

## Introducing BC Cancer Primary Care Learning Sessions

Primary care providers in BC now have a great new option to gain up to date insight into common cancers including best practices in screening, treatment and surveillance all geared to providing the best support possible to patients. The opportunity comes in the form of newly launched online learning modules called BC Cancer Primary Care Learning Sessions produced in partnership by BC Cancer's Family Practice Oncology Network and UBC's Division of Continuing Professional Development (UBC CPD).

A convenient opportunity to gain current oncology knowledge and resources specifically for primary care: [ubccpd.ca/oncology/primary-care](http://ubccpd.ca/oncology/primary-care)

The first two modules, Colorectal and Breast Cancer are now available at [ubccpd.ca/oncology/primary-care](http://ubccpd.ca/oncology/primary-care) at no charge with a Prostate Cancer module soon to follow. Only minutes are required to create an account with UBC CPD and enroll in these interactive modules. Each is certified for up to 1 Mainpro+ credit each and requires an hour to complete. Real-life case studies are featured throughout and each module includes an abundance of helpful resources. Though the content is tailored to the needs of primary care, anyone looking to increase their understanding of these cancers is welcome to enroll.

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## Communication: An essential cancer care skill

*by Dr. Geneviève Chaput and Tristan Williams*

Last year, after months of suspicion, we were informed in a hurried manner that Tristan had metastatic thyroid cancer recurrence. The news hit us hard, but for reasons beyond the diagnosis itself. Here we share a sliver of our experience to highlight the importance of communication.

First, listening is key to effective communication. Patients and caregivers provide essential information to help guide your care. Months leading to the cancer recurrence diagnosis, we both noticed subtle but worrisome changes in Tristan's health. We voiced our concerns on numerous occasions to all physicians involved. Regrettably, we seemed to be in a tunnel of deafness, where no one could hear our concerns but us. Weight loss, increasing fatigue, and new-onset symptoms were met with non-reassuring explanations such as, "probably due to suboptimal synthroid adherence" or "interactions with natural supplements". Our sense of uneasiness grew over time, as did Tristan's symptoms. After much advocacy, a work-up was organized, which ultimately confirmed our initial concerns of cancer



recurrence. While there is no denying that cancer care is complex, evidence has shown active listening can improve both patient experiences and outcomes. Thus, there is value in patients listening to your instructions and as much value in you listening to your patients' concerns.

Second, in an era of increasing use of technology,  
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Sincere appreciation  
to all our healthcare  
colleagues in Times  
of COVID-19

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# The Inside Passage: not just a bucket-list holiday destination



By Dr. Pippa Hawley, Medical Leader, BC Cancer Pain and Symptom Management/Palliative Care Program

Constipation is a much-feared consequence of cancer and its therapies. For many patients it is the worst experience of their cancer journey, and is a huge contributor to impairment of quality of life consuming vast amounts of time and money (both for the patient and the system) to address. Just as a cruise can turn from the experience of a lifetime to a nightmare overnight, a bowel crisis can occur unpredictably and be catastrophic. The following “Top Ten Tips” tips will help you prevent and manage constipation in your cancer patients, and are

transferable to your other patients living with chronic illness:

1. Get into the habit of always asking your patients about their bowels.
2. Document their “normal” when you first meet them so you know what to compare with later. Comparing to your own “normal” bowel habit is not helpful. Some people go four times a day, and I once knew a patient who only went once every 2 weeks, perfectly happily.
3. Use an easy person-centred reporting tool such as the Victoria Bowel Performance Scale so that you can track changes in a consistent and reproducible way.
4. “What do you produce? How often do you pass it? How does it feel on the way out?” These questions cover most of what you need to know.
5. The hand that writes the opioid prescription and fails to write the laxative plan is the one that does the manual evacuation. Enough said.

6. The mantra above also applies to other constipating drugs, especially ondansetron and anticholinergic agents.
7. In patients with a slow transit time who don’t drink much, fibre (such as Metamucil) will form chip-board in the bowel.
8. Sennosides and PEG work equally well as first-line laxatives, but PEG is more expensive and requires the ability to drink a fair volume of liquid. Select according to patient preference and finances. If one doesn’t work, switch to, or add the other.
9. Maximize the dose of your first choice laxative before adding another one: keep it simple.
10. Docusate doesn’t work for opioid-induced constipation.

The last point is to remember that, just like another familiar over-the-counter remedy, lactulose tastes awful, but it works, and is a useful salvage therapy for a constipation crisis. It can also mitigate hepatic encephalopathy.

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## Communications continued from page 1

verbal communication remains undisputedly essential. Trust, empathy, expertise, and shared-decision making are valued attributes of patient-doctor relationships. Cancer care is undoubtedly associated with high demands, often accompanied with a sense of inadequate time to communicate with patients. The thing is, it’s not how much time you spend per se, but more about how, to whom, and why you deliver information. The “how” is the backbone of communication, as receiving cancer-related news is stressful. Communicating in a clear and compassionate manner is of utmost importance, as it can significantly reduce distress. In our situation, being told: “Tristan will probably never be able to walk again” was far more daunting than the subsequent clarification: “May or may not lose some or all function of his legs”. Physicians are not



expected to be “perfect” communicators, but brief sentences such as “I wish I had better news” and “I’m sorry to have to tell you this” go a long way in one’s cancer experience.

The “to whom” also comes into play: whether delivering difficult news or supportive interventions, including caregivers in these discussions is considerate and essential, as cancer affects families and loved ones too. Caregivers provide approximately 70% of cancer care and their meaningful

contribution helps your patients reach the best possible outcomes. Caregivers are your patients’ allies and always remember they are also your allies, too. Thus, include and encourage them to seek support for themselves as well. Lastly, the “why” of communication is personal to you and ultimately boils down to the core reasons you chose to become a physician in the first place. It reflects your motivational drivers and what inspires you to continue doing

the important work that you do. Nurture that moral compass, and let it be your ever-present guide to delivering both exceptional clinical communication and cancer care.

Ultimately, a practice focused on incorporating evidence-based medical knowledge and effective clinical communication can help save time and prevent distress for all parties involved. As cancer care providers you work hard for us, and we hope sharing a bit of our story reminds you that as patients and caregivers we are right here working with you too.

*Gen is a family physician with a dedicated cancer care practice. She is chair elect of the Canadian Association of General Practitioners in Oncology, and vice-chair of the Cancer Care Member Interest Groups section of the College of Family Physicians of Canada. Tristan is a cancer survivor, also living with multiple sclerosis. He is a motivational speaker. He is co-chair of the cancer care mission patients’ committee and acts as patient representative for OPAL, an app to empower patients, at the McGill University Health Centre. Gen and Tristan live in Quebec.*

# Resources supporting patient education on breast density and screening mammography



By Dr. Colin Mar, Medical Director,  
BC Cancer Breast Screening Program

The BC Cancer Breast Screening Program provides a breast density assessment with screening mammography results. An independent review<sup>1</sup> commissioned by the Breast Screening Program to evaluate the evidence surrounding breast density and breast cancer risk recommended the development of materials supporting the education of patients on breast density. To facilitate provider and patient understanding of breast density and its risks, the following resources have been developed:

- **Breast Density Discussion Guide**

The purpose of this guide is to facilitate

conversations around breast density between providers and patients. The guide contains information on the differences between breast density categories, breast density as a risk factor and supplemental testing. The guide can be accessed at [www.screeningbc.ca/breast](http://www.screeningbc.ca/breast) (under Guidelines, Breast Screening Resources).

