



Adolescent and
Young Adult Program

Treatment of Sarcoma in Young Adults

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Staff Oncologist, PM and Sickkids

Windsor Regional Cancer
Education Day
November 2020

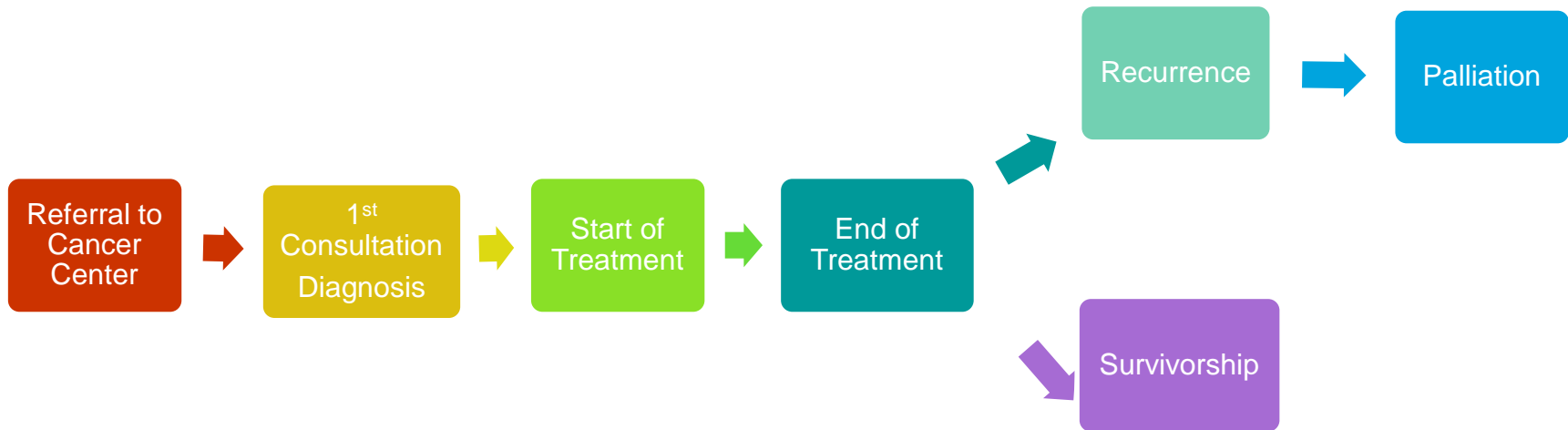
Presenter Disclosure

- **Relationships with financial sponsors:**
 - **Grants/Research Support:** N/A
 - **Speakers Bureau/Honoraria:** Windsor Regional Hospital
 - **Consulting Fees:** N/A
 - **Patents:** N/A
 - **Other:** N/A

