, financial concerns such as insurance denials, from an organization perspective, were raised. In such CPGs, CS/HIPEC has been referred to as “experimental”, making acceptance of the technique by insurance companies challenging. Also from a financial perspective at the organizational level, the procedure is known to be resource intensive, and having such resources such as interventional radiology, critical care, and other ancillary services available for the care of these patients can be costly.

In addition, within the financial concerns barrier, if a patient has a surgical complication or mortality, the concern of lost revenue to the organization from future treatments that cannot be administered was raised, especially by medical oncologists. The final barrier concepts within the adherence section were found to be related to logistics of referrals. Given that many CS/HIPEC referrals occur from one center to another as the procedure is not offered at all centers, the lack of correspondence or response regarding a possible referral was felt to deter future referrals. In addition, for patient cases that are not straightforward, requiring a pre-referral conversation between the referring physician and CS/HIPEC surgeon, difficulty with arranging such discussions or lack of response of emails or phone calls was cited to be a barrier. The workflow issue of arranging referral to a CS/HIPEC center, especially for complex patients with large amounts of medical records, was further cited as a barrier from the individual clinician and practice group levels. Related to this issue, the lack of an electronic platform through which to review outside radiologic imaging or records was
cited as a barrier at the organizational level. Such a platform would make the referral process smoother overall, and would assist in communication between referring physicians and CS/HIPEC surgeons, especially in cases of complicated patients that are not straightforward referrals.

A total of three clinicians agreed with the concept of referrals for CS/HIPEC and evidence to support it. One of these, Subject 3 (adopted and agreed) was a surgical oncologist within the first two years of practice, mainly completing lower GI surgery. The two adherent clinicians that were in agreement, Subjects 2 and 15, were both medical oncologists, the first previously in private practice now in academic practice, the second a medical oncologist in private practice, both having large proportions of GI patients in their practice (25 and 100% respectively).

4.4: Conclusions

Although from different clinical backgrounds, types of practice, and experience in the field of oncology, several common factors for each of the Pathman 4 A’s were noted, many contributing to a barrier at many levels of practice. These concepts and ideas collected and summarized from the interviews can be found in Figure 3.
Chapter 5: Study Part II – Using a survey to quantitate prevalence of B/F factors for CS/HIPEC among referring clinicians in Western New York State.

For this portion of the study we used a survey to determine the prevalence of factors (i.e., barriers and facilitators influencing referral for CS/HIPEC) at the population level identified during tailoring grid interviews, as described in the previous chapter. The planned design was to translate responses and issues raised during the tailoring grid interviews directly into several types of survey questions, for quantification at the population level of referring physicians.

5.1: Survey design and methodology

Study Setting

Given the current referral patterns to an overall small number of CS/HIPEC centers in New York State, this was felt to be an excellent setting and system in which to administer this survey. RPCI has an established CS/HIPEC center, having received referrals for this procedure from Western New York State, but also from New York State as a whole. However, given the demonstrated variable rates of referral of patients for CS/HIPEC from various counties, at least with respect to CRC, discordance exists that deserves study in this system.

Sample Population

The target population for administration of the survey included the following stakeholders: medical oncologists, general surgeons, colorectal surgeons, and surgical oncologists. This group was chosen as the target population, because all patients that would be suitable for referral for CS/HIPEC would at some point in the diagnosis or treatment of their condition be managed by one or all of these clinicians. With the
exception of self-referral, the majority of referrals would originate from one of these clinicians. RPCI continually updates a list of all medical and surgical specialists practicing in New York State based on membership to professional societies (American Medical Association, American College of Surgeons). We used this list to identify relevant medical and surgical specialists who potentially treat this group of patients, and who thus could potentially refer patients for CS/HIPEC. This list contained contact information for 1607 individuals, but approximately 600 were eliminated for the following reasons: half for duplicate email addresses or email addresses no longer in use, the remainder for non-clinical practice (research, administration), or physician extenders. This left 1007 clinicians that had relevant practices for participation in the survey. Although under-coverage of the sample population is a concern by using a compiled email list from one of the CS/HIPEC institutions, either by under-sampling or by sampling from a biased group that has connections to the referring institution for any particular reason, this list was felt to be a good representation of practicing stakeholders in New York State given their specialties, and nature of practice. Potential subjects included in this list had no particular referral pattern or practice associated with RPCI. Some were even from potentially competing institutions or practices.

Survey Distribution

Email was selected as the most appropriate manner in which to distribute the survey and obtain and collate responses. The positive aspects of using email for this purpose includes that in general high volumes of information pertaining to practice is transmitted in this manner, and that these email accounts can be accessed for completion of the survey on tablets, smart phones, or home computers, rather than needing to be
completed in the office. The cost of using email for distribution is minimal, related mainly to the cost of using Survey Monkey, which is less expensive than postage and return postage costs for mailed surveys. The negative aspects of using email as a method for distribution of the survey is related to the ease of disregarding such emails by deleting them (Dykema, Jones, Piche, & Stevenson, 2013).

To encourage good response rates, the Dillman Method was undertaken, designing the survey with an introductory letter written by the PI with the goals of the study delineated clearly and how collected data were planned to be used (Dillman, 2007). After the initial emailing, reminder emails were sent at intervals of 2 weeks for the total of 8 weeks of the study. Paper copies of the survey were sent to individuals upon request.

Regarding surveys of health care professionals, a recent meta-analysis indicates that in the last 50 years, the average overall response rates for such surveys was 53 %, trending downward with time (Cho, Johnson, & Vangeest, 2013). Using web-based surveys in the last decade, response rates in health care professionals have been found to be less than 20 % (Klabunde, Willis, & Casalino, 2013). Reasons for this low response rate has been postulated to be related to several factors, including lack of time, perception of the survey having low value, perception of the survey questions being biased, and concern regarding confidentiality of responses. However, these barriers have not been validated. One manner in which to improve response rates to surveys in health care professionals is to offer monetary incentives (Klabunde et al., 2013). However, given the survey questions center on referrals for CS/HIPEC, monetary incentives would be considered conflict of interest, and could not be used in this study.
The recent CS/HIPEC survey by Spiegle and colleagues in this similar population
of medical oncologists and surgeons had a response rate of 44 %, but was completed in
the province of Ontario where CS/HIPEC was not already available, and the program was
in the process of being developed by the authors (Spiegle et al., 2013). For the present
study, given the target population of busy clinicians working in a variety of settings
including private and academic practice, a survey response rate of 15-20 % was felt to be
attainable.

Survey Design and Format

For the survey design and layout, Survey Monkey was used (Survey Monkey,
2014). This provided an electronic platform for designing the questions, and providing
them to subjects in a clear and concise manner.

To determine the characteristics of respondents, basic demographic questions
were utilized, including information regarding medical specialty, training, current
practice, and proportion of patients within their practice with GI malignancies (as most
indications for CS/HIPEC are for GI malignancies including appendix, colorectal).

To determine basic prevalence of respondents’ position within the Pathman 4 A’s
at the population level of referring physicians, simple “yes” or “no” questions were
utilized, asking if a respondent was aware, in agreement, an adopter, or adherent to a
referral practice for CS/HIPEC. Questions involving responses such as “choose all that
apply” or ranking questions were used for tailoring grid themes that appeared very
heterogeneous. All such questions included an option for “none of the above” or “other”
to allow for free-text answers.
For direct patient-care related actions, vignettes designed around patient cases were used. The rationale for their use was although clinicians may select particular answers to questions based on thoughts or philosophies, when put in a clinical scenario, answers may be different and can assist in obtaining more realistic or truthful information. To tailor vignettes directly to a participant’s practice, skip logic was used (Groves et al., 2009), so vignettes regarding surgical decision-making were provided to surgeons, whereas vignettes regarding chemotherapy prescription were provided to medical oncologists.

All respondents were provided with demographic questions and position within the Pathman 4 A’s. The last set of questions regarding “adherence” were only posed to those respondents who answered “yes” to the question of regular referral practice for CS/HIPEC given specificity to regular referral practices.

Once a draft of the survey was created, it was piloted on 4 clinicians who provided feedback on survey content, format, clarity, and flow. Representation of tailoring grid answers and topics related to survey questions can be found in Table 2. Feedback was obtained and changes were incorporated into the final draft of the survey. The final draft of the survey can be found in Appendix D.

5.2: Survey administration

For the purposes of distributing the survey and having accurate information regarding number of emails opened, bounce-backs, opt-outs, and information regarding when responses to the survey came in with respect to send-outs and reminder emails, Constant Contact email program was used (Constant Contact., 2014). A link to the final
survey in Survey Monkey was embedded in this email, along with the personalized letter from the PI explaining the nature and goals of the study.

The survey was sent out in an initial email on 1/13/2014, and then subsequent reminder emails were sent on 1/26/2014, 2/9/2014, and 2/22/2014. Given the target sample of busy practicing clinicians, these emails were generally sent out on a Sunday. Responses have been found to be more likely to be obtained for surveys sent early in the week, and thus Sunday can provide a free day that may results in responses, or provide an email present in a subject’s inbox early in the week for potential response (Survey Monkey, 2014).

5.3: Statistical analysis

For the statistical analysis of results, respondents were divided for an initial analysis into medical and surgical cohorts. A second analysis was completed using the cohorts of early (first two emailings) or late (final two emailings) responders. Results of these analyses were reported using frequencies and relative frequencies. Where appropriate, comparisons between cohorts were made using Fisher’s exact test using SAS v9.3 (Cary, NC). A significance level of 0.05 was used, and thus a value of less than 0.05 was considered statistically significant.

5.3: Results of survey

Response rates

For each of the four emailings (1/13, 1/26, 2/9, 2/22), the message was opened by approximately 1/3 of clinicians (353, 360, 350, and 322 subjects respectively). The number of clinicians that clicked on the survey link to complete the survey was significantly lower, (54, 42, 26, and 22 respectively, totaling 144). As per Survey
Monkey results, a total of 119 clinicians completed the survey. This corresponds to an overall response rate of 12 % (119 of 1000). A total of 83 % (119 of 144) of clinicians that clicked on the survey link actually completed the survey. The timing of responses related to email send-outs can be found in Figure 4.

Considering “early” (response to one of the first two email requests) versus “late” responders (response to the third or last email requests), approximately 2/3 of clinicians were early responders (n=76; 64 %).

Respondent demographics

Demographic information for respondents can be found in Table 3. Academic and private/community practices were equally represented in the sample. Two thirds of the sample was comprised of surgeons (surgical oncologists, colorectal or general surgeons; n=77; 65 %), while the remainder were medical specialists (gastroenterologists or medical oncologists, with the majority being medical oncologists). For the overall sample, 15 % of clinicians were junior, in practice for 0-5 years. The majority of respondents (59 %) were senior, in practice for greater than 10 years. There was no statistical difference between medical oncology and surgery cohorts in terms of type of practice or years in practice (p=0.06 and p=0.63 respectively). Regarding types of patients seen in current practice, the majority of respondents (68 %) saw a substantial number of patients with GI cancers on a regular basis (10-50 % or greater than 50 % of patients in practice). This was broken down differently between the two groups, as medical oncologists were more likely to see 10-50 % of GI cancer patients in their practice (n = 24; 57 %), whereas surgeons were more likely to see larger proportions of GI cancers, greater than 50 % (n = 28; 36 %; p = 0.009).
Regarding prior training of clinicians, the majority (64%) trained in a major academic or university center associated with a cancer center. This was not different between the medical oncology and surgery cohorts.