- **Educational Video**

An animated video has been developed to educate patients on breast density. The video contains information on the risks associated with breast density and provides information to patients on what they can do if they have higher breast density. The video is accessible through the Screening BC website and is also available in French, Cantonese, Mandarin and Punjabi: [www.screeningbc.ca/breast](http://www.screeningbc.ca/breast)

These two materials join an existing collection of resources on breast density for providers and patients which can be found on the Screening BC website. Both the Breast Density Discussion Guide and educational video are outcomes of the work of the Breast Density Communication Working Group. The purpose of the working

group was to provide consultation and expertise toward the development of educational resources on breast density. Specifically, the group was tasked to determine areas of focus for breast density communication and identify strategies to increase understanding of breast density assessments. The group consisted of patients, public advocates, primary care providers, radiologists, technologists and program and ministry staff. This development was followed by focus group testing by a similarly diverse group of representation.

The Breast Screening Program is confident that these materials will be useful for supporting providers and their patients' breast health decisions in the context of breast density. In addition, the program will continue to assess the performance of the Breast Imaging Reporting and Data System (BI-RADS) density scoring system currently utilized, and monitor the scientific literature for ongoing developments in this area.

1. Coldman, A. Report on Breast Density. 2018 July 12. Available at [www.screeningbc.ca/health-professionals](http://www.screeningbc.ca/health-professionals) (under Reports, Breast Screening Resources)

## "This was a great little read for my night shift!"

Introducing BC Cancer Primary Care Learning Sessions continued from page 1

"Our goal with these Learning Sessions is to maximize accessibility of high quality, current cancer care information for primary care," notes Dr. Cathy Clelland, BC Cancer's Program Medical Director for Primary Care. "We developed these modules based on the successful series of in-community workshops we presented with UBC CPD, 2012-16, attracting over 1,200 primary care providers in 90 communities across BC."

Much of the credit for these online modules goes to our working groups of family physicians, oncologists, surgeons, and patient partners who, together with UBC CPD, and chaired by our then Medical Lead of Education, Dr. Raziya Mia, brought them to life in a learning style I know you'll enjoy."

Feedback is welcome as we plan for anticipated in-community workshops and new modules uniting oncology and primary care to enhance cancer care.

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### Case Study: Chad



Click on the tabs below to reveal them:

Question 1

Question 2

Question 3

Question 4

Chad is a 45 year old rectal cancer survivor who is up-to-date with surveillance, having completed active treatment 4 months ago. He has several issues that are troubling him, including renewed concern about his cancer recurrence risk and what the future holds. Adjusting to a permanent colostomy continues to be a struggle and consequently he has been avoiding sexual intimacy. He has ongoing fingertip numbness and is concerned about his ability to return to work as a mechanic. All of this has had an impact on his mood. Chad was adopted at birth and no biological family history is available.

**Question 1: How would you address Chad's concern about his recurrence risk?**

Type an answer, it's just reflective

Show feedback

# Supportive care: enhancing and extending cancer care

Effective care of cancer patients extends well beyond diagnosis and core treatment to include services which address the emotional, spiritual and physical impacts that cancer and its treatment can bring to the forefront. At BC Cancer, these services are known as Supportive Care and include Patient and Family Counselling, Spiritual Care, Psychiatry, Pain and Symptom Management/Palliative Care, Nutrition and Speech and Language Pathology. All are available through each of BC Cancer's six Centres including options to connect in-person, by telephone or online.

See [bccancer.bc.ca/supportivecare](http://bccancer.bc.ca/supportivecare) for contact and referral details.

## Patient and Family Counselling

Patient and Family Counselling helps patients, couples, and families cope with the emotional, practical, and social distress that a cancer diagnosis and treatment can trigger. Counsellors help manage challenges such as financial and travel issues, fear, anxiety and depression, family and relationship tensions, and lifestyle changes. Individual counselling and group-based programs – including stress reduction – are available at every BC Cancer Centre. No referral is needed and patients, their families, or caregivers can call for an in-person or telephone appointment up to eighteen months following treatment.

**Supportive Care Patient Newsletter:**  
Subscribe to receive updates on BC Cancer Supportive Care programs and educational events,  
[bccancer.bc.ca/supportivecare](http://bccancer.bc.ca/supportivecare)

## Spiritual Health

Spiritual Health Practitioners (multi-faith) work with Patient and Family Counselling, supporting patients, families, and health care staff emotionally and spiritually in moments of need, based on the person's beliefs, cultural background, values, and practices.

## Psychiatry

BC Cancer psychiatrists provide mental health support for patients suffering from complex situations related to cancer and cancer treatment. Their services are available to patients during active treatment and into early post-treatment with a referral from the patient's family physician or oncologist.

## Pain and Symptom Management/Palliative Care

Pain and Symptom Management Clinics help patients improve pain control and cope with problems such as severe nausea, shortness of breath, and fatigue. Staff also counsel on care planning and decision making during care transitions. The aim is to transfer patients back to their family physician once their needs are addressed. Referrals are accepted from any member of a patient's care team.

### Learning Opportunity

- Take the free, one-hour, accredited online course – [methadone4pain.ca](http://methadone4pain.ca) – to become more confident in prescribing methadone for analgesic purposes. Federal exemption no longer required.

## Nutrition

BC Cancer dietitians help patients improve and maintain their nutritional status during treatment providing support for issues such as decreased appetite and unintentional weight loss, dry mouth, taste changes, nausea and vomiting, and constipation or diarrhea. Patients with head and neck, esophageal or gastric cancer are directly referred to these services. Others can self-refer and make an appointment by calling the closest Nutrition Services team.

### In Your Community

- Patients can call 811 – Health Link BC – to speak with a registered dietitian at no charge. Patients and family members can also speak directly with a cancer care dietitian working in partnership with BC Cancer.

## Speech-Language Pathology (SLP)

BC Cancer, and its Health Authority partners, help patients improve speaking and swallowing difficulties caused by cancer or cancer treatments. Patients with head and neck cancer are directly referred while others can self-refer by contacting the appropriate SLP location.

### In Your Community

The Canadian Cancer Society helps Canadians manage life with cancer, providing community and connection, and building wellness and resilience throughout the cancer journey. Services are either free or low-cost and are available to people with cancer, their families, friends and caregivers and many are available in multiple languages. Services include:

- a peer match program to connect people living with cancer and their families with trained volunteers who offer encouragement and share ideas for coping;
- an online peer support community to share experiences;
- accommodation for people who need to travel for cancer treatment;
- a transportation service to help people with cancer get to and from their appointments;
- a toll-free helpline at 1-888-939-3333 where information specialists can answer questions about cancer and help find community support services;
- a community services locator with over 4,000 cancer-related services listed; and
- informative resources and booklets

Visit [cancer.ca](http://cancer.ca), Supportive Care, How We Can Help for full details.



**Canadian  
Cancer  
Society**

# Cariboo cancer care: where once there was one, now there are four – GPOs

For years, systemic cancer therapy and supportive care in Williams Lake, 100 Mile House, and surrounding communities were provided by one highly regarded General Practitioner in Oncology (GPO), Dr. Gord Hutchinson, with back-up coverage from Williams Lake GPO, Dr. Emil LaBossière. Times and personnel changed, however, all while the need for local cancer care increased.

Now, there is a team of four GPOs for this region; three based in Williams Lake: Dr. LaBossière, Dr. Ghaida Radhi, and (just recently) Dr. Francina van der Merwe; and Dr. Adrienne Montgomery, an hour's drive south in 100 Mile House.