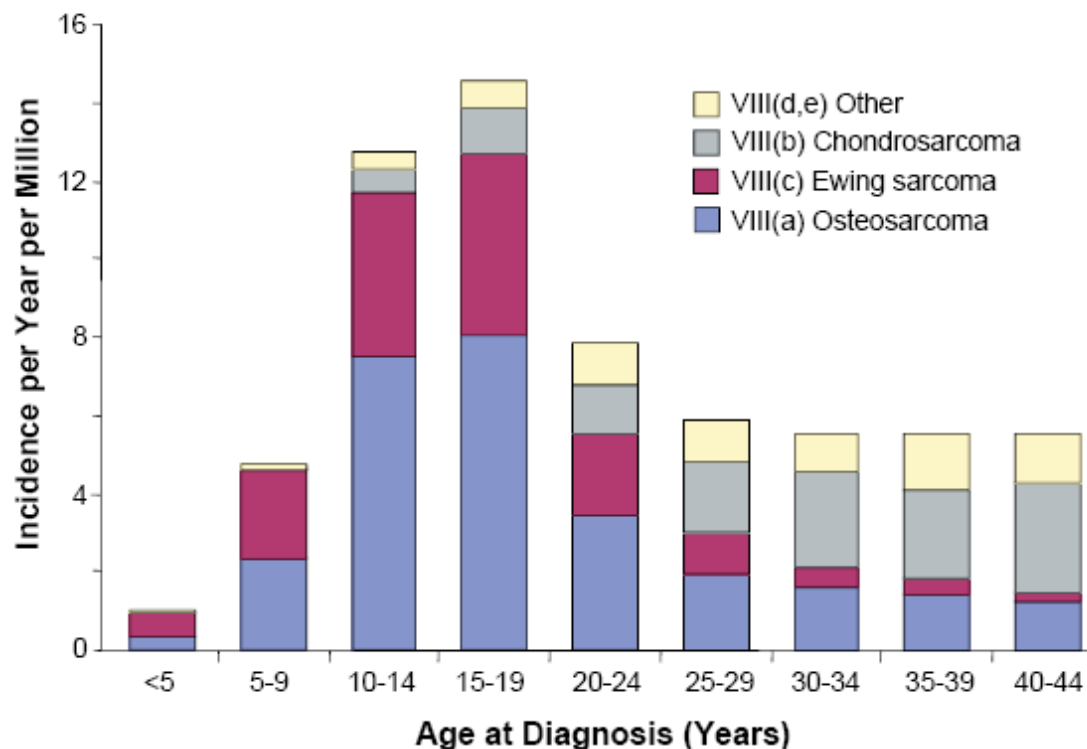
Objectives

- How to identify/treat sarcomas and bone tumours
- How we can facilitate primary care provider referrals for patients with a potential bone cancer
- Knowing that surgery usually occurs in Toronto followed by treatment at the Windsor Regional Cancer Centre, what could be done to streamline this process for our patients?

The Cancer Journey



Incidence of Bone Sarcomas, SEER 1975-2000



Incidence

- 1 in a million – Ewing sarcoma
- 5 in a million - osteosarcoma

The Usual Story

- “I was playing hockey, and my knee hurt”
- Took advil, got better.
- Still played.
- Knee started swelling.
- Went to walk-in clinic. Took advil.
- Went to local ER. Took more advil. Told to rest, ice.
- Still swollen. Still hurt.
- 3 months later, went to my family doctor and got an xray.

There is NO

- Weight loss
- Fever
- Night sweats
- Pallor
- Bruising
- Fatigue
- Anorexia

Red Flags

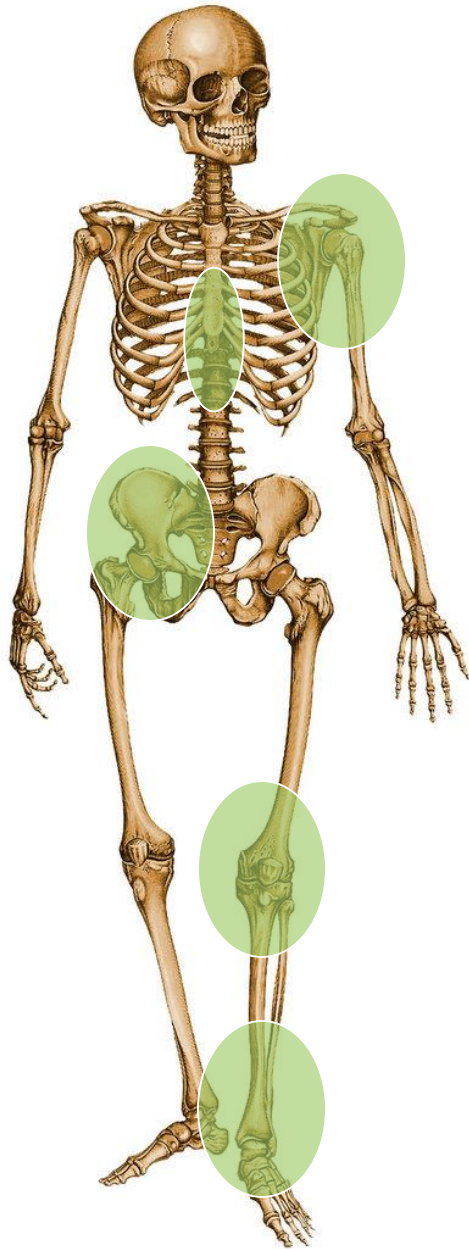
- Persistent pain
 - Neurological weakness
 - Can they walk?
 - Swelling?
 - Back pain...
 - Just doesn't seem right
-
- Not sure? Call. Email. Text. Fax. Skype. Tweet. Instagram.



EWING'S SARCOMA



OSTEOSARCOMA



Most common sites of disease.

Delay to Diagnosis

- Median duration of symptoms: 9 months
- Delay to diagnosis does not change overall survival

VOLUME 32 · NUMBER 18 · JUNE 20 2014

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Time to Diagnosis of Ewing Tumors in Children and Adolescents Is Not Associated With Metastasis or Survival: A Prospective Multicenter Study of 436 Patients

Jean-François Brasme, Martin Chalumeau, Odile Oberlin, Dominique Valteau-Couanet, and Nathalie Gaspar

- But, delay can impact:
 - Surgical resectability, function, morbidity
 - Field of radiotherapy
 - Family distress
 - Chronic pain

Some comments on first steps.

- AYA with bone sarcoma should be seen urgently.
- Every week counts.
- When in doubt, please email. Abha.Gupta@uhn.ca
- If x-ray highly suggestive of malignant bone tumour in a young adult, consider urgent referral to medical oncology even before biopsy results.
 - ****gives time to discuss fertility preservation****

The diagnosis is key.