*Pathman 4 A’s of awareness, agreement, adoption, and adherence*

The vast majority of respondents were aware of CS/HIPEC as a treatment option, 95% overall, with only a slight difference between medical oncologists (91%) versus surgeons (97%), which was not statistically significant (Table 4). Considering respondent-reported agreement with the concept of CS/HIPEC, a difference that was found to be statistically significant was found – 76% (n=32) medical oncologists versus 92% (n=71) surgeons were in agreement with the procedure (p=0.02). Regarding adoption of a referral practice for CS/HIPEC, no difference existed between medical oncologists or surgeons (p=0.21), with overall 70% having referred a patient for consideration of CS/HIPEC in the past or presently.

Finally, regarding adherence to a more routine or regular practice of referring patients for a CS/HIPEC opinion, this was not found to be different between medical oncologists and surgeons (49% vs 56%, p = 0.53).

*Awareness*

Regarding awareness of new techniques or available treatments as a facilitator, the method in which clinicians keep up to date was felt to vary within the tailoring grid interviews, and a more detailed investigation of this in the practice of respondents was sought, and final survey results can be found in Table 5. The most common method in which to keep up to date of new practices or techniques was reading journal or review articles (93%), whereas attending national or international meetings (91 of 111) or
utilizing electronic resources such as websites (85 of 111) was selected by approximately 76 % of respondents. No statistically significant differences existed between medical oncologists and surgeons for any selection. Reliance on colleague interaction, advertisements for new techniques or treatments offered at particular centers, and other less represented options such as audiotapes or local meetings were very infrequently chosen.

During tailoring grid interviews, attendance at MCCs, and discussion of novel techniques at such colleague-to-colleague interaction meetings were felt to be a facilitator of patient referrals and lack of availability of such meetings or lack of attendance at such meetings was felt to represent a barrier to referrals. Interestingly, approximately 70 % of medical oncologists regularly attended MCCs, whereas 83 % of surgeons regularly attended (p = 0.15, 111 total respondents of 119). Just fewer than 10 % of respondents (8 of 111) did not participate in any interaction whatsoever to discuss patients. The use of informal meetings between colleagues did not appear to differ between the two groups, nor was this used frequently in place of standard MCC (7 of 111, 6 %).

Exposure to trainees within one’s practice was felt to act as a facilitator for keeping abreast of new techniques. At least 30 % of respondents had infrequent or no exposure to trainees, which may act as a barrier – however, survey respondents in general, had high rates of awareness of CS/HIPEC, and could not be demonstrated in this group.

The barrier of aggressive initial management of patients with PM, or lack of recognition of options for patients with PM was addressed in two clinical vignettes. For surgeons, a vignette involving options that would equate to an initial aggressive surgical
management in an asymptomatic patient was used, and for medical oncologists, a vignette regarding if surgery was ever felt to be an appropriate treatment modality for patients with PM was used.

The vignette for medical oncologists involved the barrier of PM in colorectal cancer as being futile to treat, and not a surgically managed disease process. This vignette involved a case presentation of a female patient found to have a colonic mass and limited PM. Biopsy indicates the tumor is a colonic adenocarcinoma. More than half of respondents felt the patient should be started on first-line chemotherapy after recovery (22 of 39 medical oncologists, 56%). In addition to this 38% felt that re-referral back to the surgeon to consider resection of the primary tumor after chemotherapy was appropriate. Only a very small proportion (8%) felt that surgery would never be warranted in this patient, unless an emergency occurred such as obstruction, bleeding. An additional 7% of respondents felt that referral for CS/HIPEC for this patient would be appropriate, as well as discussion of the patient case amongst colleagues in an MCC setting.

The surgical vignette centered on the barrier identified by surgeons in the tailoring grid interviews regarding lack of awareness of what to do when encountering unexpected PM in the operating room. Barriers within this concept included overly aggressive management of asymptomatic or minimally symptomatic patients with debulking/cytoreduction potentially causing surgical morbidity or mortality, or on the opposite end of the spectrum patients being identified as having PM and no further involvement in treatment or management occurs.
This vignette for surgeons involved an intraoperative scenario where a gynecology colleague asks for assistance with a patient for which he planned a hysterectomy and bilateral salpingo-oophorectomy. The patient is noted at time of surgery to have PM, and a non-obstructing mass of the cecum. This vignette was utilized to directly evaluate the rates of “overly aggressive” approaches to a patient with this presentation, as this was an awareness barrier to referral for CS/HIPEC. Approximately 30% of respondents selected resection of the non-obstructing cecal mass, whereas almost half (35 of 72 surgeons, 49%) would cytoreduce the patient including hysterectomy, bilateral oophorectomy, resect cecal mass, remove peritoneal nodules. Almost two-thirds of respondents selected the option of exploring the abdomen (including pelvis, diaphragms, liver capsule) for an evaluation of extent of PM. Grouping the various options into the “aggressive” options of hysterectomy / bilateral oophorectomy, resection of cecal mass, and/or cytoreduction, 56% of respondents selected at least one of these options. For the “extent of PM/diagnosis” options including intraoperative biopsy and frozen section, and explore the abdomen for extent of PM, 69% of respondents selected at least one of these options. A total of 44% of respondents selected the option of consulting medical oncology post-operatively. A small minority of 7% selected they would do nothing and close the patient. A total of 17 respondents selected the “other” category, where 13 respondents said they would refer the patient for CS/HIPEC or to another specialist for management, and 3 would complete a colonoscopy or further work-up of the patient.
Agreement

The tailoring grid interviews discussed the issue of “lack of high level evidence” in the form of published studies supporting CS/HIPEC in support of the technique as a barrier to referral, especially from the individual practicing clinician level. The majority of respondents of the survey felt that the literature was limited to retrospective or poorly designed prospective studies (47 of 108 respondents total, 44%) or biased towards patients with good tumor biology, good performance status, or would otherwise do well with any treatment (37 of 108, 34%). Those responses were not different between medical oncologists and surgeons. However, there was a statistically significant difference between those two groups, as medical oncologists were far less likely to identify that the evidentiary basis for CS/HIPEC was comprised of good quality prospective studies (3 of 38, 8%) versus surgeons (19 of 70, 27%; p = 0.03).

A second survey question centering on agreement with CS/HIPEC involved the respondent’s interpretation of the procedure and its application, particularly the idea of “futility of treatment” or nihilistic attitude towards PM and the paradigm shift the procedure represents. A large proportion of those selecting other options in the question felt that select patients that have good outcomes with CS/HIPEC would likely have good results with all therapies (44 of 108, 41%) but was not different between medical oncologists and surgeons (p=0.25). The concept of PM being a disease that can be treated with systemic chemotherapy only identified in the tailoring grid interviews was not validated in the survey responses, with only 6% of respondents selecting this option. When posing a question regarding what the intraperitoneal (HIPEC) portion of the procedure adds to the surgical (CS) portion, surgeons were more likely to select this
option as compared with medical oncologists (21 % versus 8 %). Many respondents did not feel any option within the question appropriately represented their opinion, with approximately one third selecting “none of the above”. Final results can be found in Table 6.

Adoption

Survey questions regarding adoption of a practice of referring patients either currently or in the past for CS/HIPEC took the form of two questions and one vignette. Regarding referrals and frequency of such referrals, this was posed as a direct question asking respondents to select all listed options that applied to their situation and practice. Half of respondents felt they did not see enough patients that fit the criteria or indications for the procedure, which was not different between medical oncologists or surgeons (p=0.68, p=0.12). Medical oncologists were significantly more likely to feel that morbidity and mortality from CS/HIPEC is prohibitively high for this group of patients (26 of 105 25 %, p = 0.04). Medical oncologists were more likely to be unaware of whom to refer in the surgical community to obtain a CS/HIPEC opinion, compared with surgeons, but this was not statistically significant (18 % vs 6 %, p = 0.05). The option of a lack of centers nearby offering CS/HIPEC was only selected by 12 % of respondents, not different between surgeons and medical oncologists. A large proportion of surgeons were more likely to choose none of the above for this question, compared with medical oncologists (47 %, p = 0.03).

Thoughts regarding adoption of referrals for CS/HIPEC with respect to “futility of treatment” for PM were asked as a survey question in this section. The majority of respondents felt that all patients with PM should receive some form or duration of
systemic chemotherapy, with a select group appropriate for CS/HIPEC, and was not different between medical oncologists or surgeons (75 %, \( p = 0.53 \)). Only a very small minority of respondents felt that all treatment for PM is futile, and that treatment should restricted to systemic chemotherapy alone with no option for surgical management (1 %).

Lastly, a vignette was used to further characterize the barrier of uncertainty of when to initiate a referral. From the tailoring grid interviews, it was felt that this uncertainty could lead to lack of initiating a referral at all, or too late in a patient’s treatment plan. The vignette posed involved a patient case of a presentation of acute appendicitis, with the intraoperative finding of a solid appendix mass and PM. A right hemicolecctomy was performed, leaving PM behind. Referral for CS/HIPEC and timing of this with respect to other treatments was posed in this question. Approximately 14 % of respondents felt this patient would never be a candidate for CS/HIPEC.

The “timing” options (immediately following surgery, after 3 months of systemic chemotherapy, after 6 months of systemic chemotherapy, and after 6 months of systemic chemotherapy with no evidence of progressive disease or distant metastatic disease) were relatively equally represented, and no option was selected more frequently in medical oncologists versus surgeons. Approximately one quarter (22 %) were not sure when to refer, and the majority of these respondents were medical oncologists. Final results can be found in Table 7.

Adherence

Considering clinicians who consider themselves regular referring physicians for CS/HIPEC, overall 54 % of respondents, 49 % medical oncologists, and 57 % surgeons,
barriers to the regular referral process were evaluated through 4 survey questions. Using skip logic, these questions were only posed to those with regular referral practices.

The first question included a ranking of factors that make logistics of continued referrals easier. Four parts to this question were asked, and a rank from 1 (most important) to 4 (least important) were options. The option of not applicable (N/A) was available for selection for each of the four parts. There were no statistically significant differences between ranking of these four parts between medical oncologists or surgeons. The more consistently ranked “most important” factor was knowing the CS/HIPEC surgeon or practice group by name, location and reputation, selected by 69 % of respondents. Second most commonly chosen as most important was having a contact person (physician extender, referral coordinator, or means in which to contact the CS/HIPEC surgeon directly for opinion prior to referral), selected by 49 % of respondents. Having a standard referral form that can be filled out to capture all relevant information needed by the CS/HIPEC center to expedite referrals was felt to only be the most important factor in 18 % of respondents.

