A New Paradigm of Cancer Care for Adolescents and Young Adults (AYA): A Framework for Action

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Co-Chair Canadian National Taskforce for AYA with Cancer
Adolescents and Young Adults (AYA) with cancer and survivors of cancer are distinct from the pediatric and the older adult cancer populations with respect to their spectrum of diseases due to the biology of their cancers, their developmental status, their particular psychosocial needs and their long-term complications of their cancer and treatment thereof. Moreover they are poorly served by the dichotomy of the pediatric and adult oncology services.
In many parts of the world AYA with cancer and survivors of cancer in childhood, adolescence, and young adulthood face disparities of care affecting quality of life and other outcomes. In Canada, AYA with cancer experience these disparities in a health care system that is population-based rather than patient-centric. Improving this situation will necessitate that AYA can benefit not only from the current state of knowledge regarding optimal cancer care, but also from research directed to the biology, treatment and specific needs of this population.
Adolescents and young adults (AYAs) aged 15-29 years are a largely understudied population with regard to cancer. In 2005, nearly 2300 cancer cases (1.5% of all cases in Canada) and approximately 300 deaths due to cancer were reported in AYAs. AYA cancer is both an acute life threatening event and a chronic disease due to delayed complications.
Adolescents and Young Adults

Definition:
Lower age limit – 15 years
Upper age limit – 29 (39) years
Who Are AYA with Cancer?

- 15-29 year olds
- 2,075 new cases per year
- 2% of all invasive cancers
- 326 deaths per year
- 16,000 potential years of life lost due to cancer

“We may be rare but we ARE still there”
(Survivor, March 2010, AYA workshop)

(Bleyer, O’Leary, Barr, & Ries, 2006; Canadian Cancer Society’s Steering Committee, 2009; Oeffinger, Hudson, & Landier, 2009)
So what is unique about AYA cancer?

- Unique life stage
  - Identity and independence
  - Higher education/career development
  - Romantic relationships and family planning

- Unique medical and psychosocial needs
  - Delayed diagnosis
  - Lack of clinical trials/slower gains in survival rates
  - Forced dependence, limited finances, isolation, risk of infertility
So what is unique about AYA?

- AYA are at a very important and often turbulent developmental stage of life
- AYA’s developmental status and their particular psycho-social needs are unique to this age group
- AYA are affected by a different spectrum of cancers, and the biology of their cancers may actually be different
- AYA are not well served by the traditional dichotomy of the health care system, pediatric vs. adult
Cancers in AYA are frequently detected later in their course because young people

- sometimes delay seeking medical advice (cost or denial)
- do not have consistent medical care during which cancer symptoms can be identified

Also, health care providers are not cognizant of cancer in this age cohort.
The small number of cancers in this age group does not appropriately reflect the personal and societal costs of cancer in this population, as reflected in:

- the potential years of life lost or saved
- decreased productivity and QOL due to the impact of the disease during formative years and long-term complications or disabilities.
Mortality

After homicides, suicides and unintentional injury (accidents) CANCER IS THE COMMONEST CAUSE OF DEATH IN THE 15-39 YEAR AGE GROUP IN INDUSTRIALISED SOCIETIES.
Why Does It Matter?

- In Canada and the USA only 30-40% of adolescents are treated in pediatric cancer centres
- Survival advantage in some instances
  - Pediatric v. adult protocols e.g. A.L.L (USA, France, Italy, the Netherlands, Denmark, UK) and soft tissue sarcomas (INT, Italy)
  - Pediatric v. adult centres e.g. Ewing sarcoma (Germany)
Malignant hematologic diseases in adolescents and young adults