Williams Lake team (left to right): Dr. Francina van der Merwe, GPO, Muriel Overton, Chemotherapy Nurse, GPOs, Dr. Emil LaBossière, and Dr. Ghaida Radhi

Together, with their valued nursing and pharmacy staff, these GPOs provide enhanced cancer care for patients throughout the region, some coming from as far away as Bella Coola – a six-hour drive. They work in partnership with oncologists from BC Cancer, enabling patients to receive systemic therapy and supportive care as close to home as possible. “We are a focus of cancer care for the area,” notes Dr. LaBossière. “Having GPOs in these communities saves patients from travelling to BC Cancer, reducing hardship exponentially (especially in winter), and enables the feasibility of receiving care for many.”

Each Williams Lake GPO also maintains a family practice rotating days per week in the GPO Clinic. Dr. Montgomery, in 100 Mile House, divides her time between the GPO role, and serving as the local palliative care lead. She also provides outreach care to a

local First Nations reserve, runs a women's gynaecologic clinic, and fills occasional shifts in the local emergency department.



100 Mile House crew (left to right): Patti Randle, RN, Nicole Leduc, Pharmacist, Gisele Polisen, Clerk and 'do-er of everything extra', Leah Martin, RN, and Dr. Adrienne Montgomery, GPO

## What They Like Most About the Job

Dr. LaBossière: *I really like the variety of the GPO role. The work is different than office-based practice and forces me out of my comfort zone every day.*

Dr. Radhi: *I like having another focus to complement my family practice. I'm learning every day in the GPO role, and am impressed by how rapidly cancer care is evolving.*

Dr. Montgomery: *I like the patient focus of the GPO role, being able to fully prepare and getting to know each person. Patients often have no recollection of their first oncology consult, and I can serve as a translator explaining their prognosis and our plan in way that provides empowerment and stress relief.*

*I worried when I took on this role whether I would be suited, but it's a great fit. There is strong community support, good balance with my young family (I sometimes bring my kids on rounds!), and never a dull moment.*

## Sharing Care with BC Cancer Oncologists Works Well

These GPOs all express appreciation for the timely expertise provided by their BC Cancer colleagues.

Dr. LaBossière: *The oncologists at BC Cancer are fantastic. They get back to us quickly, and almost always take my calls.*

Dr. Radhi: *I met so many oncologists through the GPO Education Program making it easy to get support. The relationships we've built are very helpful.*

Dr. Montgomery: *I have only praise for the oncologists. They provide rationale for their position, and answer even my silliest questions. They offer solid guidance providing me, and our patients, with a sense of security.*

## On Being a Cancer Care Resource for Community Physicians

Dr. LaBossière: *We have a strong relationship with our community physicians, and work in close partnership. They call us with oncology questions, and we can help – or get help – quickly.*

Dr. Radhi: *We are a resource for our medical community – easy to contact, able to answer questions and connect quickly with an oncologist if need be.*

Dr. Montgomery: *There are always questions, and I am always glad to help connect with our oncologist colleagues.*

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## Next GPO Education course begins September 14, 2020

The GPO Education Program is an eight-week course offering rural family physicians and newly hired BC Cancer GPOs the opportunity to strengthen their oncology skills and knowledge, and provide enhanced cancer care. The program covers BC and the Yukon and includes a two-week Introductory Module held twice yearly at BC Cancer – Vancouver followed by 30 days of flexibly scheduled clinical rotation. Full details at [www.fpon.ca](http://www.fpon.ca)

# Radiation-induced lung injury: an elusive diagnosis

By Dr. Hamid Raziee, Radiation Oncologist, and Dr. Aaron Pelman, GPO, BC Cancer – Surrey

A.P. is a 54 year-old female with left-sided breast cancer. Following surgery, she underwent radiotherapy to the left chest wall and lymphatic areas. Seven weeks after radiation, she presented to the emergency room with a non-productive cough, dyspnea-on-exertion, and a fever. The chest x-ray was normal. Further investigation with chest CT angiogram ruled out pulmonary embolism, but demonstrated consolidative changes with surrounding ground-glass opacity at the left apex, and the anterior surface of the left upper lobe (Figure 1A). She was discharged on antibiotic therapy with a diagnosis of possible pneumonia. Although respiratory symptoms improved with treatment, cough and exertional dyspnea continued. After consultation with a respirologist, she was diagnosed with radiation pneumonitis (RP), started on oral prednisone, and obtained significant relief.

## Nomenclature

Radiation-induced lung injury (RILI) is a potential toxicity of thoracic radiation for treatment of lung and breast cancers, and hematological malignancies. RILI manifests as RP in the sub-acute setting, and as radiation-induced pulmonary fibrosis (RIPF) in the chronic setting.

## Pathophysiology

Initial radiation injury occurs “in-field”. Through the production of reactive free radicals, ionizing radiation creates cytotoxic damage of pneumocytes and endothelium. This leads to surfactant and exudate release into the alveoli, and creates interstitial edema. This phase begins shortly after radiation exposure, and is not clinically evident.<sup>1</sup>

In the acute exudative or pneumonitis phase, the inflammatory response elicited by cytokines leads to capillary obstruction, alveolar septal thickening and shrinking of alveolar spaces.<sup>2,3</sup> This is the classic RP phase. Fibrosis develops as a consequence of pathological repair of the pneumonitis phase<sup>4</sup> and is a late event. The pneumonitis phase in most patients will resolve without progression to fibrosis (RIPF), which is irreversible if it occurs.

## Presentation and Clinical Assessment

Symptoms of acute RILI may include exertional dyspnea, non-productive cough, fever, malaise, and pleuritic chest pain, typically occurring 4- 12 weeks after the completion of radiation therapy.<sup>5</sup>

Signs may include tachypnea, hypoxemia and fever. Pulmonary examination may demonstrate dullness to percussion and/or crackles on auscultation. Skin changes such as hyperpigmentation or erythema corresponding to the radiation treatment fields may also be observed.<sup>5</sup>

The differential diagnosis for the above and examination findings is broad, and may include lower respiratory tract infections, exacerbation of chronic obstructive pulmonary disease, congestive heart failure, or thromboembolic disease.<sup>5</sup>

## Investigations

Laboratory tests are non-specific for RP, however, they may help rule out differential diagnoses. A chest radiograph may be normal, or could demonstrate consolidation and/or ground-glass opacities. Classically, the radiographic border corresponds to the radiation volume (Figure 1B). With modern radiation planning, there may be no distinct ‘field border’ due to an irregularly-shaped high-dose radiation volume, making the diagnosis challenging. Radiologic changes are limited to the radiated volume.

Chest CT is more sensitive, and is the diagnostic modality of choice for RP. It is indicated for patients with respiratory symptoms following radiation who do not respond to initial management. CT angiogram may be obtained to rule out

pulmonary embolism. Comparing CT findings to radiation volumes/doses helps with diagnosis.

## Diagnosis

The diagnosis of RILI is based on consistent respiratory symptoms and signs in a patient with a history of thoracic radiation while excluding other causes. Imaging findings that correspond to radiation fields can be pathognomonic for RILI.<sup>5</sup>

## Management

For mildly symptomatic patients, supportive care measures may be sufficient. For those with symptoms interfering with activities or a decrease in pulmonary function, oral steroid therapy such as 1 mg/kg oral prednisone for 2-4 weeks followed by a slow taper of 6-12 weeks is warranted. Prophylaxis against pneumocystis has been suggested for patients on more than 20 mg of prednisone per day for more than a month.<sup>6</sup> Close monitoring after diagnosis is important regardless of treatment modality.