- Pathology review at Mount Sinai is mandatory for any patient we see (regardless of center of origin – even UHN!)
- Dedicated sarcoma pathologists are required to confirm diagnosis

Molecular analysis: standard of care

Test	Genes
Expanded RAS/BRAF	NRAS, KRAS, BRAF
MSI	BAT-25, BAT26, MON0-27, NR-21, NR-24
MLH1 Promoter methylation	MLH1
GIST	BRAF, CKIT, PDGFRA, KRAS, NRAS
Tumor BRCA1 and BRCA2	BRCA1, BRCA2
Illumina RNA Fusion Panel (Sarcoma/Salivary/Lymphoma)	>500 genes
HER2 FISH	HER2
MDM2 FISH	MDM2

Mis-Diagnosis

- EWSR1+ by FISH
- Presumed to be Ewing's
- RNA fusion panel: t(12;22)(q13;q12) EWSR1/AFT1
- Diagnosis: **CLEAR CELL SARCOMA**

Other examples in last few months

1. ABC – not osteosarcoma
2. Melanoma, not PECOMA
3. Synovial sarcoma, not NOS
4. Carcinoma, not sarcoma (very often)

Multi-disciplinary Tumour Board

- Sarcoma is the most complicated cancer.
- Every patient has a different diagnosis, different treatment, different story, different site of disease!

Multi-D discussions
Standard of care
Cancer Care Ontario

The Toronto Sarcoma Program



The Princess Margaret
Cancer Foundation  UHN

Treatment: No Change for 40 years

Chemotherapy



Local Control – surgery (RT)



Chemotherapy

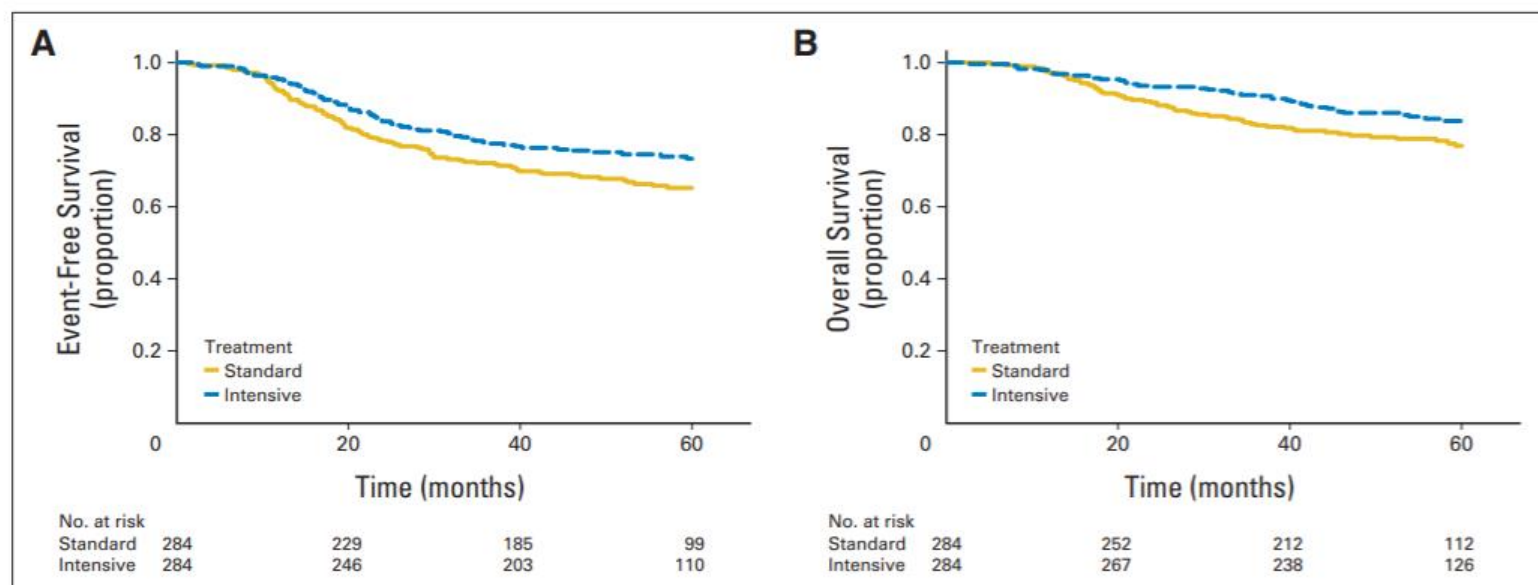
EWING SARCOMA

1. Chemotherapy

- Alternating cycles of VDC with IE
- Goal: 14 cycles
- Cap doxorubicin at 375 mg/m²

Randomized Controlled Trial of Interval-Compressed Chemotherapy for the Treatment of Localized Ewing Sarcoma: A Report From the Children's Oncology Group

Richard B. Womer, Daniel C. West, Mark D. Krailo, Paul S. Dickman, Bruce R. Pawel, Holcombe E. Grier, Karen Marcus, Scott Sailer, John H. Healey, John P. Dormans, and Aaron R. Weiss