The concept of the “downstream” effects of a surgical complication from CS/HIPEC limiting a patient’s future suitability to receive more systemic chemotherapy for medical oncologists, and from a surgeon’s perspective having to manage another surgeon’s complications having to be managed by the referring physician arose as a barrier. For this question, the “balance” between good oncologic outcome and surgical outcomes (morbidity, mortality) was evaluated. One third of respondents felt that patients had good outcomes both oncologically and surgically (7 medical oncologists, 14 surgeons, 38 %), and a further third felt that for those that did experience surgical
complications, oncologic outcomes were still good (36 %). Very few felt that no good outcomes emerged from regular CS/HIPEC referrals (2 of 56 respondents, 4 %). There was no difference between the experience of medical oncologists and surgeons (p=0.87).

A further question in this section involved how numbers of referrals could be increased compared with current practice. Nearly half of all respondents, both medical oncologist and surgeons, felt that inclusion of CS/HIPEC into CPGs for a specific disease site (colorectal, appendiceal) would be a positive step to increase frequency or consideration of referrals (46 %, p = 0.62). A common electronic information platform and a CS/HIPEC surgeon at one’s own center were felt to be low priority. The idea of “loss” of patients to a center offering CS/HIPEC to future therapy or therapeutic relationships identified in the tailoring grid interviews was not validated (4 % of respondents).

Considering the financial implications of CS/HIPEC, a large proportion of respondents (36 %) did not feel any option reflected their opinion. Many clinicians felt that they were unaware of the “return on investment” for the costs and resources put in to a CS/HIPEC procedure provided to a patient (33 %, p =0.47). Insurance denials causing undue stress on patients was not well represented (6 %). Final results can be found in Table 8.

Early versus Late responders

Early responders to the survey were considered those that responded to the survey within the first month, including the first two emailings, whereas the late responders were those that responded in the second month, in the last two emailings. Considering these two groups, approximately two thirds of respondents were early, and there were no
differences in demographics between early and late groups. Respondents’ specialties were similar in the early versus late respondents groups. There were also no differences seen in rates of awareness, agreement, adoption or adherence.
Chapter 6:

6.1: Discussion

6.1: i. Clinical aspects of study

The current study utilizes the opinions of practicing clinicians to systematically evaluate barriers and facilitators to CS/HIPEC referral. Although an evaluation of barriers to awareness of the procedure was evaluated in the province of Ontario prior to the initiation of the CS/HIPEC program at Mount Sinai Hospital in Toronto, a comprehensive evaluation of barriers and facilitators to referral for this procedure from the clinician practicing at various stages of awareness, agreement, adoption, or adherence has not been completed to date (Spiegle et al., 2013). This is the first study fully to evaluate this through the main clinical stakeholders of the procedure.

The subjects that participated in the tailoring grid interviews had clinical practices very relevant to this discussion, as a good proportion of their practices included patients that could potentially be candidates for the procedure, namely gastrointestinal primary cancer cases. Both medical oncologists and surgeons were easily engaged in these interviews regarding referral practices. Fellows, both in medical oncology and surgery, were utilized to contribute to the ideas and concepts noted from the tailoring grid interviews, and how such ideas potentially differed during training as compared with practice.

Regarding the topics that emerged from the tailoring grid interviews, many clinicians had similar ideas regarding barriers and at which level each was at work. It was evident from these interviews all clinicians were aware of the procedure of CS/HIPEC at the most basic level, and at the population level, the survey indicates over 90% of
participating clinicians were aware. Surgeons were more likely to be aware than medical oncologists. Several topics that emerged from interviews clearly contributed to this awareness, including prior training at a center offering CS/HIPEC and exposure during residency or fellowship. Although CS/HIPEC centers are becoming more common, for those clinicians that continue to train in centers without this practice, educational interventions could be designed to promote awareness to address this gap. Identified manners in which clinicians keep up to date of novel techniques or treatments from the interviews vary from conferences, published studies and reviews, and electronic resources such as websites. Such avenues can be used to circulate information regarding CS/HIPEC, as the stakeholders in the referral process clearly utilize them. It is also interesting to note that true advertisements and marketing of a program were not felt to be useful for respondents for the purposes of keeping up to date of novel techniques or treatments.

Another clear barrier to referral for CS/HIPEC identified during interviews was the lack of availability and attendance of MCCs, as a “net” to discuss and catch patient cases that would be appropriate for referral, especially important to medical oncologists. The survey indicates that 15% of clinicians do not attend MCCs for discussion of their cancer patients. The survey was not designed to specifically characterize or define barriers to MCC at individual centers, but it can be postulated from previous research that by utilizing virtual or electronic MCCs, some of these individuals may be encouraged to present difficult patient cases, including those where CS/HIPEC may be appropriate (Francescutti et al., 2014).
Although exposure to trainees for discussion of novel techniques during rounds and journal clubs was felt to be a facilitator during interviews, the survey indicates that overall less than 10% of sampled practicing clinicians have no exposure to trainees. This signifies that exposure to trainees may not contribute significantly to awareness of novel techniques at the population level of clinicians, or that the majority of those potentially referring physicians practice in settings where they have at least occasional exposure to trainees.

Two other clinical issues emerged in interviews specific to awareness of CS/HIPEC, and were addressed by vignettes in the survey. Overall, the majority of survey respondents considered themselves aware of referrals for CS/HIPEC; 90.5% of medical oncologists and 97.4% of surgeons. The vignettes were presented to all individuals regardless of self-reported awareness or lack of awareness. For medical oncologists, a case was presented as a patient who appears to be a good candidate for consideration of CS/HIPEC, and options aimed to identify the barrier of nihilistic treatment and no possibility for surgical management for such patients with PM. More than half of respondents felt systemic chemotherapy was warranted. Interestingly, two respondents recommended the patient could be considered for CS/HIPEC in the “other” category, validating that this was an appropriate group of stakeholders chosen for this study. Although the concept of surgery being reserved for palliative or emergency indications did emerge, especially from medical oncologists in the tailoring grid portion of the study, this was only the opinion of 3 respondents in the survey.

From the perspective of the surgical vignette, the concept of overly “aggressive” initial management of patients presenting with intraoperative “surprise” findings of PM
was felt to represent a barrier to referral for CS/HIPEC, either due to the patient experiencing complications from an initial surgery that precluded further surgical or medical treatments, or from an underlying lack of understanding or awareness of the disease process and what treatments may be useful in the future. Again, this vignette was posed to a sampling of surgeons wherein 97% considered themselves aware of CS/HIPEC as a treatment option. In this vignette, 9 respondents felt this patient could be referred on for a CS/HIPEC opinion, and similarly 4 felt the patient should be “closed” and referred on to another specialist for management. This group indicated awareness of other options not listed. A large group of nearly 45% of surgeons felt they would “cytoreduce” the patient including hysterectomy, colon resection, and removal of peritoneal nodules, which was the option representing an aggressive approach to a non-obstructed potentially asymptomatic patient. Interestingly less than half of surgeons overall would recommend a medical oncology consultation for this patient with PM. For the group choosing at least one of the resection procedures as part of the management plan for this patient (56% of surgeons), only 61% of this group would consult medical oncology post operatively. Although considered aware of the novel CS/HIPEC technique, this suggests that many clinicians may be unaware of the possibility of harm from aggressive management, and possibly the importance of systemic chemotherapy in the overall management of a patient fitting this profile. This also may show that awareness of the option of a procedure does not necessarily include awareness of indications or applications of the procedure, where educational interventions may be appropriate even in aware individuals, regarding how to approach a patient such as the one presented, and what may be considered unnecessary surgical management.
Regarding agreement with CS/HIPEC, the majority of ideas collected from the tailoring grid interviews centered on the strength and quality of the available evidentiary basis for the procedure, specifically clinical trials comparing CS/HIPEC to systemic chemotherapy. The first factor that emerged from the tailoring grid interviews was the type or design of study (ex: prospective or randomized controlled trial versus retrospective studies) and the second was the study design bias to include only patients that would do well with any surgical or medical treatment. At the population level, medical oncologists were much less likely to feel that good prospective studies existed compared with surgeons. Whether these clinicians were not aware of such publications, or were aware but felt the overall quality of such studies were poor is not clear. This difference may be related to how studies in medical oncology are designed as compared with surgery, and what each group interprets as strong evidence. For example, large prospective or randomized studies are rarely completed for surgical procedures to prove safety or effectiveness, and results of retrospective series can be representative and appropriate. This difference in what information or results medical oncologists “require” to feel comfortable with a treatment compared with surgeons may be driving this result.

For future development in similar procedures that involve stakeholders from several disciplines, alternate strategies may be necessary to address fundamental differences in how these groups interpret published evidence.

The second question in the agreement section of the survey was in regards to futility of care and overall ultimate poor outcomes and nihilism in patients with PM. The idea of futility of all treatments that was raised in the interviews was not reflective of the opinions of most clinicians in the survey. Most felt that a select group of these patients
will have good outcomes with all therapies, surgical or medical, supporting the idea of a selection bias in patients chosen for inclusion into many trials.

Considering barriers to adoption of referrals for CS/HIPEC, a few key issues deserve mention. At the population level, medical oncologists were less likely to have information regarding to whom (which center or which surgeon) to refer a patient for CS/HIPEC. As compared with surgeons, this may reflect the fact that surgeons are part of a “community” of surgeons where word of mouth plays a role in this process. Medical oncologists also were significantly more likely to be concerned regarding the morbidity and mortality associated with CS/HIPEC as compared with surgeons, acting as a barrier for adoption of a referral practice. Surgeons may be more comfortable with surgical complications and have better knowledge regarding outcomes and management, and future interventions could investigate medical oncologists’ perceptions and interpretations of these complications.

A final vignette was used for both medical oncologists and surgeons to address the barrier identified in tailoring grid interviews of when to refer a patient for a CS/HIPEC opinion, given the many points in time during a patient’s treatment. Various time points were provided in the vignette as “windows” for referral for CS/HIPEC, including immediately following initial surgery, after half a planned systemic chemotherapy regimen, after a full 6 months of systemic chemotherapy or after 6 months of systemic chemotherapy provided restaging scans were negative for progression of disease. There were a small proportion of respondents (~15 %) that felt the patient should never be sent for a CS/HIPEC opinion, and the reason for this is not clear. However, a quarter of respondents were unsure when referral could occur, which identifies a rather
substantial group that may be receptive to information and education regarding how such a treatment can fit into current treatment regimens or pathways.