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see References on page 13



Figure 1A: CT angiography at the time of respiratory symptoms

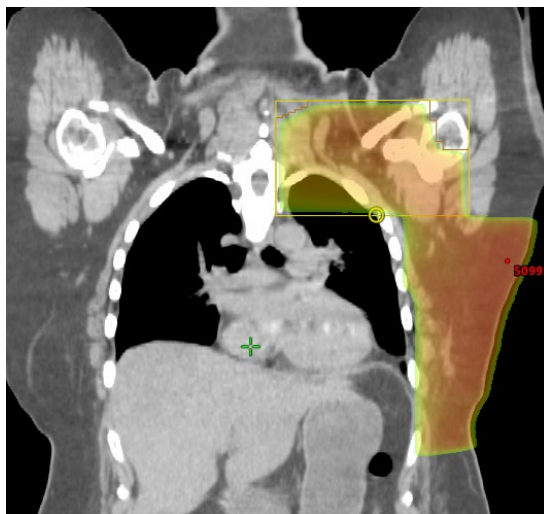


Figure 1B: Radiation dose coverage

# Screening for new primary cancers in patients with metastatic cancer

By Dr. Megan Tesch, PGY4, Medical Oncology, BC Cancer – Vancouver

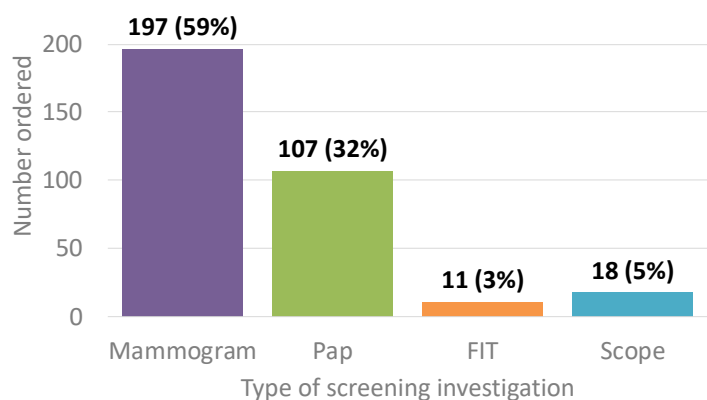
**Screening saves lives.** That is the message that drives healthcare providers to order screening investigations for breast, cervical, and colorectal cancers, as such tests have been shown to reduce cancer-related mortality in healthy patients. It is also this message that motivates patients to undergo at times cumbersome or uncomfortable mammograms, pap smears, flexible sigmoidoscopies/ colonoscopies, or fecal immunohistochemical tests (FIT).

But what if the patient undergoing the pap smear has metastatic lung cancer? It has been shown that the time lag to a survival benefit from screening investigations like mammography and flexible sigmoidoscopy ranges from 9.4 years to 10.7 years.<sup>1,2</sup> In simpler terms, a life expectancy of approximately 10 years is needed to profit from cancer screening. In addition, many potential adverse events are associated with screening investigations, including anxiety secondary to false positives, unnecessary follow-up tests and procedures, and procedural complications such as bowel perforation.

These considerations led Choosing Wisely Canada to make the recommendation to avoid routine cancer screening and surveillance for a new primary cancer in patients with metastatic disease (<https://choosingwiselycanada.org/oncology/>).<sup>3</sup> In such patients, the survival benefit from screening investigations is generally outweighed by the potential harms of these tests and the competing mortality risks of metastatic disease.

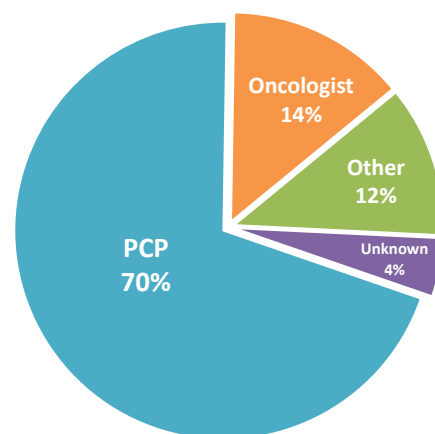
## Real-Life Experience

A recent study examined cancer screening practices for a subset of patients with metastatic cancer at the Dr. H. Bliss Murphy Cancer Centre in St. John's, Newfoundland and Labrador.<sup>4</sup> For the 305 metastatic breast cancer patients included in the study, it was assessed whether screening with any one or a combination of screening mammography, Pap test, flexible sigmoidoscopy/ colonoscopy, or FIT were performed at any point after diagnosis of metastatic disease. Overall, 114 patients (37.4%) underwent at least 1 screening investigation (mean, 2.92 investigations per screened



**Figure 1:** Number of screening or surveillance investigations ordered by type. Pap = Papanicolaou test; FIT = fecal immunohistochemical test; Scope = flexible sigmoidoscopy or colonoscopy.

patient) over a median follow-up time 21 months (range, 0-178 months). The most common screening investigations were mammography and Pap test [Figure 1]. Primary care providers ordered most of the screening investigations, compared to oncologists and other specialists [Figure 2], likely stemming from their preventive care focus. In this cohort, median overall survival after a diagnosis of metastatic disease was 42 months, with a 5-year overall survival of 35.9%, demonstrating the life expectancy of this patient population is too short for any predictable survival benefit from screening.



**Figure 2:** Proportion of screening or surveillance investigations ordered, by physician specialty. PCP = primary care provider; Other = other specialists.

It is important to note the Choosing Wisely Canada recommendations acknowledge screening can be considered for a small subset of patients with relatively indolent metastatic disease.<sup>3</sup> Of the 333 screening investigations ordered for patients in the aforementioned study, a portion might have been appropriate. That portion would presumably consist of the tests ordered by oncology specialists, who would be most cognizant of an individual patient's metastatic disease burden. Factors that could possibly be contributing to unnecessary screening include lack of explicit instructions by medical oncologists to other physicians about the discontinuation of screening and surveillance investigations upon development of metastatic disease, unfamiliarity with the metastatic disease status of the patients, and lack of awareness regarding Choosing Wisely Canada guidelines.

## Choosing Wisely for Metastatic Cancer Patients

In BC, a formal assessment of the rate of inappropriate and potentially harmful screening investigations for new primary malignancies in patients with metastatic disease has not been conducted; however, anecdotally, this scenario is frequently encountered among oncology patients. Healthcare providers—oncologist and family physician—should discuss the overriding risks of screening tests with their metastatic cancer patients. Most patients are willing to talk about unnecessary testing and may be reassured by their healthcare team's aligning goals. Shared decision-making between healthcare providers and oncology patients regarding the value or lack thereof in screening for new primary cancers ensures the care being delivered is both patient-centred and impactful.

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see References on page 13

# Following through with Primary Care Learning Sessions

By Dr. Cathy Clelland, Program Medical Director, Primary Care

With the development of personalized care and immunotherapy, cancer management options have grown significantly. More patients are surviving longer, while many are cured of cancers previously considered “incurable”. As a result, cancer is fast becoming a co-morbid chronic condition requiring primary care expertise. Key asks from our 2018 Primary Care Needs Assessment, published with UBC’s Division of Continuing Professional Development (UBC CPD), encouraged access to education and information on rapidly changing oncology management,



Dr. Cathy Clelland

and support for increased and improved shared care.

Following this feedback, BC Cancer’s Primary Care Program partnered again with UBC CPD to update, and redesign its community-based workshops into self-directed, online education modules targeted to the needs of primary care (see Primary Care Learning Sessions on page 1). Never has online CME been more pertinent! The first two modules - Colorectal Cancer and Breast Cancer - are freely available at [ubccpd.ca/course/oncology](http://ubccpd.ca/course/oncology) with a Prostate Cancer module soon to follow. All explore the role of primary care providers in supporting patients through their cancer

journey plus highlight best practices in screening, treatment, and surveillance.