2. Maintain dose intensity

- Offer q2 weekly therapy to young fit patients

3. Ensure local control within 3 months of diagnosis

Comparative Study

> [Cancer. 2010 Jul 1;116\(13\):3189-94. doi: 10.1002/cncr.25144.](#)

Clinical outcome of children and adults with localized Ewing sarcoma: impact of chemotherapy dose and timing of local therapy

Abha A Gupta ¹, Alberto Pappo, Natasha Saunders, Sevan Hopyan, Peter Ferguson, Jay Wunder, Brian O'Sullivan, Charles Catton, Mark Greenberg, Martin Blackstein

offered (surgery or radiotherapy, vs both). However, local therapy occurred earlier in pediatric patients compared with adults (3.7 months vs 7.4 months; $P = .0003$). The 3-year event-free survival (EFS) rate in pediatric and adult patients was 70% +/- 9% and 43% +/- 13% ($P = 0.1$), respectively. The 3-year overall survival rate was 81% +/- 7.7% and 59% +/- 12% ($P = .02$) for pediatric and adult patients, respectively. Factors found to be significantly associated with EFS on univariate analysis included pelvic site, cyclophosphamide dose, and time to local therapy. On multivariate analysis, only pelvic disease (hazard ratio [HR] 4.26; $P = .018$) and time to local therapy (HR, 1.19; $P = .002$) were found to be significant.

4. Options for relapsed disease

1. Irinotecan/temodal
2. Cyclophosphamide/topotecan
3. Gemcitabine/docetaxel
4. cabozantinib

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ARTICLES | [VOLUME 21, ISSUE 3, P446-455, MARCH 01, 2020](#)

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Cabozantinib in patients with advanced Ewing sarcoma or osteosarcoma (CABONE): a multicentre, single-arm, phase 2 trial

Prof Antoine Italiano, MD   • Olivier Mir, MD • Prof Simone Mathoulin-Pelissier, MD • Prof Nicolas Penel, MD
Sophie Piperno-Neumann, MD • Emmanuelle Bompas, MD • et al. [Show all authors](#)



OSTEOSARCOMA

1. HD MTX: teens vs. young adults

- MAP chemotherapy remains standard in pediatrics
- HD MTX 12 g/m²/course x 12 courses
- The role for HD MTX in osteosarcoma, especially in adults remains unclear.

2. Do NOT change therapy based on poor necrosis

Comparison of MAPIE versus MAP in patients with a poor response to preoperative chemotherapy for newly diagnosed high-grade osteosarcoma (EURAMOS-1): an open-label, international, randomised controlled trial

Neyssa M Marina, Prof, MD, Sigbjørn Smeland, Prof, MD, [...], and Jeremy S Whelan, Prof, MD

and etoposide. Our findings do not support the intensification of postoperative chemotherapy by adding ifosfamide and etoposide for patients with a poor response to preoperative chemotherapy.

3. 2 new options for relapsed disease

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ARTICLES | [VOLUME 20, ISSUE 1, P120-133, JANUARY 01, 2019](#)



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Efficacy and safety of regorafenib in adult patients with metastatic osteosarcoma: a non-comparative, randomised, double-blind, placebo-controlled, phase 2 study

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Prehab and Rehab

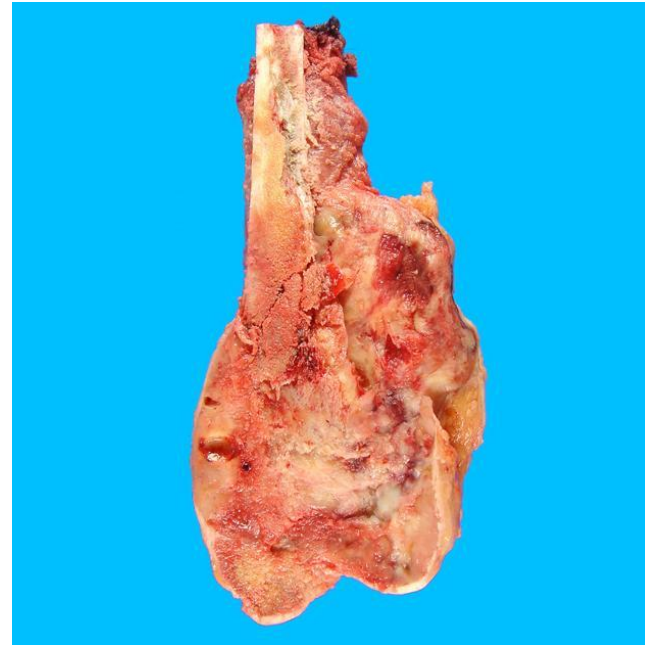
- important to consider fitness and nutrition both before and after surgery
- Need active physiotherapy post-operatively