Regarding ideas specific to clinicians who regularly refer patients for CS/HIPEC, considering themselves adherent, information regarding surgeon name, practice group, and reputation appear to be the most important logistical factor in predicting future and ongoing referrals. In this same vein from the tailoring grid interviews, surgical and oncologic outcomes were felt to be a barrier to adoption of referrals for CS/HIPEC. However, when evaluating this outcome issue in adherent clinicians in the survey, this represented the opinion in only about one third of clinicians as a barrier, as most (~70 %) of respondents stated patients had good outcomes, or at least acceptable surgical complications in the face of good oncologic outcomes. This may be reflective of a clinician’s definition of “acceptable” complication rates, or conversely related to ongoing good outcomes in particular patient cases, could be a reason why clinicians routinely refer. Those clinicians with several patients that had poor outcomes may have stopped routinely referring, although this is difficult to conclude from the current available information.

When comparing early versus late responders, it appeared that approximately two-thirds of respondents were early, and there was little difference regarding timing of response and specialty. In addition, no key significant differences existed in answers for any questions dependent on the respondent being in the early or late group.

6.1: ii. Methodologic aspects of the study

Considering the tailoring grid methodology that was used in the first portion of this study, this structure provided an excellent way to organize interviews. As more
interviews were completed, the interview time decreased, likely in part due to redundancy in answers, but also from interviewer experience with the tailoring grid and structure. Overall this was an efficient manner in which to obtain this information. Given the manner in which this was organized, the “grid” facilitated straightforward summary of topics of relevance, and organization into where or at which Grol “level” these best contributed to the overall picture of barriers and facilitators. It was clear that within each barrier or facilitator topic that was mentioned in an interview, there were contributions from various levels, at the individual clinician, practice group, and organizational level. To fully address these with a tailored intervention in the future would require a thorough understanding of the issue, from a variety of perspectives. Thus, using Grol “levels” within this framework was extremely useful in obtaining a comprehensive view of a particular issue for this purpose.

Regarding the logistics of completing the tailoring grid interviews, many clinicians, despite busy schedules, were willing to participate. Refusal to participate usually occurred through the subject’s secretary, so direct refusal from the clinician was difficult to ascertain. More refusals were obtained via telephone and message rather than email, so it may be postulated that direct contact with the clinician rather than a “screening process” through a secretary may be more efficacious in encouraging participation.

The second portion of the study, the design and administration of the survey to referring or potentially referring physicians, identified as the “stakeholders”. The overall response rate of 12 % is lower than initially hypothesized. Various methods for improving response rates were utilized in this study, including Dillman methods of a
letter from the investigator regarding the goals of the survey and how information would be used. Reminder emails were sent out every 2 weeks during the study period, each resulting in more responses. Although the absolute rate of survey response may be considered suboptimal, the fact that those responding were all in the relevant groups of medical oncology and surgery (general, colorectal, or surgical oncology) that would provide appropriate and useful information is important.

Regarding the translation of themes and ideas from the tailoring grid interviews into survey questions, this process occurred easily due to the structure of the grid and ease of organization. A similar structure of the survey using the Pathman 4 A’s assisted to achieve this continuity. For questions that did not contain an appropriate answer for selection by survey respondents, the category of “other” was used to allow for free-text answers. Interestingly, for many of these questions offering an “other” option, very similar responses from respondents were obtained, reflecting good concordance between the tailoring grid answers and survey questions, and very little of relevance not included into possible responses.

Some questions with the option of “none of the above” or “none of these reflects my opinion” including agreement questions involving published literature and interpretation of CS/HIPEC and its applications did have relatively high rates of selection (18.5 % and 37.0 % respectively). This unfortunately only gives information regarding the unsuitability of the other options, not the true answer or option that best represents the respondent’s opinion. This may have been better posed as an “other” option allowing for free-text answers to clarify.
A separate analysis of early versus late responders did not show any tangible differences between the two groups. The difference in timing of responses may have more to do with busy clinician schedules rather than any specific characteristics of the respondent. Many potential respondents may be interested in participating, and a reminder email timed appropriately based on their schedule may be a driving factor in increasing response rates.

The current study aimed to evaluate and characterize barriers and facilitators to referral for CS/HIPEC specifically in medical oncologists and surgeons. Other possible stakeholders in this process, including patients, primary care physicians, and other surgeons such as gynecologists, may provide useful insight into this process.

6.1: iii. Limitations and Future Directions

In this study, the use of a tailoring grid methodology proved useful, as an efficient manner in which to obtain information from a targeted group of busy clinicians in an organized fashion. One limitation of this approach is that although it is organized and efficient, it does not have the same evidence base or proven use compared with other qualitative research methodology, including focus groups. However, given the wealth of information gleaned from the tailoring grid interviews in short periods of time, on average 30 to 40 minutes for this study, for such interviews involving busy clinicians, higher participation rates and valuable information gained may outweigh these limitations. The integration of the Pathman 4A’s and Grol framework was particularly helpful in evaluating barriers and facilitators to use of a novel surgical technique. Use of this tailoring grid methodology in other clinical situations with similar positive experiences may further validate this approach in the future.
One further limitation of the tailoring grid interviews was they were completed by a single interviewer. Some were completed by telephone and others in-person. There was no real difference in interview time or depth of questioning based on in-person or telephone interviewing. However, some bias regarding how questions are posed and interpretation of responses by a single interviewer could be perceived as a limitation. For future tailoring grid interviews, more than one interviewer could be utilized, or interpretation of results could be completed from audio recordings of the interview by more than one individual. This may make the research methodology more robust, but the interpersonal interaction during an interview in a non-threatening environment may be compromised with this approach.

The administration of the survey and response rate was limited by the aforementioned busy practices and obligations of clinicians. It is known that the addition of an incentive for completing a survey will increase response rates. However, given this survey involves referral practices and opinions; the use of incentives was prohibited, and was a limitation that unfortunately could not be addressed.

Within the design of the survey questions, a small number of questions created from ideas raised in the tailoring grid interviews were not substantiated in survey responses. This was for a small number of questions (questions 18 and 19), where a large number of respondents selected (up to one third) selected “none of these reflect my opinion”. Although this response assists with understanding the lack of suitability of the other options to the respondent, it does not clarify what a true response may be, thereby limiting information that can be gained from the question. To contrast, questions that offered an “other” option with space for free-text answers generally had low rates of
This study has provided a wealth of factors organized within a Pathman and Grol framework that characterize barriers and facilitators to referral for CS/HIPEC. A future direction for the current study and within KT science involves how to take the generated list of barriers and facilitators in a particular topic area and prioritize them. Valuable information emerged within the tailoring grid interviews, including financial concerns, clinical practice guidelines, quality measures, interpersonal interactions through trainees and MCCs, etc. However, there is currently no accepted way in which to prioritize these barriers. Although many barriers were selected by respondents in the survey, the question remains as to should barriers that are most popular be selected to design interventions, or those that have the most impact on the desired outcome (referrals, etc).

In addition to prioritization of barriers and facilitators, little evidence exists regarding how barriers should subsequently be selected for tailored interventions. Should barriers in similar topic areas be grouped for intervention, or should available interventions be used to assist in sub-classifying identified and prioritized barriers? Further research taking into account these issues will assist in translating information from studies such as the current one into tailored interventions to direct affect outcomes of interest.
6.2: Conclusions

The current study uses tailoring grid interviews to elicit detailed information regarding barriers and facilitators to referral for a complex surgical innovation with variable uptake, namely CS/HIPEC, from key stakeholders. The results of these interviews include organized information within a Pathman and Grol framework. A survey was subsequently created from topics obtained from interviews and administered to a larger group of clinicians representing the population level, and the response rate obtained for this survey was felt to be appropriate given the busy schedules of the selected population.

Questions translated from the tailoring grid interviews into survey questions showed good concordance with very few questions and responses that were not selected and validated by respondents. This tailoring grid interview and survey methodology provides an excellent and efficient manner in which to comprehensively evaluate barriers and facilitators and measure how such are represented at the population level of clinicians.

The current study provides several actionable barriers and facilitators organized within the framework of uptake of novel innovation for future design and implementation of tailored interventions for KT.
References


Table 1: Demographic information of tailoring grid interview participants

<table>
<thead>
<tr>
<th>Subject Number</th>
<th>Specialty</th>
<th>Center</th>
<th>Current Position</th>
<th>Years in Practice</th>
<th>Proportion of GI cancer patients in practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Surgery</td>
<td>Academic</td>
<td>Adherent</td>
<td>7</td>
<td>100 %</td>
</tr>
<tr>
<td>2</td>
<td>Medical Oncology</td>
<td>Academic/Private</td>
<td>Adherent</td>
<td>3</td>
<td>100 %</td>
</tr>
<tr>
<td>3</td>
<td>Surgery</td>
<td>Academic</td>
<td>Adopter</td>
<td>1.5</td>
<td>100 %</td>
</tr>
<tr>
<td>4</td>
<td>Medical Oncology</td>
<td>Academic</td>
<td>Aware</td>
<td>7</td>
<td>100 %</td>
</tr>
<tr>
<td>5</td>
<td>Surgery</td>
<td>Academic</td>
<td>Adopter</td>
<td>15</td>
<td>80 %</td>
</tr>
<tr>
<td>6</td>
<td>Surgery</td>
<td>Academic</td>
<td>Adherent</td>
<td>19</td>
<td>100 %</td>
</tr>
<tr>
<td>7</td>
<td>Medical Oncology</td>
<td>Academic</td>
<td>Adherent</td>
<td>3</td>
<td>80 %</td>
</tr>
<tr>
<td>8</td>
<td>Surgery</td>
<td>Academic</td>
<td>Aware</td>
<td>Fellow</td>
<td>N/A</td>
</tr>
<tr>
<td>9</td>
<td>Surgery</td>
<td>Private</td>
<td>Aware</td>
<td>5</td>
<td>50 %</td>
</tr>
<tr>
<td>10</td>
<td>Medical Oncology</td>
<td>Academic</td>
<td>Not Aware</td>
<td>Fellow</td>
<td>N/A</td>
</tr>
<tr>
<td>11</td>
<td>Medical Oncology</td>
<td>Private</td>
<td>Aware</td>
<td>20</td>
<td>20 %</td>
</tr>
<tr>
<td>12</td>
<td>Surgery</td>
<td>Private</td>
<td>Adopter</td>
<td>10</td>
<td>60 %</td>
</tr>
<tr>
<td>13</td>
<td>Surgery</td>
<td>Academic</td>
<td>Aware</td>
<td>30</td>
<td>30 %</td>
</tr>
<tr>
<td>14</td>
<td>Medical Oncology</td>
<td>Private</td>
<td>Aware</td>
<td>21</td>
<td>10 %</td>
</tr>
<tr>
<td>15</td>
<td>Medical Oncology</td>
<td>Private</td>
<td>Adherent</td>
<td>10</td>
<td>30 %</td>
</tr>
<tr>
<td>16</td>
<td>Medical Oncology</td>
<td>Private</td>
<td>Adherent</td>
<td>25</td>
<td>25 %</td>
</tr>
<tr>
<td>17</td>
<td>Medical Oncology</td>
<td>Private</td>
<td>Agreement</td>
<td>30</td>
<td>10 %</td>
</tr>
<tr>
<td>18</td>
<td>Surgery</td>
<td>Academic</td>
<td>Aware</td>
<td>5</td>
<td>25 %</td>
</tr>
<tr>
<td>19</td>
<td>Surgery</td>
<td>Private</td>
<td>Aware</td>
<td>25</td>
<td>50 %</td>
</tr>
<tr>
<td>20</td>
<td>Medical Oncology</td>
<td>Academic</td>
<td>Aware</td>
<td>2</td>
<td>100 %</td>
</tr>
</tbody>
</table>

A total of 20 participants in the tailoring grid interviews regarding referral practices for CS/HIPEC. Participants were chosen based on medical specialty and nature of practice (academic versus private practice). Classification of current position is participant’s self-reported position within Pathman’s 4 A’s of Awareness, agreement, adoption, adherence.
Table 2: Representation of Tailoring Grid responses in final survey questions

This table provides a summary of themes and topics from tailoring grid interviews, classified according to Pathman 4 A’s and Grol level at which each was felt to work. The survey question that reflects the barrier or facilitator is identified and referenced.