William A. Wood and Stephanie J. Lee
<table>
<thead>
<tr>
<th>Trial</th>
<th>Pediatric</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRALLE-93/LALA-94(^{28})</td>
<td>5-y EFS: 67%</td>
<td>5-y EFS: 41%</td>
</tr>
<tr>
<td>CALGB/CCG(^{34})</td>
<td>7-y EFS: 63%</td>
<td>7-y EFS: 34%</td>
</tr>
<tr>
<td>MRC ALL 97-99/UKALLXII-E2993(^{29})</td>
<td>5-y EFS: 65%</td>
<td>5-y EFS: 49%</td>
</tr>
<tr>
<td>GIMEMA/AIEOP(^{30})</td>
<td>2-y OS: 80%</td>
<td>2-y OS: 71%</td>
</tr>
<tr>
<td>HOVON/DCOG(^{31})</td>
<td>5-y EFS: 71%</td>
<td>5-y EFS: 38%</td>
</tr>
<tr>
<td>Adult ALL Grp/NOPHO-92(^{32})</td>
<td>5-y OS: 74%</td>
<td>5-y OS: 39%</td>
</tr>
<tr>
<td>Finnish Leukemia/NOPHO(^{33})</td>
<td>5-y OS: 67%</td>
<td>5-y OS: 60%</td>
</tr>
</tbody>
</table>
## Estimated Five-Year Observed Survival Proportion (95% Confidence Interval) for Selected Cancers in Adolescents and Young Adults (15-29 Years), by Calendar Period, Canada (Excluding Quebec*)

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>All Cancer</td>
<td>80 (79-81)</td>
<td>85 (84-85)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>100 (99-100)</td>
<td>99 (99-100)</td>
</tr>
<tr>
<td>Testis</td>
<td>94 (92-96)</td>
<td>95 (94-97)</td>
</tr>
<tr>
<td>Hodgkin Lymphoma</td>
<td>95 (93-96)</td>
<td>95 (93-96)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>93 (90-94)</td>
<td>93 (91-95)</td>
</tr>
<tr>
<td>Cervix</td>
<td>87 (83-90)</td>
<td>87 (83-90)</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>66 (62-71)</td>
<td>78 (74-81)</td>
</tr>
<tr>
<td>Breast</td>
<td>69 (63-75)</td>
<td>73 (67-78)</td>
</tr>
<tr>
<td>Soft Tissue &amp; Other Extraosseous Sarcoma</td>
<td>63 (57-68)</td>
<td>72 (67-77)</td>
</tr>
<tr>
<td>Central Nervous System</td>
<td>65 (60-69)</td>
<td>68 (64-72)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>57 (52-61)</td>
<td>67 (63-72)</td>
</tr>
</tbody>
</table>
# 10yr K-M Survival by age and era for “pediatric” type malignancies

<table>
<thead>
<tr>
<th>Age yrs.</th>
<th>overall</th>
<th>‘70-’79</th>
<th>‘80-’89</th>
<th>’90-’95</th>
<th>’96-‘05</th>
</tr>
</thead>
</table>
| 12-16    | 65.1% +/- 2.2% (468pt) | 49.1% +/- 3.9% (167pt) | 68.9% +/- 3.5% (177pt) | 82.3% +/- 3.4% (124pt) | ????
| 17-24    | 62.4% +/- 1.7% (850pt)  | 53.1% +/- 2.9% (286pt)  | 67.3% +/- 2.5% (349pt)  | 67.1% +/- 3.4% (215pt)  | ????
| p =      | 0.259       | 0.333    | 0.438    | 0.004    | ????

Locus of Care

Determines access to age and disease appropriate care

- Health care system and providers
- Infrastructure, such as physical facilities
- Treatment including access to clinical trials
Locus of Care

(Place and People)

1. Urban vs. Rural
2. Public vs. Private Institution
3. Academic vs. Non-Academic Institution
4. Pediatric vs. Adult vs. AYA Units
5. Clinical Trial Availability at Institutions
6. Health Care Professional Expertise
TABLE III. Number of Registrations as a Surrogate for Locus of Treatment. Five Year Aggregate Data (1997–2001)

<table>
<thead>
<tr>
<th>Age at diagnosis (years)</th>
<th>15</th>
<th>16</th>
<th>17</th>
<th>18</th>
<th>19</th>
</tr>
</thead>
<tbody>
<tr>
<td>POGO</td>
<td>121</td>
<td>81</td>
<td>37</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>OCR</td>
<td>141</td>
<td>138</td>
<td>156</td>
<td>182</td>
<td>160</td>
</tr>
</tbody>
</table>