Chemotherapy After Surgery

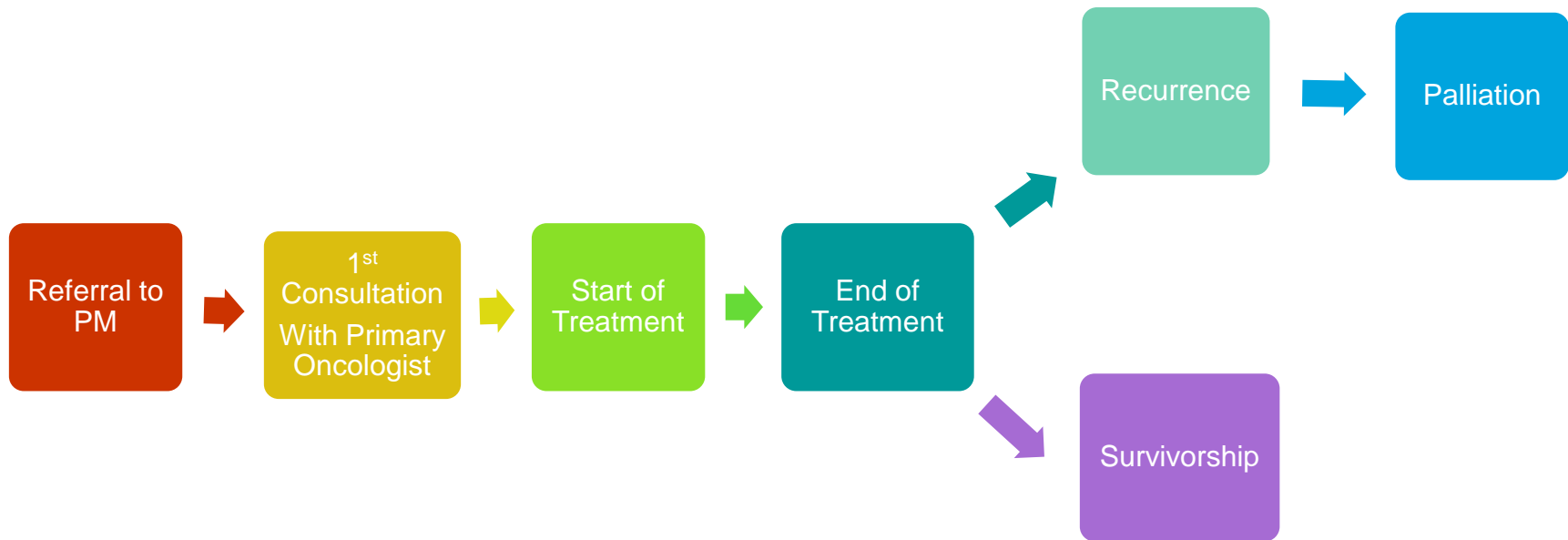
- Life over limb
- We tolerate wound infections/minor dehiscence in order to resume chemotherapy ~ 2 weeks post-operatively
- Patients are good about taking photos of wounds and sending to us
- Hard to get chemo after surgery.

Surgical options

- Amputation
- Endoprosthesis
- Autograft
- Allograft
- Rotationplasty



The Cancer Journey



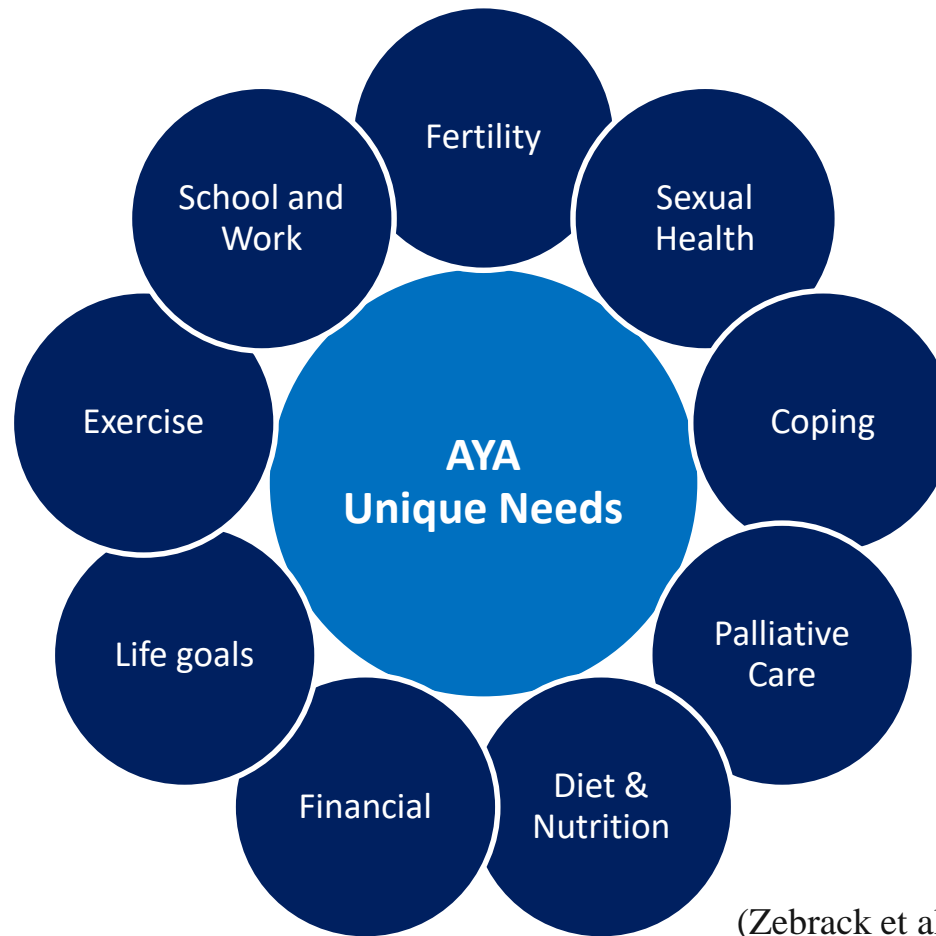
The Young Adult with Sarcoma.