<table>
<thead>
<tr>
<th>Topic</th>
<th>Individual</th>
<th>Social</th>
<th>Organizational</th>
<th>Reflected in Survey Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Awareness</td>
<td>Interaction with colleagues</td>
<td>-Solo practice</td>
<td>-Exposure to trainees</td>
<td>10/11/14/15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-Use of conferences and other resources to keep up to date of new techniques</td>
<td>-MCC availability at center</td>
<td></td>
</tr>
<tr>
<td>Advertising / Marketing</td>
<td></td>
<td></td>
<td>-Training at center that offers HIPEC procedure</td>
<td>9/13</td>
</tr>
<tr>
<td>Lack of knowledge and indications</td>
<td>-Personal thoughts regarding futility, unaware of potential benefit of procedure</td>
<td>-General surgeons consulted intraoperatively for carcinomatosis by other surgeons/gynecologists can be overly aggressive with debulking, etc, knowledge gap</td>
<td>12/16</td>
<td></td>
</tr>
<tr>
<td>Agreement</td>
<td>Published studies: issues with design</td>
<td>-Personal interpretation of results, inability to compare with personal patient population</td>
<td>-Lack of appropriate study design by agencies and groups, lack of accrual to studies make for slow results and outdated systemic treatments being used</td>
<td>17</td>
</tr>
<tr>
<td>Carcinomatosis as a systemic disease</td>
<td></td>
<td>-Training / practice group interpretation of futility of treatment of carcinomatosis, treatment must be a systemic treatment as carcinomatosis is a systemic disease</td>
<td></td>
<td>18</td>
</tr>
<tr>
<td>Adoption</td>
<td>Cytoreduction/HIPEC surgeon profile</td>
<td>-Availability and accessibility of HIPEC surgeon to referring physicians</td>
<td>-Reputation of HIPEC surgeon in community / area where he or she practices vs. being an “unknown”</td>
<td>19,21</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-Having ability to obtain prompt feedback regarding a patient and candidacy (phone call, email)</td>
<td>-Outcomes of individual surgeons and cytoreduction/HIPEC programs not readily available (both surgical and oncologic)</td>
<td></td>
</tr>
<tr>
<td>Lack of reflection of cytoreduction/HIPEC in treatment algorithm</td>
<td>-Personal algorithm may not include HIPEC due to low volume of</td>
<td></td>
<td>19,21</td>
<td></td>
</tr>
<tr>
<td>Category</td>
<td>Description</td>
<td>Reference(s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>--------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morbidity/Mortality associated with procedure</td>
<td>Historically was felt to have high morbidity and mortality, deemed “outlier” or “overly aggressive” in the past and this reputation has not changed in some practice groups</td>
<td>19, 20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adherence</td>
<td>Lack of reflection of cytoreduction/HIPEC in clinical practice guidelines (CPGs) - Associated with personal algorithm issue in Adoption barriers; no obviously recommended time to consider</td>
<td>25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Financial concerns</td>
<td>- Resource intensive, many hospital and center resources used for these patients - Insurance denials as “experimental” in CPGs, not widely accepted</td>
<td>26</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality measures/outcomes</td>
<td>- Individual practitioner (potentially referring) has connection to patient, trust they will be sent to a surgeon with good outcomes - No accepted threshold of morbidity, mortality, what a center requires to be a “HIPEC” center</td>
<td>24, 25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Logistics of referrals</td>
<td>- Workflow issues, hassles with referrals, what to do if referring physician is unsure of referring a patient or not - Lack of correspondence from HIPEC surgeon - No electronic platform by which to provide notes and review records – would make referral process easier especially with complicated patients</td>
<td>23, 25</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 3: Demographics of survey respondents

Demographics and practice characteristics of survey respondents, including 42 medical oncologists and 77 surgeons (colorectal, general surgery and surgical oncology). P-value of <0.05 indicates statistical significance.

<table>
<thead>
<tr>
<th>Question</th>
<th>Medical Oncology</th>
<th>Surgery</th>
<th>Overall</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>42 (35.3 %)</td>
<td>77 (64.7 %)</td>
<td>119</td>
<td></td>
</tr>
<tr>
<td><strong>1) nature of current practice</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private or Community Practice</td>
<td>35 (59.5 %)</td>
<td>31 (40.3 %)</td>
<td>56 (47.1 %)</td>
<td>0.06</td>
</tr>
<tr>
<td>Academic Practice</td>
<td>17 (40.5 %)</td>
<td>46 (59.7 %)</td>
<td>63 (52.9 %)</td>
<td></td>
</tr>
<tr>
<td><strong>2) years in practice</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trainee</td>
<td>3 (7.1 %)</td>
<td>7 (9.1 %)</td>
<td>10 (8.4 %)</td>
<td>0.63</td>
</tr>
<tr>
<td>0-5 years</td>
<td>4 (9.5 %)</td>
<td>14 (18.2 %)</td>
<td>18 (15.1 %)</td>
<td></td>
</tr>
<tr>
<td>Between 5-10 years</td>
<td>5 (11.9 %)</td>
<td>5 (6.5 %)</td>
<td>10 (8.4 %)</td>
<td></td>
</tr>
<tr>
<td>Greater than 10 years</td>
<td>26 (61.9 %)</td>
<td>44 (57.1 %)</td>
<td>70 (58.8 %)</td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>4 (9.5 %)</td>
<td>7 (9.1 %)</td>
<td>11 (9.2 %)</td>
<td></td>
</tr>
<tr>
<td><strong>3) training setting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private or community practice</td>
<td>8 (19.0 %)</td>
<td>8 (10.4 %)</td>
<td>16 (13.4 %)</td>
<td>0.29</td>
</tr>
<tr>
<td>Academic or university-based practice</td>
<td>7 (16.7 %)</td>
<td>20 (26.0 %)</td>
<td>27 (22.7 %)</td>
<td></td>
</tr>
<tr>
<td>Academic or university-based practice associated with a cancer center</td>
<td>27 (64.3 %)</td>
<td>49 (63.6 %)</td>
<td>76 (63.9 %)</td>
<td></td>
</tr>
<tr>
<td><strong>4) proportion of GI cancer patients in current practice</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>3 (7.1 %)</td>
<td>4 (5.2 %)</td>
<td>7 (5.9 %)</td>
<td>0.009</td>
</tr>
<tr>
<td>Less than 10 %</td>
<td>10 (23.8 %)</td>
<td>21 (27.3 %)</td>
<td>31 (26.1 %)</td>
<td></td>
</tr>
<tr>
<td>10-50 %</td>
<td>24 (57.1 %)</td>
<td>24 (31.2 %)</td>
<td>48 (40.3 %)</td>
<td></td>
</tr>
<tr>
<td>Greater than 50 %</td>
<td>5 (11.9 %)</td>
<td>28 (36.4 %)</td>
<td>33 (27.2 %)</td>
<td></td>
</tr>
<tr>
<td><strong>5) medical specialty</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical Oncology</td>
<td>41 (97.6 %)</td>
<td></td>
<td>34.5 %</td>
<td></td>
</tr>
<tr>
<td>Surgical Oncology</td>
<td>42 (54.5 %)</td>
<td></td>
<td>35.3 %</td>
<td></td>
</tr>
<tr>
<td>Gastroenterology</td>
<td>1 (2.4 %)</td>
<td></td>
<td>0.8 %</td>
<td></td>
</tr>
<tr>
<td>General Surgery</td>
<td>24 (31.2 %)</td>
<td>20.2 %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colorectal Surgery</td>
<td>11 (14.3 %)</td>
<td>9.2 %</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 4: Respondents’ position with respect to Pathman 4 A’s

Self-reported position of respondents within Pathman’s framework of 4 A’s of awareness, agreement, adoption and adherence to referrals for CS/HIPEC, p-value of < 0.05 is considered significant.

<table>
<thead>
<tr>
<th></th>
<th>Medical Oncology</th>
<th>Surgery</th>
<th>Overall</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aware</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>38 (90.5 %)</td>
<td>75 (97.4 %)</td>
<td>113 (95.0 %)</td>
<td>0.18</td>
</tr>
<tr>
<td>No</td>
<td>4 (9.5 %)</td>
<td>2 (2.6 %)</td>
<td>6 (5.0 %)</td>
<td></td>
</tr>
<tr>
<td><strong>Agree</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>32 (76.2 %)</td>
<td>71 (92.2 %)</td>
<td>103 (86.6 %)</td>
<td>0.02</td>
</tr>
<tr>
<td>No</td>
<td>10 (23.8 %)</td>
<td>6 (7.8 %)</td>
<td>16 (13.4 %)</td>
<td></td>
</tr>
<tr>
<td><strong>Adoption</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>26 (61.9 %)</td>
<td>57 (74.0 %)</td>
<td>83 (69.7 %)</td>
<td>0.21</td>
</tr>
<tr>
<td>No</td>
<td>16 (38.1 %)</td>
<td>20 (26.0 %)</td>
<td>36 (30.3 %)</td>
<td></td>
</tr>
<tr>
<td><strong>Adherent</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>17 (48.6 %)</td>
<td>39 (56.5 %)</td>
<td>56 (53.8 %)</td>
<td>0.53</td>
</tr>
<tr>
<td>No</td>
<td>18 (51.4 %)</td>
<td>30 (43.5 %)</td>
<td>48 (46.2 %)</td>
<td></td>
</tr>
</tbody>
</table>
Table 5: Awareness questions

Numbers and frequency of answers to awareness barrier questions in survey. P-value of < 0.05 is considered significant.