The Prostate Cancer module is especially exciting as we recently completed development of a Primary Care Prostate Cancer Guideline in partnership with BC’s Guidelines and Protocols Advisory Committee. The content of this guideline is integrated and included as a core resource for this module.

Next steps include exploring options to prototype and deliver an in-person, case-based workshop focusing on cancer as a chronic disease and using the online modules to identify local opportunities and challenges that primary care and specialists can address together.

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## Implementation of oncology biosimilars at BC Cancer

By Dr. Anne Dar Santos, Oncology Drug Information Specialist, Provincial Pharmacy, BC Cancer

In the Fall 2019 issue of the *Journal of Family Practice Oncology*, Dr. Helen Anderson outlined tips to help physicians speak with patients about oncology biosimilars. Since then, BC Cancer has implemented bevacizumab biosimilar for patients with colorectal, brain, ovarian, cervical and soft tissue cancers – the first oncology biosimilar to be funded in British Columbia.

A new web page, educational sessions, patient literature and e-mail blasts were utilized to prepare BC Cancer staff and patients for the adoption of the first biosimilar product at BC Cancer. Patients starting a new treatment protocol were started on the bevacizumab biosimilar product. Patients who had started a planned course of bevacizumab treatment prior to November 2019 were not switched over to the biosimilar product, and instead continued to receive the bevacizumab reference product. The uptake and implementation of the bevacizumab biosimilar for patients was smooth and successful.

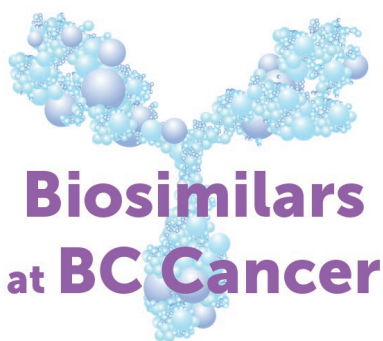
More recently, in February 2020, trastuzumab biosimilar became available at BC Cancer for patients with breast and gastrointestinal cancers. As with its predecessor, patients starting a new treatment protocol received the trastuzumab biosimilar product, whereas patients who had started a planned course of treatment prior to February were continued on the trastuzumab reference product. In the case of trastuzumab, a treatment plan may consist of a trastuzumab-containing chemotherapy regimen (e.g., doxorubicin, cyclophosphamide, paclitaxel and trastuzumab), followed by single-agent

trastuzumab given in a sequential regimen. Patients receiving trastuzumab for early breast cancer will typically complete their trastuzumab treatment in one year. However, patients receiving trastuzumab in the advanced breast cancer setting will continue to receive trastuzumab until their disease progresses. In addition, all patients who are, or will be, receiving maintenance combination trastuzumab and pertuzumab in the advanced HER2-positive breast cancer setting will continue to receive the reference brand of trastuzumab, as this combination is supplied as a kit.

Eventually as patients complete or discontinue treatment with the branded reference drugs, the biosimilars will become the predominant products at BC Cancer. However, physicians are also encouraged to discuss with patients the option of switching to a biosimilar product. Evidence and experience support the switch to biosimilars, and increased savings will support re-investment in cancer drugs that are proven to improve patient outcomes.

Biosimilar rituximab, used in the treatment of patients with lymphoma, is anticipated to be available in early summer 2020.

Visit [www.bccancer.bc.ca/biosimilars](http://www.bccancer.bc.ca/biosimilars)



Biosimilar	Entry at BC Cancer
Bevacizumab	November 2019
Trastuzumab	February 2020
Rituximab	Early summer 2020



# Long term follow-up of hematopoietic stem cell transplant recipients

By Dr. Gagan Kaila, MD, FRCPC, Leukemia/Bone Marrow Transplant (L/BMT) Program of BC

Allogeneic hematopoietic stem cell transplant (HSCT) recipients who are disease-free five years post-transplant have a greater than 80% 10-year survival.<sup>1</sup> However, life expectancy among 5-year survivors remains 30% lower than the general population, regardless of current age and years since HSCT.<sup>2</sup> Cardiovascular diseases and secondary malignancies are among the leading causes of late mortality following HSCT.

There is a 5-10% cumulative incidence of cardiovascular disease at ten years post-HSCT, which is 3.5 times higher than in the general population.<sup>3</sup> Broadly, this can include coronary artery disease, cardiomyopathy, congestive heart failure, valvular dysfunction, arrhythmia, strokes, and peripheral arterial disease. Major risk factors for cardiovascular disease in this population include anthracycline exposure and chest radiation. The L/BMT Program recommends adherence to healthy lifestyle recommendations (diet, exercise, maintenance of healthy weight, smoking cessation) and regular monitoring and early treatment of cardiovascular risk factors (obesity, hypertension, dyslipidemia, or diabetes). We also recommend having a low threshold for ECG, echocardiogram, and/or cardiology referral if cardiovascular symptoms develop, particularly with a history of anthracycline exposure or chest radiation.

Overall, HSCT recipients have twice the risk of malignancy compared with the general population. The cumulative incidence of malignancy continues to rise over time and without plateau.<sup>4</sup> Risk factors include myeloablative total body irradiation, young age at transplant, chronic GVHD, and prolonged immunosuppression beyond two years. The most common sites of second malignancy include skin, oral cavity, breast, and thyroid. Adapting from the American Society for Transplantation and Cellular Therapy's long term follow up recommendations<sup>5</sup> and Canadian cancer screening guidelines, we recommend the following screening following HSCT:

- Brain: if a history of TBI or whole-brain radiation, annual history and screening neurologic exam with a low threshold to obtain brain MRI if concerns;
- Skin: annual head to toe skin exam for signs of skin cancer (BCC, SCC, and melanoma). Reinforcement of sun-safe practices, such as regularly wearing sunscreen and avoiding excess sun exposure;
- Oral: Dental assessment every 6-12 months;
- Thyroid: if a history of TBI or neck radiation, annual neck palpation with a low threshold to investigate any discovered thyroid nodules (ultrasound +/- biopsy);
- Breast (females only): screening based on general population guidelines and/or family history; if TBI or chest radiation, annual mammograms starting at age 25 or eight years following radiation (whichever is later), but no later than age 40;
- Colon: screening based on general population guidelines and family history;

- Prostate (males only): screening based on general population guidelines if available, family history, and patient preference;
- Testicles (males 25-40): regular self-exam and clinical follow up if concerns; and
- Cervix (females only): annual pap smears for two years following transplant or as long as on systemic immunosuppression (e.g. prednisone, cyclosporine), whichever is later, followed by general population intervals.

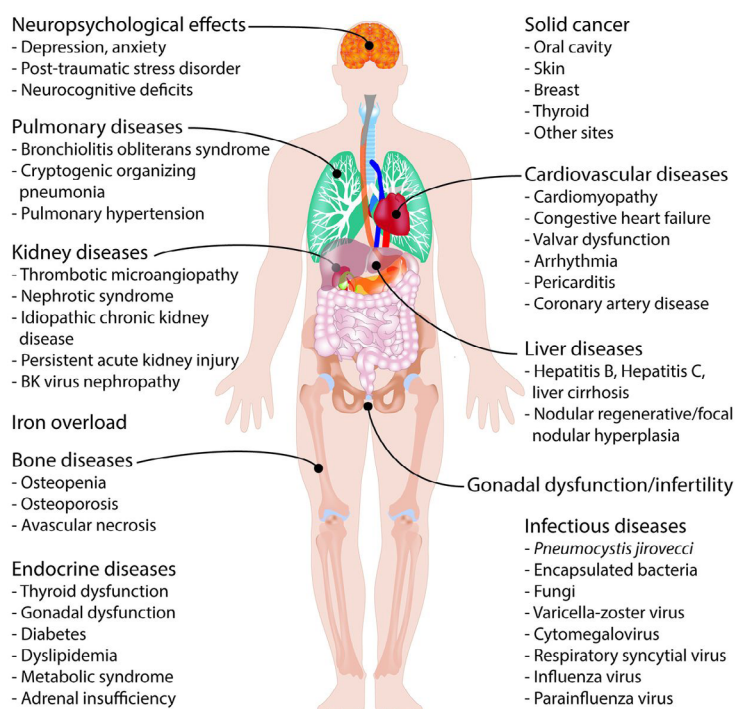
View the full 2019 webcast on this topic at [www.fpon.ca](http://www.fpon.ca) – Continuing Medical Education.