POGO, Pediatric Oncology Group of Ontario (five pediatric treatment centres); OCR, Ontario Cancer Registry (all cases of cancer). The proportion of the total registrations (OCR) captured by POGO falls progressively with age, from almost 85% of 15 year olds to fewer than 25% of 17 year olds.
Clinical trial accrual in the U.S.
(Courtesy of Dr Archie Bleyer)

No. Accruals

Patient Age (Years)

2001-2003
2004-2006 decreasing
2004-2006 increasing

Courtesy of A. Bleyer, MD
Survival improvement is correlated with clinical trial participation (Courtesy of Dr Archie Bleyer)
AAPC – Two disease cluster

- High survival rates: Hodgkin lymphoma, testicular tumors, thyroid cancer and melanoma
  - More than 40% of incident cases aged 15 – 29 years
  - Range of 5-year survival rates is 90 – 99%

- Lower survival rates: all other diseases
  - Less than 60% of incident cases aged 15 – 29 years
  - Range of 5-year survival rates is 40 – 75%
Why is age a poor prognostic factor?

- Pharmacology and pharmacogenetics drug distribution, delivery and metabolism may be different
- Supportive care may be greater in pediatric population
- Fewer patients entered onto clinical trials
- Locus of care
- Unknown factors
Why is age a poor prognostic factor?

- May represent different biological spectrum i.e. different disease
- Rx given may be different, less available or less effective in older age patients
- Pediatric type Rx to older age patients may not be tolerated
- Delayed diagnosis
- May be a greater problem of patient compliance
AYA survivors

- Adding to the challenge of providing appropriate health care to this population is the recognition of the needs of survivors of malignant diseases in childhood (0-14 years).

- It has been estimated that 1 in 640 of the population between the ages of 20 and 39 years is a survivor of cancer in childhood.
Survivors of Cancer in AYA

- ~1/640 individuals between the ages of 20 and 39 years is a survivor of childhood cancer
- ~1/3 will have 1 adverse sequelae from the treatment for their disease

“It totally blindsided me... It’s the last thing you expect when you’re 25... I felt cheated... I watched friends getting married, going on trips, advancing in their careers – and I was in a stalemate.”

SS, age 25, non-Hodgkin lymphoma

(Canadian Cancer Society’s Steering Committee, 2009; Oeffinger, Hudson, & Landier, 2009)
Chronic Health Conditions in Adult Survivors of Childhood Cancer

Kevin C. Oeffinger, M.D., Ann C. Mertens, Ph.D., Charles A. Sklar, M.D.,
Toana Kawashima, M.S., Melissa M. Hudson, M.D., Anna T. Meadows, M.D.,
Debra L. Friedman, M.D., Neyssa Marina, M.D., Wendy Hobbie, C.P.N.P.,
Nina S. Kadan-Lottick, M.D., Cindy L. Schwartz, M.D., Wendy Leisenring, Sc.D.,
and Leslie L. Robison, Ph.D., for the Childhood Cancer Survivor Study*

Idea to fruition: 1998 - 2006
## CCSS and Dutch Cohorts

<table>
<thead>
<tr>
<th></th>
<th>CCSS</th>
<th>PLEK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>10,397</td>
<td>1,362</td>
</tr>
<tr>
<td>Yrs of DX</td>
<td>1970-86</td>
<td>1966-96</td>
</tr>
<tr>
<td>Ascertainment</td>
<td>Self-report</td>
<td>Med Eval</td>
</tr>
<tr>
<td>Mean age</td>
<td>26.6 yrs</td>
<td>24.4 yrs</td>
</tr>
<tr>
<td>Interval</td>
<td>17.5 yrs</td>
<td>17.0 yrs</td>
</tr>
<tr>
<td>Any late effect</td>
<td>62.3%</td>
<td>74.5%</td>
</tr>
<tr>
<td>Serious late effect</td>
<td>27.5%</td>
<td>40.0%</td>
</tr>
<tr>
<td>&gt; 3 late effects</td>
<td>23.8%</td>
<td>44.7%</td>
</tr>
</tbody>
</table>

*Geenen MM, et al. JAMA 2007*
Adverse sequelae in survivors

Approximately one third of survivors of cancer in childhood and adolescents will have one or more important adverse sequelae from the treatment for their disease.
Through linkage studies, outcome data are available for patients aged 0-24 yrs diagnosed in BC from 1970 to 1995.