<table>
<thead>
<tr>
<th>Respondents</th>
<th>Medical Oncology</th>
<th>Surgery</th>
<th>Overall</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keeping up to date of new treatments</td>
<td>National/International Meetings</td>
<td>28 (67.0 %)</td>
<td>63 (87.5 %)</td>
<td>91 (82.0 %)</td>
</tr>
<tr>
<td></td>
<td>Journal articles or reviews</td>
<td>38 (97.4 %)</td>
<td>65 (90.3 %)</td>
<td>103 (92.8 %)</td>
</tr>
<tr>
<td></td>
<td>Electronic resources</td>
<td>33 (84.6 %)</td>
<td>52 (72.2 %)</td>
<td>85 (76.6 %)</td>
</tr>
<tr>
<td></td>
<td>Trainee/Colleague interactions</td>
<td>18 (46.1 %)</td>
<td>43 (59.7 %)</td>
<td>61 (55.0 %)</td>
</tr>
<tr>
<td></td>
<td>Flyers/advertisements</td>
<td>0</td>
<td>4 (5.6 %)</td>
<td>4 (3.6 %)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>3 (7.7 %)</td>
<td>2 (2.8 %)</td>
<td>5 (4.5 %)</td>
</tr>
<tr>
<td>MCCs</td>
<td>Regularly attend</td>
<td>27 (69.2 %)</td>
<td>60 (83.3 %)</td>
<td>87 (78.4 %)</td>
</tr>
<tr>
<td></td>
<td>Rarely/infrequently attend</td>
<td>6 (15.4 %)</td>
<td>3 (4.2 %)</td>
<td>9 (8.1 %)</td>
</tr>
<tr>
<td></td>
<td>Informal meetings with colleagues</td>
<td>2 (5.1 %)</td>
<td>5 (6.9 %)</td>
<td>7 (6.3 %)</td>
</tr>
<tr>
<td></td>
<td>No discussion</td>
<td>4 (10.3 %)</td>
<td>4 (5.6 %)</td>
<td>8 (7.2 %)</td>
</tr>
<tr>
<td>Exposure to trainees</td>
<td>Regular exposure</td>
<td>22 (56.4 %)</td>
<td>50 (69.4 %)</td>
<td>72 (64.9 %)</td>
</tr>
<tr>
<td></td>
<td>Infrequent/occasional</td>
<td>8 (20.5 %)</td>
<td>14 (19.4 %)</td>
<td>22 (19.8 %)</td>
</tr>
<tr>
<td></td>
<td>No exposure</td>
<td>7 (17.9 %)</td>
<td>3 (4.2 %)</td>
<td>10 (9.0 %)</td>
</tr>
<tr>
<td></td>
<td>Current trainee</td>
<td>2 (5.1 %)</td>
<td>5 (6.9 %)</td>
<td>7 (6.3 %)</td>
</tr>
<tr>
<td>Vignette (Med Onc, q12)</td>
<td>Surgery to resect primary tumor</td>
<td>18 (46.1 %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>First-line chemotherapy</td>
<td>22 (56.4 %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Re-referral for resection of primary tumor after chemo</td>
<td>15 (38.5 %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Surgery only if emergency occurs</td>
<td>3 (7.7 %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>3 (7.7 %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vignette (Surgery, q 16)</td>
<td>Complete TAH/BSO</td>
<td></td>
<td>20 (27.8 %)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Resect cecal mass</td>
<td>22 (30.6 %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cytoreduce patient</td>
<td>35 (48.6 %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Biopsy</td>
<td>45 (62.5 %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Explore abdomen</td>
<td>47 (65.3 %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Do nothing, close</td>
<td>5 (6.9 %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Consult Med Onc</td>
<td>34 (47.2 %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>17 (23.6 %)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 Other = CS/HIPEC (2); tumor board (1)

2 Other = CS/HIPEC (9); refer to specialist (4), colonoscopy/further workup (2); not applicable to my practice (2)
Table 6: Agreement questions

Numbers and frequency of answers to barriers to agreement questions in survey. P-value of < 0.05 is considered significant.

<table>
<thead>
<tr>
<th>Respondents</th>
<th>Medical Oncology</th>
<th>Surgery</th>
<th>Overall</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Interpretation of available published literature in CS/HiPEC</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Literature limited to retrospective studies and poor quality prospective studies</td>
<td>12 (31.6 %)</td>
<td>35 (50.0 %)</td>
<td>47 (43.5 %)</td>
<td>0.08</td>
</tr>
<tr>
<td>Literature includes good prospective studies including RCTs</td>
<td>3 (7.9 %)</td>
<td>19 (27.1 %)</td>
<td>22 (20.4 %)</td>
<td>0.03</td>
</tr>
<tr>
<td>Literature biased towards patients with good PFS, tumor biology, and low volume carcinomatosis</td>
<td>14 (36.8 %)</td>
<td>23 (32.9 %)</td>
<td>37 (34.3 %)</td>
<td>0.84</td>
</tr>
<tr>
<td>Comparisons between groups in trials not relevant to current practice (outdated chemotherapy, non-standardized surgical approaches)</td>
<td>6 (15.8 %)</td>
<td>10 (14.3 %)</td>
<td>16 (14.8 %)</td>
<td>1.00</td>
</tr>
<tr>
<td>None of the above</td>
<td>9 (23.7 %)</td>
<td>13 (18.6 %)</td>
<td>22 (20.4 %)</td>
<td>0.62</td>
</tr>
<tr>
<td><strong>Application of CS/HiPEC procedure to patients with carcinomatosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinomatosis is stage IV, disseminated, and treatment can only include systemic chemotherapy</td>
<td>2 (5.3 %)</td>
<td>4 (5.7 %)</td>
<td>6 (5.6 %)</td>
<td>0.25</td>
</tr>
<tr>
<td>Select patients have good outcomes with CS/HiPEC, and likely with all therapies</td>
<td>19 (50.0 %)</td>
<td>25 (35.7 %)</td>
<td>44 (40.7 %)</td>
<td></td>
</tr>
<tr>
<td>Unclear role of intraperitoneal chemotherapy, surgery can deal with carcinomatosis</td>
<td>3 (7.9 %)</td>
<td>15 (21.4 %)</td>
<td>18 (16.7 %)</td>
<td></td>
</tr>
<tr>
<td>None of the above</td>
<td>13 (34.2 %)</td>
<td>27 (38.6 %)</td>
<td>40 (37.0 %)</td>
<td></td>
</tr>
</tbody>
</table>
Table 7: Adoption questions
Numbers and frequency of answers to barriers to adoption questions in survey. P-value of < 0.05 is considered significant.

<table>
<thead>
<tr>
<th>Respondents</th>
<th>Medical Oncology</th>
<th>Surgery</th>
<th>Overall</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>38</td>
<td>69</td>
<td>105</td>
<td></td>
</tr>
<tr>
<td><strong>Barriers to adopting referral plan</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low appropriate patient volume</td>
<td>11 (28.9 %)</td>
<td>24 (34.8 %)</td>
<td>35 (33.3 %)</td>
<td>0.68</td>
</tr>
<tr>
<td>Low volume of patients that fit criteria CS/HIPEC</td>
<td>14 (36.8 %)</td>
<td>15 (21.7 %)</td>
<td>29 (27.6 %)</td>
<td>0.12</td>
</tr>
<tr>
<td>Do not know where / to whom to refer</td>
<td>7 (18.4 %)</td>
<td>4 (5.8 %)</td>
<td>11 (10.5 %)</td>
<td>0.05</td>
</tr>
<tr>
<td>Do not have resource to discuss</td>
<td>5 (13.2 %)</td>
<td>4 (5.8 %)</td>
<td>9 (8.6 %)</td>
<td>0.28</td>
</tr>
<tr>
<td>Unsure of patient benefit</td>
<td>8 (21.1 %)</td>
<td>8 (11.6 %)</td>
<td>16 (15.2 %)</td>
<td>0.26</td>
</tr>
<tr>
<td>CS/HIPEC centers far distance</td>
<td>7 (18.4 %)</td>
<td>7 (10.1 %)</td>
<td>14 (13.3 %)</td>
<td>0.24</td>
</tr>
<tr>
<td>Concern regarding morbidity/mortality</td>
<td>14 (36.8 %)</td>
<td>12 (17.4 %)</td>
<td>26 (24.8 %)</td>
<td>0.04</td>
</tr>
<tr>
<td>None of the above</td>
<td>9 (23.7 %)</td>
<td>33 (47.8 %)</td>
<td>42 (40.0 %)</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Thoughts regarding patients with carcinomatosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment is futile with or without treatment</td>
<td>1 (2.6 %)</td>
<td>4 (5.8 %)</td>
<td>5 (4.8 %)</td>
<td>0.53</td>
</tr>
<tr>
<td>Only efficacious treatment is systemic chemotherapies</td>
<td>1 (2.6 %)</td>
<td>0</td>
<td>1 (1.0 %)</td>
<td></td>
</tr>
<tr>
<td>All patients should receive systemic chemotherapies, select group considered for CS/HIPEC</td>
<td>28 (73.7 %)</td>
<td>51 (73.9 %)</td>
<td>79 (75.2 %)</td>
<td></td>
</tr>
<tr>
<td>None of the above</td>
<td>6 (15.8 %)</td>
<td>14 (20.3 %)</td>
<td>20 (19.0 %)</td>
<td></td>
</tr>
<tr>
<td><strong>Vignette (q 21)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediately following surgery</td>
<td>8 (21.1 %)</td>
<td>18 (26.1 %)</td>
<td>26 (24.8 %)</td>
<td>0.35</td>
</tr>
<tr>
<td>After 3 months chemo</td>
<td>7 (18.4 %)</td>
<td>5 (7.2 %)</td>
<td>12 (11.4 %)</td>
<td></td>
</tr>
<tr>
<td>After 6 months chemo</td>
<td>2 (5.3 %)</td>
<td>8 (11.6 %)</td>
<td>10 (9.5 %)</td>
<td></td>
</tr>
<tr>
<td>After 6 months chemo and rescan</td>
<td>5 (13.2 %)</td>
<td>14 (20.3 %)</td>
<td>19 (18.1 %)</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>4 (10.5 %)</td>
<td>11 (15.9 %)</td>
<td>15 (14.3 %)</td>
<td></td>
</tr>
<tr>
<td>Not sure</td>
<td>10 (26.3 %)</td>
<td>13 (18.8 %)</td>
<td>23 (21.9 %)</td>
<td></td>
</tr>
</tbody>
</table>
Table 8: Adherence questions

Numbers and frequency of answers to barriers to adherence questions in survey. P-value of < 0.05 is considered significant.