As with screening in the general population, consider life expectancy when deciding which screening strategies to pursue. Most general population guidelines do not recommend screening if life expectancy is less than ten years.

The L/BMT Program's Long Term Follow-Up (LTFU) Clinic is located at Vancouver General Hospital and provides annual follow-up for adult allogeneic HSCT recipients for at least ten years post-transplant, and provides individualized recommendations for their primary care providers in the community. In the coming months, the Program's website will be updated with comprehensive post-transplant long-term follow-up guidelines, which will be available for HSCT recipients and their care providers.

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Credit: Late effects of blood and marrow transplantation, Yoshihiro Inamoto, Stephanie J. Lee, *Haematologica* April 2017 102: 614-625

# Lim's top 10 list of things I wish I had known about rectal cancer (Butt Cancer 101)

By Michelle Lim

The following is submitted by Michelle Lim, who was treated for rectal cancer in 2017. She is now a Patient Partner with BC Cancer and played a significant role in developing our first online Primary Care Learning Session on Colorectal Cancer (see page 1). She shares her perspective below. Thank you Michelle!

1. Rectal cancer is messy, scary, difficult to discuss, and unpleasant – but survivable. Keep this in mind as countless people see your butt, and do unthinkable things to it while you adjust to life with a modified or removed rectum.
2. Break the disease into phases so its duration is less overwhelming: diagnosis, treatment, life with a bag, and hopefully, the reversal (plus the hard month following with 20+ bowel movements daily). Focus on the end goal: survival.
3. Being around supportive people helps. Friends and family will be shocked and saddened by your diagnosis, and many won't know what to say or do. There is also the "ick" factor with rectal cancer which is challenging. Strongly consider accepting help from others. This makes them feel better, and will help you as fatigue, worry and discomfort take their toll. Short visits and walks are helpful, as is



laughter which is truly the best medicine. Continue living!

4. There is no right way to get through this challenge. Talking with a counsellor or your family doctor can help, as can speaking with others who have experienced this same journey.
5. While it is natural to hate having a stoma (I named mine Ramona) and bag, seeing them as tools to achieve a better outcome helps. Being able to change your bag is also helpful, as is eating a few

marshmallows about 15 minutes prior (reduces liquidity). Candles also help mask the "unique" odour relating to the bag.

6. Napping is beneficial. If an ileostomy is planned, and you always sleep on your right side, get used to sleeping on your back or left side before the procedure.
7. On the subject of intimacy, nothing says sexy like a bag of poop on your waist, or an adult diaper. It is important that your partner understand you may feel fatigued, worried, distracted and sore below-the-belt. This improves with time, but possibly never to pre-diagnosis status (hugs are helpful).
8. Be kind to your behind: cotton underwear, soft toilet tissue and creams help as do soaking baths, potty stools, and plain yoghurt. Also, loperamide, aka Imodium, costs far less as a prescription, and one pill per dosage often suffices.
9. Always note where bathrooms are, avoid belts and extra buttons. Learn which foods trigger your bowels, and allow extra time to get places.
10. Be honest with people about your diagnosis. Talking about rectal cancer creates awareness and reduces stigma. This is a hard journey, but you can get through it.

Contact Michelle Lim at [the\\_lims@hotmail.com](mailto:the_lims@hotmail.com)

## Corridor Consult – Oncology Q&A

**Q** Why are my patients who have completed adjuvant breast cancer therapy receiving zoledronic acid infusions, and why at 3- or 6- month intervals?

**A** Answer from Dr. Karen Gelmon, Medical Oncologist, BC Cancer – Vancouver

In the early 1990s, studies showed that bisphosphonates decreased skeletal events such as pain, fractures, or the need for radiation in persons with metastatic breast cancer. This stimulated research into the mechanism of action



Dr. Karen Gelmon

of these drugs. A large body of preclinical evidence shows that bisphosphonates exert a variety of direct and indirect anticancer activities, affecting both tumour

cells and the surrounding microenvironment and stimulating immune reactions.

As bone metastases are the most frequent site of metastatic relapse in persons with breast cancer, researchers questioned whether administering bisphosphonates in the adjuvant setting could decrease disease recurrence and improve survival. A

number of small studies suggested a decrease in the occurrence of bone relapses, while others suggested this effect lasted only for the duration of adjuvant bisphosphonate therapy.

Gnant published a study in the New England Journal of Medicine that randomized premenopausal women to ovarian suppression plus either anastrozole or tamoxifen, with a second randomization to zoledronic acid. Although the two endocrine agents showed similar benefits, the addition of zoledronic acid resulted in a 36% decrease in recurrence at 3 years, a magnitude of benefit similar to the addition of adjuvant chemotherapy. A large study,

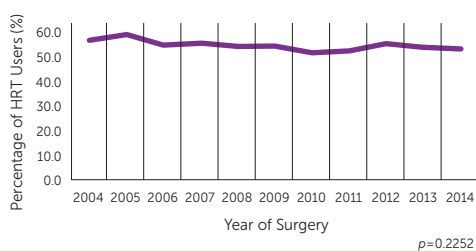
*continued on page 11*

# How to survive premature surgical menopause: role of the family physician and GPO

By Dr. Ji-Hyun Jang, Gynecologic Oncology Fellow, Nimisha Arora, Research Assistant, Dr. Gillian Hanley, Assistant Professor, all at University of British Columbia, and Dr. Janice Kwon, Gynecological Surgical Oncologist, BC Cancer – Vancouver

Women undergo premature surgical menopause because of the removal of their ovaries (bilateral oophorectomy), with or without fallopian tubes, for both benign and malignant reasons. They may have benign ovarian cysts or tumours, or primary or secondary malignancies in the ovaries. They may have a genetic predisposition to ovarian cancer because of a pathogenic variant (mutation) of the BRCA gene, or Lynch Syndrome, and therefore undergo bilateral oophorectomy at a young age to avoid the diagnosis of ovarian cancer. However, this surgical procedure can deprive young women of natural estrogen for decades. This estrogen deprivation puts them at increased risk for short-term adverse effects such as poor quality of life from vasomotor symptoms or sexual dysfunction and long-term health risks, including osteoporosis and cardiovascular disease.

## HRT Use During 10-Year Study Period



Never HRT User	N=5738 (44.7%)
Estrogen User	N=4204 (32.7%)
Estrogen and Progesterone User	N=2895 (22.6%)

We recently conducted a population-based study of British Columbian women between the ages of 19 and 50 years who underwent bilateral oophorectomy in 2004-2014. We assumed that these women underwent premature surgical menopause as a result of their surgery. We then evaluated Pharmanet data to determine how many of these women filled hormone replacement therapy (HRT) prescriptions following their surgery, and Medical Services Plan data to investigate health services use (inpatient admissions and outpatient clinic visits) according to use of HRT following surgery.