- Has no co-morbidities.
- Has normal organ function.
- Can handle the chemotherapy.
- *But, young adults have many unique needs that deserve programmatic attention.*

The Expanded AYA Team

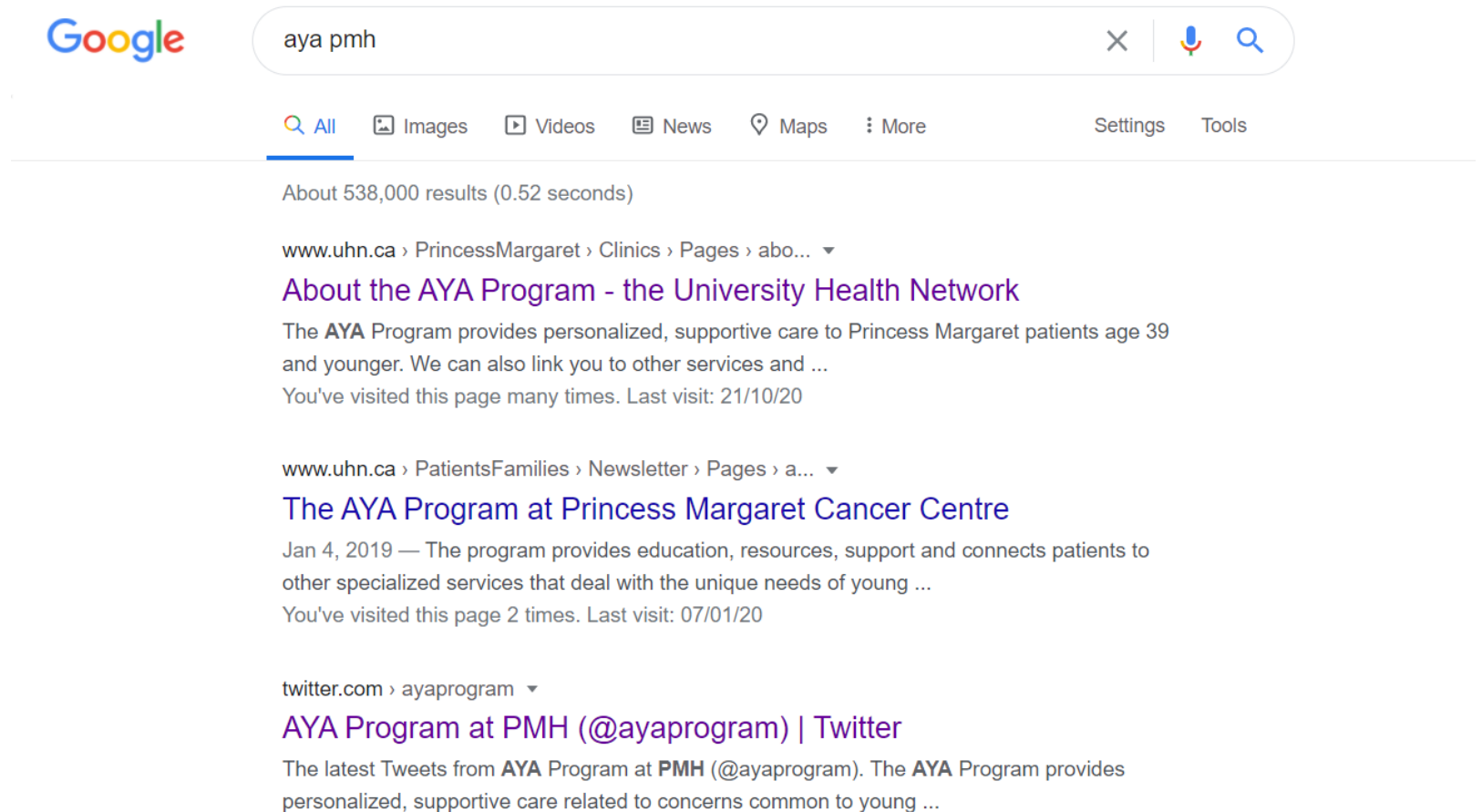




AYA: Many Areas of Need



(Zebrack et al., 2006; Gupta et al., 2011)