<table>
<thead>
<tr>
<th></th>
<th>Medical Oncology</th>
<th>Surgery</th>
<th>Overall</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>17</td>
<td>39</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td><strong>What has/could make logistics of referral easier?</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Knowing surgeon/practice group by name, location, reputation</td>
<td>13 (81.3 %)</td>
<td>25 (64.1 %)</td>
<td>38 (69.1 %)</td>
</tr>
<tr>
<td></td>
<td>Having contact person for questions</td>
<td>12 (75.0 %)</td>
<td>15 (38.5 %)</td>
<td>27 (49.1 %)</td>
</tr>
<tr>
<td></td>
<td>Response to referral within 24-48 hrs</td>
<td>6 (37.5 %)</td>
<td>8 (20.5 %)</td>
<td>14 (25.5 %)</td>
</tr>
<tr>
<td></td>
<td>Standardized referral form for submission</td>
<td>4 (25.0 %)</td>
<td>6 (15.4 %)</td>
<td>10 (18.2 %)</td>
</tr>
<tr>
<td><strong>What characterizes experience of patients having undergone CS/HIPEC?</strong></td>
<td>Good results, surgically and oncologically</td>
<td>7 (43.8 %)</td>
<td>14 (35.9 %)</td>
<td>21 (38.2 %)</td>
</tr>
<tr>
<td></td>
<td>Complications, but good oncologic results</td>
<td>5 (31.3 %)</td>
<td>15 (38.5 %)</td>
<td>20 (36.4 %)</td>
</tr>
<tr>
<td></td>
<td>Complications and no good oncologic results</td>
<td>0</td>
<td>2 (5.1 %)</td>
<td>2 (3.6 %)</td>
</tr>
<tr>
<td></td>
<td>Not deemed candidates</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>None of the above</td>
<td>4 (25.0 %)</td>
<td>8 (20.5 %)</td>
<td>12 (21.8 %)</td>
</tr>
<tr>
<td><strong>What may change number or frequency of referrals most?</strong></td>
<td>Inclusion of procedure into CPGs</td>
<td>7 (43.8 %)</td>
<td>18 (46.2 %)</td>
<td>25 (45.5 %)</td>
</tr>
<tr>
<td></td>
<td>Having quality measures for outcomes data</td>
<td>2 (12.5 %)</td>
<td>9 (23.1 %)</td>
<td>11 (20.0 %)</td>
</tr>
<tr>
<td></td>
<td>Having common info platform</td>
<td>1 (6.3 %)</td>
<td>2 (5.1 %)</td>
<td>3 (5.5 %)</td>
</tr>
<tr>
<td></td>
<td>Having CS/HIPEC surgeon at my center</td>
<td>3 (18.8 %)</td>
<td>2 (5.1 %)</td>
<td>5 (9.1 %)</td>
</tr>
<tr>
<td></td>
<td>Continuing to be involved in my patient’s care</td>
<td>0</td>
<td>2 (5.1 %)</td>
<td>2 (3.6 %)</td>
</tr>
</tbody>
</table>
and treatments

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other(^2)</td>
<td>3 (18.8 %)</td>
<td>6 (15.4 %)</td>
<td>9 (16.4 %)</td>
</tr>
</tbody>
</table>

**Financial aspects of CS/HIPEC**

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS/HIPEC is costly and resource intensive</td>
<td>2 (12.5 %)</td>
<td>8 (20.5 %)</td>
<td>10 (18.2 %)</td>
</tr>
<tr>
<td>Unaware of return on investment</td>
<td>6 (37.5 %)</td>
<td>12 (30.8 %)</td>
<td>18 (32.7 %)</td>
</tr>
<tr>
<td>Patients experience stress due to denials</td>
<td>0</td>
<td>3 (7.7 %)</td>
<td>3 (5.5 %)</td>
</tr>
<tr>
<td>Current chemo is as costly as CS/HIPEC</td>
<td>0</td>
<td>4 (10.3 %)</td>
<td>4 (7.3 %)</td>
</tr>
<tr>
<td>None of the above</td>
<td>8 (50.0 %)</td>
<td>12 (30.8 %)</td>
<td>20 (36.4 %)</td>
</tr>
</tbody>
</table>

\(^1\)ranked “most important”\(^2\) Other = more evidence (5); nothing, I already refer as frequently as I can (4)
Figure 1: Map of Upstate New York
Map of counties in Upstate New York, including the number of NYS Department of Health reported new cases of colon cancer from 2006-2010, and the number of patients overall referred for opinion of CS/HIPEC to Roswell Park Cancer Institute from 2008-2013. Based on prior analyses, approximately 50% of CS/HIPEC referrals to Roswell Park Cancer Institute are for colorectal cancers.
The Knowledge-to-Action (KTA) cycle including two parts: the knowledge creation portion (central funnel of inquiry, synthesis and tools or products involving tailoring knowledge) and knowledge action portion (adapting in a local context, evaluation of barriers, implementing, evaluating and sustaining knowledge use). Note this process is dynamic.
Figure 3: Tailoring Grid results
Topics emerging from tailoring grid interviews, sub-classified based on Pathman’s 4 A’s of awareness, agreement, adoption and adherence. Further subdivision based on Grol levels of individual practicing clinician, social/practice group, organization.
Figure 4: Timing of survey responses

# Appendix A: Final Version Tailoring Grid

## Principles

<table>
<thead>
<tr>
<th>Physician Position</th>
<th>BARRIERS / FACILITATORS – Tailoring Grid</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aware, Agree, Adopt, Adhere</strong></td>
<td><strong>Individual</strong></td>
</tr>
<tr>
<td>- Knowledge</td>
<td>- Pressure from other surgical or medical colleagues</td>
</tr>
<tr>
<td>- Lack of evidence, relevance</td>
<td>- Pressure or resistance from other disciplines</td>
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<tr>
<td>- Workload pressure</td>
<td>- Patient preference</td>
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### Principle: Cytoreduction/HIPEC may be an appropriate treatment option for patients with peritoneal metastases

- Are you **aware** that cytoreduction/HIPEC exists as a treatment option for patients with peritoneal metastases /carcinomatosis?
- Are you **aware** of which patients may benefit from this procedure?
- Are you **aware** of what centers in your state offer this procedure?

### Principle: Referral to a center offering cytoreduction/HIPEC for select patients for an opinion may be appropriate during other therapies (chemotherapy)

- Do you **agree** with the adequacy of published literature regarding cytoreduction/HIPEC?
- Do you **agree** with available trials comparing cytoreduction/HIPEC to standard IV chemotherapy?

- Have you **adopted** the plan of referring select patients in your practice for cytoreduction/HIPEC?
At what point in a patient’s treatment have you **adopted** the practice of considering referring for an opinion regarding cytoreduction/HIPEC?

If you had initially **adopted** referring patients for the procedure, and then stopped, why did this happen?

**Principle:** Sustained / ongoing referral practice for cytoreduction/HIPEC, receiving input and feedback from surgeons completing the procedure to assist in further refinement of referral practices

Did any of the patients you have referred or have seen referred for cytoreduction/HIPEC have significant complications, resulting in a change in your opinion of the procedure? [adherence]

Do you face any barriers or roadblocks to referral for cytoreduction/HIPEC that affects the number or frequency of referrals for this procedure? [adherence]

---

**Final tailoring grid structure used for interviews of 20 participants, this grid included the structure of Pathman’s 4 A’s of awareness, agreement, adoption, adherence with the Grol “level” in which the issue was felt to be working, namely the individual clinician level, practice group, or organization.**
Appendix B: Ethics approval documents from RPCI and McMaster University

From: Malema, Ayoma
Sent: Thursday, April 18, 2013 1:53 PM
To: Francescutti, Valerie
Cc: Pantano, Janet; Brady, William; Singh, Deepnepaul
Subject: I 235113- Initial Submission Activation

I 235113 - Barriers and Facilitators to Referral in Cytoreduction / Hyperthermic Intraperitoneal Chemotherapy (HIPEC) in Patients with Peritoneal Surface Malignancies--Initial Submission has been IRB approved and is now active and open to patient accrual.

The study materials are now available on the clinical trials website.

RRA – please check the web and email me back along with a cc to Jan Pantano verifying accuracy.

Best wishes,

Ayoma Malema

Clinical Research Associate I
Roswell Park Cancer Institute
CRS Compliance Office
Phone: 716-845-1094
SRC FINAL APPROVAL MEMORANDUM

INVESTIGATOR NAME: Valerie Francescutti, MD

FROM: Mary Reid, Ph.D., Meir Wetzler, M.D.
Co-Chairs; Scientific Review Committee

DATE: 04/09/2013

STUDY #/ TITLE:
I235113- Barriers and Facilitators to Referral in Cytoreduction / Hyperthermic Intraperitoneal Chemotherapy (HIPEC) in Patients with Peritoneal Surface Malignancies

The Executive Board of the Scientific Review Committee reviewed the above mentioned study on 03/20/2013

Your study received final approval on 04/04/2013
The dated documents below will be sent to ORSP for IRB review.

Protocol dated: 3/25/13

Consent V.1 dated: N/A

Confirmation of Approval: R. Schiske for L. Musial, RN, MS, CCRP, AVP; CRS Date 04/09/13
Laurie Musial, RN, MS, CCRP; AVP Clinical Research Services or Designee
**Amendment Approval**

<table>
<thead>
<tr>
<th>Date:</th>
<th>03 December 2013</th>
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<tbody>
<tr>
<td>REB Number:</td>
<td>13-358-S</td>
</tr>
<tr>
<td>Title of Study:</td>
<td>Barriers and facilitators to referral in cytoreduction/hyperthermic intraperitoneal chemotherapy (HIPEC) in patients with peritoneal surface malignancies.</td>
</tr>
<tr>
<td>Student PI:</td>
<td>Valerie Francescutti</td>
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<tr>
<td>LPI:</td>
<td>Marko Simunovic</td>
</tr>
<tr>
<td>Comments:</td>
<td></td>
</tr>
<tr>
<td>Version date:</td>
<td></td>
</tr>
<tr>
<td>25 Nov 2013</td>
<td>Protocol Amendment</td>
</tr>
<tr>
<td>08 Nov 2013</td>
<td>HIPEC Survey</td>
</tr>
</tbody>
</table>

Dear Valerie:

We have completed our review of your amendment and are pleased to issue our final approval. You may now continue your study as amended.

All recruitment and consent material must bear an REB stamp. You may pick up the stamped forms from our office. If you need to make changes to any of these documents, please submit them for review as an amendment.

Please cite the REB number in any correspondence.

Good luck with your research,

Kristina Trim, PhD, RSW
Chair, HiREB Student Research Committee
Health Research Services, HSC 1B7, McMaster University
Dear participant,

Thank you for considering participating in this research project. The focus of this project is to clarify possible barriers or facilitators to referral for the cytoreduction and heated intraperitoneal chemotherapy (HIPEC) procedure. This procedure is gaining popularity, but referral practices are still unclear, in terms of choice of patient and timing of referral.

You have been chosen as a prospective participant due to the characteristics of your current practice. Other medical oncologists and surgeons in your center or community may be approached as well for participation. The methodology for this interview-based project is to use a structured “tailoring grid” to determine common themes of barriers to referral, and conversely, facilitators of referral of patients with carcinomatosis to a center offering cytoreduction/HIPEC.