We included nearly 13,000 women in our study with a median age of 43 years and a median follow-up of 5 years. The most common medical indications for bilateral oophorectomy were endometriosis, benign tumours, abnormal uterine bleeding, and leiomyomata (fibroids).

We were surprised to find that only half of these women ever filled a single prescription of HRT following their surgery. Among those who ever used HRT, less than half used it for more than six months. This number did not change annually over the ten year study period.

Women were more likely to use HRT if they were carriers of BRCA pathogenic variants (i.e., underwent bilateral oophorectomy for prophylactic reasons), if they were younger at surgery, and if they had a higher income. Those who underwent concurrent hysterectomy were also more likely to use HRT. Women who used HRT had lower health services utilization rates for cardiovascular disease and fractures (approximately 50% lower) compared to those who did not use HRT. Therefore

## So what can we do?

- Offer close follow-up for women who undergo premature surgical menopause to manage short-term symptoms and to counsel them about the long-term risks of cardiovascular disease and osteoporosis.
- Women and their health care providers may be concerned about the safety of HRT, especially in the context of a genetic predisposition to breast and ovarian cancer (BRCA mutation), or gynecologic cancers with estrogen-receptor expression. Discuss these cases on an individual basis with the treating oncologist. Otherwise, for the vast majority of women (ovarian cysts or benign tumours, early-stage endometrial cancer), the rationale, risks, and benefits of HRT following premature surgical menopause should be discussed.
- The family physician and GPO have pivotal roles as front-line health care providers in supporting these women after premature surgical menopause through education, HRT, and prevention of long-term health consequences.

our study highlights that many women in our province are not prescribed HRT for premature surgical menopause and are at increased risk for significant health consequences.

Contact Dr. Ji-Hyun Jang, [ji-hyun.jang@alumni.ubc.ca](mailto:ji-hyun.jang@alumni.ubc.ca).

Corridor Consult – Oncology Q&A  
continued from page 10

Azure, did not show overall benefit from the addition of zoledronic acid; however, it did show benefit in postmenopausal women with a 25% reduction in recurrence and a 26% improvement in survival. Coleman, the principal investigator went on to do a meta-analysis which confirmed the benefit in postmenopausal women.

A number of studies looked at bisphosphonates

and denosumab in early breast cancer, using a number of different dosage schedules and routes of administration. Similar benefits were reported, although the results to date with denosumab are less impressive.

Recently, BC Cancer's Breast Tumour Group created protocols for use of zoledronic acid in naturally and medically induced menopausal high-risk women. Both the 3-month (every 3 months for 3 years) and 6-month (every 6 months for 5 years)

schedules are effective, providing patients and their doctors with options. Adjuvant bisphosphonate therapy should commence within 1 year of diagnosis, and no later than 18 months following breast cancer surgery.

Contact Dr. Karen Gelmon at [kgelmon@bccancer.bc.ca](mailto:kgelmon@bccancer.bc.ca)

see References on page 14

# Corridor Consult – Gastroenterology Q&A

By Dr. Erica Tsang, PGY-5 Medical Oncology Resident, and Dr. Howard Lim, Medical Oncologist, BC Cancer – Vancouver

## If there is a history of gastric cancer, should family members be screened for *H. pylori*?

Currently, there is not enough evidence to support routine screening for *H. pylori* in asymptomatic individuals. Consider *H. pylori* testing in symptomatic patients as per current guidelines. If a patient has a family history of gastric cancer, screening recommendations vary depending on the type (examples: *CDH1* mutation, Lynch syndrome, familial adenomatous polyposis).

A recent study showed that among individuals with *H. pylori* and a family history of gastric cancer in first-degree relatives, treatment of *H. pylori* reduced the risk of gastric cancer.<sup>1</sup> This has not yet been incorporated into routine guidelines.

## Is there any consideration for population screening for *H. pylori*?

There is not enough data to support population-wide screening for *H. pylori* in asymptomatic individuals.

## What is the best approach for managing patients who have not responded to repeated courses of antibiotic treatment for *H. pylori*?

Recommended options include bismuth quadruple therapy (protein pump inhibitor (PPI), bismuth, metronidazole, tetracycline), and levofloxacin-containing therapy



Dr. Erica Tsang



Dr. Howard Lim

(PPI, amoxicillin, levofloxacin) for 14 days.<sup>2,3</sup> Rifabutin-containing treatments are restricted to cases where at least 3 recommended options have failed.<sup>4</sup>

## Has the prevalent use of PPIs affected the rates of upper GI cancers?

There been no association between PPI use and the rate of upper GI cancers. A controversial 2008 article suggested an association between PPI use and gastric cancer, but there were concerns regarding the study's validity.<sup>5</sup> The Canadian Association of Gastroenterology subsequently released a statement debunking the article and recommended continued use of PPIs as indicated.<sup>6</sup>

## Have H2 receptor blockers decreased the incidence of upper GI malignancies?

There is no association between the use of H2 receptor blockers and the incidence of upper GI malignancies.<sup>7,8</sup>

## What is the current opinion about Barrett's esophagus as a risk factor for cancer?

Barrett's esophagus occurs when the normal stratified squamous epithelium of the esophagus is replaced by metaplastic columnar epithelium. This can transform into esophageal and gastroesophageal junction adenocarcinoma, and thus is a known risk factor for cancer.<sup>9</sup>

## Does treatment of GERD decrease the risk of esophageal cancer?

Barrett's esophagus is known to be associated with esophageal cancer, and can be a complication of chronic GERD. Thus, treating GERD secondary to Barrett's esophagus would, in turn, decrease the risk of esophageal cancer.<sup>9</sup>

## When should a patient with chronic GERD be referred for endoscopy?

Patients with GERD should be referred for upper endoscopy if there are alarm features: new onset of dyspepsia in patients who are  $\geq 60$  years of age, weight loss, anemia, dysphagia, persistent vomiting, and/or

gastrointestinal cancer in a first-degree relative. Alarm features in individuals  $< 60$  years of age should prompt consideration of an endoscopy on a case-by-case basis, as per the American College of Gastroenterology and Canadian Association of Gastroenterology joint guidelines.<sup>10</sup> Discuss with a gastroenterologist to ensure prompt referral.

## What currently available investigations are there for suspected small bowel cancer?

History, physical examination, baseline bloodwork (complete blood count, electrolytes, liver function tests) and screening for fecal occult blood are initial tests. Other investigations include CT scans, and endoscopic techniques such as capsule endoscopy and enteroscopy. CT and MR enterography can be useful if there is a high suspicion without a mass seen on conventional imaging.<sup>11</sup>

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see References on page 14

### FOR MORE INFORMATION

To learn more about the Family Practice Oncology Network or become involved please contact: Jennifer Wolfe  
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## References

1. McDonald S, Rubin P, Phillips TL, Marks LB. Injury to the lung from cancer therapy: clinical syndromes, measurable endpoints, and potential scoring systems. *Int J Radiat Oncol Biol Phys*. 1995 Mar 30;31(5):1187–203.
2. Rosiello RA, Merrill WW, Rockwell S, Carter D, Cooper JA, Care S, et al. Radiation pneumonitis. Bronchoalveolar lavage assessment and modulation by a recombinant cytokine. *Am Rev Respir Dis*. 1993 Dec;148(6 Pt 1):1671–6.
3. Rubin P, Johnston CJ, Williams JP, McDonald S, Finkelstein JN. A perpetual cascade of cytokines postirradiation leads to pulmonary fibrosis. *Int J Radiat Oncol Biol Phys*. 1995 Aug 30;33(1):99–109.
4. Abratt RP, Morgan GW, Silvestri G, Willcox P. Pulmonary complications of radiation therapy. *Clin Chest Med*. 2004 Mar;25(1):167–77.
5. Olivier KR and Peikert T. Radiation-induced lung injury. In: UpToDate, Jett JR, Schild SE and Hollingsworth H (Eds), UpToDate, Waltham, MA, 2020.
6. Limper AH, Knox KS, Sarosi GA, Ampel NM, Bennett JE, Catanzaro A, et al. An official American Thoracic Society statement: Treatment of fungal infections in adult pulmonary and critical care patients. Vol. 183, *American Journal of Respiratory and Critical Care Medicine*. 2011. p. 96–128.