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About the AYA Program - the University Health Network

The **AYA** Program provides personalized, supportive care to Princess Margaret patients age 39 and younger. We can also link you to other services and ...

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The AYA Program at Princess Margaret Cancer Centre

Jan 4, 2019 — The program provides education, resources, support and connects patients to other specialized services that deal with the unique needs of young ...

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Adolescent & Young Adult (AYA) Oncology Program

- About
- Health Information
- The Team
- Get Connected
- Personal Stories
- For Health Care Providers

AYA Resources

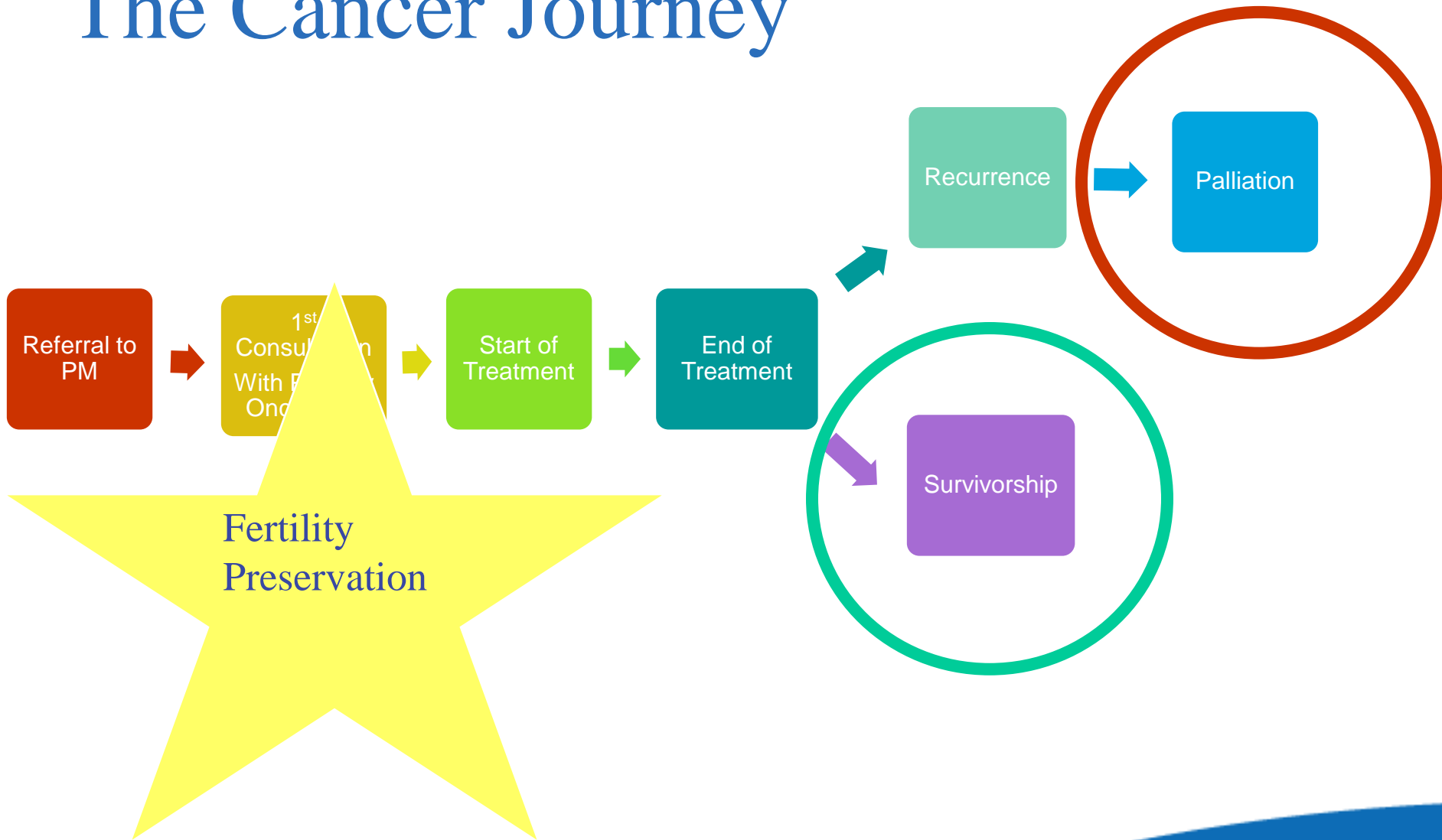
Approximately 1,500 adolescents and young adults (ages 15 to 39) are diagnosed with cancer each year at Princess Margaret. It is important to realize that these patients have unique psychosocial needs and concerns that need to be addressed.