If you choose to participate, your identity will be kept confidential, and you will never be referred to by name or practice name. The themes collected from my interview with you will be combined with those collected by me from other clinicians, and combined in an overall summary, for eventual translation into a survey of medical oncologists and surgeons in the Western New York area. You will not be compensated financially or otherwise for participation in this study.

Although you have been approached as a potential subject for the study, if you decide to not participate, there will be no ramifications.

Thank you for your consideration,

Sincerely

Valerie Francesc Cutti, MD

Roswell Park Cancer Institute
Appendix D: Final Draft of Survey

A final draft of the survey available on Survey Monkey™. All demographic questions (1-8) answered by all participants, and using skip logic, questions 9-12 and 17-21 completed by medical oncologists, 13-16 and 17-21 completed by surgeons. Those answering “yes” to Question 22 (adoption question) completed questions 23-26.

### Barriers to referral for Cytoreduction / HIPEC

1. What is the nature of your current practice?
   - J. Private or Community Practice
   - J. Academic Practice

2. How many years have you been in practice?
   - J. I am a trainee
   - J. 0-5 years
   - J. Between 6-10 years
   - J. Greater than 10 years
   - J. Retired

3. In what setting are you completing or did you complete your highest level of training?
   - J. Private or community-based practice
   - J. Academic or university-centered practice
   - J. Academic or university-centered practice associated with a cancer center

4. What proportion of patients within your practice have primary abdominal cancers (including colorectal, appendiceal, upper gastrointestinal)?
   - J. None
   - J. Less than 10%
   - J. Between 10-50%
   - J. Greater than 50%

5. I am aware that surgical cytoreduction and heated intraperitoneal chemotherapy (CS / HIPEC) is a therapeutic option for patients with gastrointestinal or peritoneal based cancers.
   - J. Yes
   - J. No

6. I agree with the concept of cytoreduction/HIPEC would refer an appropriately selected patient for this procedure.
   - J. Yes
   - J. No
7. I have adopted the practice of referring patients for cytoreduction/HIPEC in my current practice, or in the past.
   - Yes
   - No

8. What is the nature of your medical specialty?
   - Medical Oncology
   - Surgical Oncology
   - Gastroenterology
   - General Surgery
   - Colorectal Surgery
**9. How do you keep up to date of new treatment options for your patients and where such treatments may be offered? (Check ALL that apply)**

- I attend national or international meetings related to my specialty
- I read articles in journals related to my area of specialization (clinical trials, reviews)
- I utilize electronic resources including websites, and email alerts of new technologies
- I rely on interactions with trainees and colleagues
- I rely on flyers and advertisements
- Other (please specify)

**10. Regarding the care of cancer patients in your practice:**

- I attend regularly scheduled multidisciplinary cancer conferences (MCC)
- MCCs are available but I infrequently or rarely attend
- We have informal meetings within my practice group where we discuss cancer patients, but no organized MCC
- I do not participate in any formal or informal discussion of my cancer patients with colleagues

**11. Regarding your current exposure to trainees (undergraduate students, medical students, residents, fellows):**

- I have regular exposure and teaching responsibilities of trainees both in my practice and facility
- I have infrequent exposure to trainees in my practice and facility, with occasional teaching responsibilities
- I never have exposure to trainees
- I am currently a trainee
12. You are referred a 53 yo female who was found intraoperatively during a gynecologic surgical procedure to have a transverse colon mass with very limited peritoneal carcinomatosis. Biopsies were taken at the time of exploration, and are consistent with a colonic adenocarcinoma. Staging imaging indicates no evidence of visceral metastases. The patient is asymptomatic. What do you recommend (select ALL you would recommend)?

- Surgery to resect the primary tumor
- Start the patient on first line chemotherapy as soon as adequate recovery from initial exploration
- If the patient has a response to systemic chemotherapy, consider rereferral back to surgeon for resection of primary tumor
- This patient will only be a surgical candidate if an emergency occurs (ex: obstruction, bleeding)
- Other (please specify)
13. How do you keep up to date of new treatment options for your patients and where such treatments may be offered? (Check ALL that apply)
   a. I attend national or international meetings related to my specialty
   b. I read articles in journals related to my area of specialization (clinical trials, reviews)
   c. I utilize electronic resources including websites, and email alerts of new technologies
   d. I rely on interactions with trainees and colleagues
   e. I rely on flyers and advertisements
   f. Other (please specify)

14. Regarding the care of cancer patients in your practice:
   j. I attend regularly scheduled multidisciplinary cancer conferences (MCC)
   k. MCCs are available but I infrequently or rarely attend
   l. We have informal meetings within my practice group where we discuss cancer patients, but no organized MCC
   m. I do not participate in any formal or informal discussion of my cancer patients with colleagues

15. Regarding your current exposure to trainees:
   j. I have regular exposure and teaching responsibilities of trainees both in my practice and facility
   k. I have infrequent exposure to trainees in my practice and facility, with occasional teaching responsibilities
   l. I never have exposure to trainees
   m. I am currently a trainee
16. You are called into the operating room by your gynecology colleague. His patient is a 53 yo female, for which he planned to complete a hysterectomy and bilateral salpingo oophorectomy for treatment of an ovarian mass. The patient has intraoperative findings of disseminated carcinomatosis, similar to implants found on the ovari. There appears to be a mass involving the cecum that is nonobstructing. What do you recommend (select ALL you would recommend)?

- Complete the TAH-BSO
- Resect the pelvic mass
- Cytoreduce patient (TAH-BSO, resect pelvic mass, remove any peritoneal nodules)
- Biopsy peritoneal nodules, obtain frozen section if possible
- Explore the abdomen (assess liver, diaphragm, pelvis, etc)
- Do nothing, close
- Consult medical oncology postoperatively
- Other (please specify)

[ ]
17. The following reflect my feelings regarding the available published literature in the area of cytoreduction / HIPEC (select ALL that apply):

a. The literature is limited to retrospective studies and poor quality prospective studies
b. The literature includes good prospective studies including randomized controlled trials (RCTs)
c. The literature is biased to patients with good performance status, good tumor biology, low volume carcinomatosis
d. Comparisons between treatment groups in trials are not relevant to current practice (systemic chemotherapy agents used), non-standardized surgical approaches for cytoreduction
e. None of the above

18. Regarding my interpretation of the cytoreduction/HIPEC procedure and its applications:

f. Carcinomatosis is Stage IV cancer, is disseminated, and therefore treatment can only involve systemic therapy (IV chemotherapy)
g. Select patients that have good outcomes with cytoreduction/HIPEC would likely have good results with all therapies
h. It is unclear what intraperitoneal chemotherapy adds to cytoreduction, surgery can deal with carcinomatosis if resectable
i. None of the above
19. **Significant barriers to adopting a referral plan for my patients for cytoreduction/HIPEC include (select ALL that apply):**

- I do not see enough patients in my practice that would be potential candidates related to volume of specific patients
- I do not see enough patients in my practice that fit the criteria for the procedure
- I do not know where or to whom to refer (which surgeon, which facility, outcomes)
- I do not have a resource with whom I can discuss potential referrals, either in person (at multidisciplinary conferences) or over the telephone
- I am unsure my patient will benefit from the procedure
- Centers offering cytoreduction/HIPEC are a distance away from my practice and too far for patients to travel
- I am concerned about the morbidity and mortality from cytoreduction/HIPEC
- None of the above

20. **My thoughts regarding patients with peritoneal carcinomatosis from a gastrointestinal cancer primary cancer are:**

- Treatment is futile with or without treatment; the intent of treatment is palliative
- The only efficacious treatment for carcinomatosis is systemic chemotherapy
- All patients with carcinomatosis should receive systemic chemotherapy, and a select group can be considered for cytoreduction/HIPEC
- None of the above
Barriers to referral for Cytoreduction / HIPEC

21. A 45 yo male previously in good health is seen in the emergency department with appendicitis. He is taken to the operating room by an oncall surgeon. Operative findings include a perforated appendix with abscess, associated with a solid appendiceal mass and peritoneal metastases. He undergoes a right hemicolectomy rather than the planned appendectomy. After he recovers and is discharged, staging CT scan shows no evidence of visceral metastases. Final pathology indicates an appendiceal adenocarcinoma, poorly differentiated, 2/25 lymph nodes positive. He is referred to a medical oncologist and is initiated on FOLFOX chemotherapy. He completes 6 months of therapy with no issue. At what point in time might you consider sending this patient for a cytoreduction/HIPEC opinion?

J. Immediately following his right hemicolectomy
J. After 3 months of systemic chemotherapy (half of his planned regimen)
J. After 6 months of systemic chemotherapy
J. After 6 months of systemic chemotherapy only if his restaging scan shows no progression
J. Never, this patient is not an appropriate candidate
J. I’m not sure
22. I regularly refer patients or consider referral for cytoreduction/HIPEC.

J: Yes
J: No
Barriers to referral for Cytoreduction / HIPEC

23. Regarding the logistics of initiating referrals for cytoreduction/HIPEC, what has or could make this process easier for you and your patients? (please rate, 1 = most important, 4 = least important)

<table>
<thead>
<tr>
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<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>N/A</th>
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</thead>
<tbody>
<tr>
<td>Knowing the surgeon/practice group by name or location and reputation</td>
<td></td>
<td>e</td>
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<tr>
<td>Having a “goto” contact person if there are any specific questions (physician extender, referral coordinator, or direct contact with the HIPEC surgeon)</td>
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<tr>
<td>A response to a referral request within 24 hours</td>
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<tr>
<td>Having a standardized referral form that can be directly submitted that captures all required patient information</td>
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24. For patients that you have seen in your practice that have undergone cytoreduction/HIPEC, what best characterizes the experience?

- Patients have had good results, both surgically and oncologically
- Patients have had complications, but good oncologic outcomes
- Patients have had complications with no good oncologic outcomes
- Patients I have sent for the procedure were not deemed candidates

None of the above
25. What may change your number or frequency of referrals for cytoreduction/HIPEC the most?

- Inclusion of the procedure into standard clinical practice guidelines (e.g., NCCN)
- Having “quality measures” or outcomes from a cytoreduction/HIPEC center and from the individual cytoreduction/HIPEC surgeon readily available for review
- Having a common information platform (electronic medical record system) by which to share patient case-related information, imaging
- Having a cytoreduction/HIPEC surgeon at my own center
- Continuing to be involved in my patient’s care, including involvement in treatment discussion, being involved in providing future treatment
- Other (please specify)

26. Regarding the financial aspect of cytoreduction/HIPEC treatment, which of the following best reflects your opinion?

- Cytoreduction/HIPEC is costly and resource intensive
- I am unaware of the “return on investment”; I am unsure the cost matches the perceived benefit versus standard systemic chemotherapy
- Patients experience undue stress related to insurance denials and lack of coverage
- Current systemic chemotherapy is equally as costly as cytoreduction/HIPEC
- None of these reflect my opinion