This project is jointly supported by the Canadian Cancer Society (NCIC PPG #06001) and the Canadian Institutes of Health Research (MOP#49563).
CAYACS

- Compared ages 12-16 yrs (BCCH treated) to 17-24 yrs (non-BCCH treated).
- Excluded non “pediatric type pathologies” and pathologies with <10 patients in either group
- Compared 3 eras: 1970-’79; 1980-’89; 1990-’95
Hospitalization 2001-2003

Childhood cohort:
- Twice the odds of hospitalization; 40% more hospitalizations per survivor; 70% longer stays than peers

Young Adult cohort:
- 1.5 times the odds of hospitalization; 30% more hospitalizations per survivor; 70% longer stays than peers
- Region of residence, urban/rural residence, and socioeconomic status did NOT affect utilization in general
Physician Visits 2001-2003

Childhood cohort:
- Overall, 49% increased frequency of physician visits; 51% increased frequency of specialist visits (particularly neurology, internal medicine and ophthalmology)

Young Adult cohort:
- 25% increased frequency of physician visits; 30% increased frequency of specialist visits

- Region of residence, urban/rural residence, and socioeconomic status did NOT affect utilization in general
AYA NCCN Clinical Practice Guidelines-Survivors

COCIA ET AL, JNCCN 2012;10:1112-1150
Survivorship

• AYA Cancer Survivor

• Develop a ‘Cancer Treatment Summary and Survivorship Care Plan’
• Provide a periodic evaluation focusing on history, physical examination, and screening based upon treatment exposures, and risk for treatment-related late effects
• Counsel regarding lifestyle practices and methods to reduce risk (eg, avoiding smoking, increasing level of physical activity)
• Advocate for appropriate health care coverage
• Recommend a dental exam and cleaning every 6 months
## Selected Exposures

- Cranial or Craniospinal Radiation
- Cheat Radiation
- Abdominal or Pelvic Radiation

## Screening Recommendations

- Neuroendocrine axis screening
- Neuropsychological evaluation
- Females: see breast cancer screening
- Thyroid Screening
- Cardiovascular risk assessment and screening
- Screening for Cardiomyopathy
- Screening for valvulas heart disease
- Pulmonary screening
- Colorectal cancer screening
- Assessment of gonadal function
- Screening for kidney or bladder disease
Selected Exposures

- Alkylating Agents
- Anthracyclines
- Bleomycin

Screening Recommendations

- Screening for kidney or bladder disease
- Assessment of gonadal function
- Screening for t-AML or myelodysplasia
- Pulmonary screening (for selected agents)
- Screening for cardiomyopathy
- Screening for cardiomyopathy
- Screening for t-AML or myelodysplasia
- Pulmonary screening
Selected Exposures

- Cisplatin
- Epipodophyllotoxins

Screening Recommendations

- Cardiovascular risk assessment
- Screening for kidney and/or bladder disease
- Audiological evaluation
- Screening for t-AML or myelodysplasia
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<table>
<thead>
<tr>
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<th>Screening Recommendations</th>
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<tr>
<td>Cranial or Craniospinal</td>
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<td></td>
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<tr>
<td></td>
<td>• Assessment of gonadal function</td>
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<td></td>
<td>• Screening for kidney or bladder disease</td>
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Selected Exposures

- Cisplatin

- Epipodophyllotoxins

Screening Recommendations

- Cardiovascular risk assessment
- Screening for kidney and/or bladder disease
- Audiological evaluation
- Screening for t-AML or myelodysplasia

- Screening for t-AML or myelodysplasia
AYA Cancer Trust UK Model

• first Teenage Cancer Trust unit at the Middlesex Hospital in London in 1990.