These include:

- [Financial Support](#)
- [Fertility](#)
- [Exercise and Fitness](#)
- [Diet and Nutrition](#)



The Cancer Journey




Fertility Preservation

	Males	Females
Ewing Sarcoma	100% infertile	> 30 years - menopause
Osteosarcoma	<20% infertile	?>35-40 years?

Pelvic
Radiation!

ORIGINAL CONTRIBUTIONS | Care Delivery

Young Adult Experience in an Outpatient Interdisciplinary Palliative Care Cancer Clinic

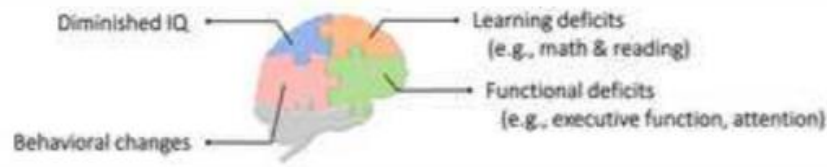



[Jonathan Avery](#), PhD^{1,2} ; [Pamela J. Mosher](#), MD, MDiv^{1,3}; [Alisha Kassam](#), MD, MPH^{4,6}; [Amirrtha Srikanthan](#), MD, MHSc⁷; [Norma D'Agostino](#), PhD¹; [Camilla Zimmermann](#), MD, PhD^{1,8}; [Yan Castaldo](#), BA²; [Rachel Aubrey](#), BSc²; [Caroline M. Rodrigues](#)²; [Adrian Thavaratnam](#)²; [Mahsa Samadi](#), MD²; [Ahmed Al-Awamer](#), MBBS, MHSc^{1,9}; and [Abha Gupta](#), MD, MSc^{1,2,6,10}

CONCLUSION:

YAs who were referred to the interdisciplinary palliative care clinic struggled with the category of palliative care but also found the care they received beneficial. Findings provide an approach to palliative care tailored to YAs with advanced cancer.

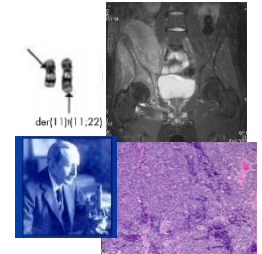
DISEASE & TREATMENT FACTORS

LATE EFFECTS SCREENING PRIORITIES

<p>Neurocognitive dysfunction</p>	<p><u>Disease:</u> CNS tumors</p> <p><u>Radiation Therapy:</u> Head & neck</p> <p><u>Chemotherapy:</u> Antimetabolites, Methotrexate</p>	
<p>Cardiovascular toxicity</p>	<p><u>Radiation Therapy:</u> Head & neck, thoracic, spinal</p> <p><u>Chemotherapy:</u> Anthracyclines, Alkylating agents, Antimicrotubule agents, Vinca alkaloids</p> <p><u>Targeted Therapy:</u> Tyrosine kinase inhibitors, mTOR inhibitors, Proteasome inhibitors, Monoclonal antibodies</p>	 <p>Cardiac Toxicity Cerebrovascular Complications Carotid Artery Disease Peripheral Vascular Disease</p>
<p>Endocrine dysfunction</p>	<p><u>Surgery:</u> Oophorectomy, Orchiectomy</p> <p><u>Radiation Therapy:</u> Head & neck, spinal, abdominal, pelvic, genital, TBI</p> <p><u>Chemotherapy:</u> Alkylating agents</p>	 <p>Ovarian Dysfunction Testicular Dysfunction Thyroid Dysfunction Diabetes Mellitus</p>
<p>Second primary malignancies</p>	<p><u>Radiation Therapy:</u> Head & neck, thoracic, axillary, abdominal, pelvic, spinal, TBI</p> <p><u>Chemotherapy:</u> Alkylating agents (e.g., cisplatin, procarbazine)</p> <p><u>Other:</u> Radioactive Iodine Therapy</p>	 <p>Breast Cancer Colorectal Cancer Lung Cancer Meningioma Thyroid Cancer</p>

Summary

1. Once patient reaches you, be fast.
2. Offer conversation regarding fertility preservation
3. Ensure multi-D tumour board discussion
4. Ensure expert pathology review
5. Consider pre-hab, rehab, survivorship, mental health, palliation for young adults



Thank you for the invitation and
for your attention.

Abha.Gupta@uhn.ca



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SickKids
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