## References

1. Lee, S. J. et al. Time lag to benefit after screening for breast and colorectal cancer: meta-analysis of survival data from the United States, Sweden, United Kingdom, and Denmark. *BMJ* 346, e8441, doi:10.1136/bmj.e8441 (2013).
2. Tang, V., Boscardin, W. J., Stijacic-Cenzer, I. & Lee, S. J. Time to benefit for colorectal cancer screening: survival meta-analysis of flexible sigmoidoscopy trials. *BMJ* 350, h1662, doi:10.1136/bmj.h1662 (2015).
3. Mitera, G. et al. Choosing Wisely Canada cancer list: ten low-value or harmful practices that should be avoided in cancer care. *J Oncol Pract* 11, e296–303, doi:10.1200/JOP.2015.004325 (2015).
4. Tesch, M. & Laing, K. Screening for new primary cancers in patients with metastatic breast cancer: a provincial analysis of the Choosing Wisely Canada recommendations. *Curr Oncol* 26, e309–e313, doi:10.3747/co.26.4289 (2019).

## References

1. Majhail, N.S. (2017). Long term complications after hematopoietic cell transplantation. *Hematology Oncology and Stem Cell Therapy*, 5(1), 1–30.
2. Martin, P.J. et al. (2010). Life expectancy in patients surviving more than 5 years after hematopoietic cell transplantation. *Journal of Clinical Oncology*, 28(6), 1011–6.
3. Bhatia, S. (2011). Long-term health impacts of hematopoietic stem cell transplantation inform recommendations for follow-up. *Expert Review of Hematology*, 4(4), 437–54.
4. Rizzo, J.D., et al. (2009). Solid cancers after allogeneic hematopoietic cell transplantation. *Blood*. 113(5), 1175–83.
5. Majhail, N.S., et al. (2012). Recommended Screening and Preventive Practices for Long-Term Survivors after Hematopoietic Cell Transplantation. *Biology of Blood and Marrow Transplantation* 18, 348–71.

## References

1. Ben-Aharon I, Vidal L, Rizel S, et al. Bisphosphonates in the adjuvant setting of breast cancer therapy--effect on survival: a systematic review and meta-analysis. *PLoS One* 2013 Aug 26;8(8):e70044.
2. Coleman R, Cameron D, Dodwell D, et al.; AZURE investigators. Adjuvant zoledronic acid in patients with early breast cancer: final efficacy analysis of the AZURE (BIG 01/04) randomized open-label phase 3 trial. *Lancet Oncol* 2014;15(9):997-1006.
3. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Adjuvant bisphosphonate treatment in early breast cancer: meta-analyses of individual patient data from randomised trials. *Lancet* 2015;386(10001):1353-61. Erratum in: *Lancet* 2016;387(10013):30.
4. Gnant M, Mlineritsch B, Stoeger H, et al.; Austrian Breast and Colorectal Cancer Study Group, Vienna, Austria. Zoledronic acid combined with adjuvant endocrine therapy of tamoxifen versus anastrozole plus ovarian function suppression in premenopausal early breast cancer: final analysis of the Austrian Breast and Colorectal Cancer Study Group Trial 12. *Ann Oncol* 2015;26(2):313-20.
5. Paterson AH, Anderson SJ, Lembersky BC, et al. Oral clodronate for adjuvant treatment of operable breast cancer (National Surgical Adjuvant Breast and Bowel Project protocol B-34): a multicentre, placebo-controlled, randomised trial. *Lancet Oncol* 2012;13(7):734-42.6. Powles T, Paterson A, McCloskey E, et al. Reduction in bone relapse and improved survival with oral clodronate for adjuvant treatment of operable breast cancer [ISRCTN83688026]. *Breast Cancer Res* 2006;8(2):R13. Erratum in: *Breast Cancer Res* 2006;8(3):406.
6. Janni W, Friedl TWP, Fehm T, et al. Extended adjuvant bisphosphonate treatment over five years in early breast cancer does not improve disease-free and overall survival compared to two years of treatment: Phase III data from the SUCCESS A study. *San Antonio Breast Cancer Symposium* 2017

## References

1. Choi IJ, Kim CG, Lee JY, Kim YI, Kook MC, Park B, et al. Family History of Gastric Cancer and Helicobacter pylori Treatment. *N Engl J Med* 2020 Jan 30;382(5):427-436.
2. Magaret N, Burm M, Faigel D, Kelly C, Peterson W, Fennerty MB. A randomized trial of lansoprazole, amoxicillin, and clarithromycin versus lansoprazole, bismuth, metronidazole and tetracycline in the retreatment of patients failing initial Helicobacter pylori therapy. *Dig Dis* 2001;19(2):174-178.
3. Fallone CA, Chiba N, van Zanten SV, Fischbach L, Gisbert JP, Hunt RH, et al. The Toronto Consensus for the Treatment of Helicobacter pylori Infection in Adults. *Gastroenterology* 2016 Jul;151(1):51-69. e14.
4. Gisbert JP, Calvet X. Review article: rifabutin in the treatment of refractory Helicobacter pylori infection. *Aliment Pharmacol Ther* 2012 Jan;35(2):209-221.
5. Cheung KS, Chan EW, Wong AYS, Chen L, Wong ICK, Leung WK. Long-term proton pump inhibitors and risk of gastric cancer development after treatment for Helicobacter pylori: a population-based study. *Gut* 2018 Jan;67(1):28-35.
6. Leontiadis GI, Veldhuyzen Van Zanten S, Hookey L, Armstrong D, Jones N, Moayyedi P. Canadian Association of Gastroenterology Statement on the Putative Link Between Proton Pump Inhibitor Treatment and Gastric Cancer after Helicobacter pylori Eradication. *J Can Assoc Gastroenterol* 2018 Dec;1(4):155-158.
7. La Vecchia C, Negri E, D'Avanzo B, Franceschi S. Histamine-2-receptor antagonists and gastric cancer risk. *Lancet* 1990 Aug 11;336(8711):355-357.
8. Colin-Jones DG, Langman MJ, Lawson DH, Logan RF, Paterson KR, Vessey MP. Postmarketing surveillance of the safety of cimetidine: 10 year mortality report. *Gut* 1992 Sep;33(9):1280-1284.
9. Armstrong D, Marshall JK, Chiba N, Enns R, Fallone CA, Fass R, et al. Canadian Consensus Conference on the management of gastroesophageal reflux disease in adults - update 2004. *Can J Gastroenterol* 2005 Jan;19(1):15-35.

10. Moayyedi P, Lacy BE, Andrews CN, Enns RA, Howden CW, Vakil N. ACG and CAG Clinical Guideline: Management of Dyspepsia. *Am J Gastroenterol* 2017 Jul;112(7):988-1013.
11. Benson AB, Venook AP, Al-Hawary MM, Arain MA, Chen YJ, Ciombor KK, et al. Small Bowel Adenocarcinoma, Version 1.2020, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw* 2019 Sep 1;17(9):1109-1133.