• Why?
  • teenagers should not have to stop being teenagers, just because they have cancer.

• How?
  • fund and build specialist units for young people in NHS hospitals, 17 to date across the UK
Roles of the AYA Cancer Unit

- Act as a named point of contact on a day-to-day basis
- Arrange appropriate support from other professionals
- Provide ongoing information and support at all stages of your care
- Listen to your views (website, Facebook, twitter accounts)
- Give you the opportunity to be involved in your care
- Promote your independence
- Support you in making decisions
- Help you cope with the physical, social and emotional effect of cancer and its treatment
Roles of the Teenage Cancer Unit

- Communicate with your school/college/university to support you through your education
- Organize teaching programs for schools/colleges about issues relating to cancer and young people
- Work with community teams to arrange support at home
- Visit you at home, hospital or in a place of your choice
- Offer advice on work, finances and other aspects of your life that can be affected by cancer
Units for teenagers and young adults (16-25)

• in a more relaxed, colorful and vibrant environment

• each bedroom has a flat screen TV, internet access and a games console with wireless controls.

• Age-appropriate environment
What about Canada

- Task force
- Recommendations
- Communication
- Framework for Action
Canadian Task Force on Adolescents and Young Adults with Cancer

A Joint Initiative of C17 and CPAC

Co-Chairs:
Ronnie Barr
Paul Rogers
Brent Schacter
Mission:

To ensure that AYA Canadians with cancer and AYA survivors of cancer have prompt, equitable access to the best care, and to establish and support research to identify how their health outcomes and health-related quality of life can be optimised.
Canadian Task Force on Adolescents and Young Adults with Cancer

Vision:
To mitigate the current disparities of care for AYA with cancer or survivors of childhood cancer through advances in treatment and research, respecting the unique circumstances and needs of this population, enacted across all health care jurisdictions in Canada.
AYA Task Force Survey

- A questionnaire about services available to AYA cancer patients, and for follow-up care of survivors of cancer as children or AYA was developed by a working group of the AYA Task Force
- Questionnaires were mailed between April 15 and May 13, 2009 to:
  - C17 Council members, representing all pediatric cancer centres in Canada;
  - all cancer treatment institutions listed by the Canadian Association of Provincial Cancer Agencies (CAPCA) and La lutte contre le cancer
Challenges faced by institutions who reported treating patients outside their institutional age limit

- Getting other specialties to see patient
- Getting patient admitted
- Getting patient seen in the emergency dept
- Staff's lack of comfort in providing age-appropriate medical and psychosocial support
- Financial barriers
- Hospital rules/policies
- Other
Dedicated AYA resources available at centre

- Age-specific health education materials
- Peer mentoring service (AYA to AYA)
- Support Group
- Family or individual counseling with AYA focus
- Standardized process to teach AYA to manage their own healthcare
- Age-specific programs to help with school-related issues
- Age-specific programs to help establishing financial independence

[Bar chart showing percentage of resources available for Pediatric and Adult.]
1. followed in dedicated survivor clinic

2. followed in a disease-specific active treatment clinic

3. discharged and transferred back to their family physician

4. followed periodically in active treatment clinic but are also followed by their family physician

5. discharged from cancer centre without a formal plan for follow-up care

other mechanism

both option 1 and 2

both option 2 and 3
Where are patients seen in your facility, if you see patients who received all therapy at a pediatric center?

- 41.2% dedicated survivor clinic
- 47.1% disease-specific active treatment clinic
- 11.8% other
Does your centre accept, for ongoing care and follow-up patients who have received all of their therapy at a pediatric oncology facility?

- YES: 78.3%
- NO: 21.7%
QB3/7. In your facility how important are the following in the diagnosis and treatment of AYA (15-29 years old) with pediatric/adult type cancers?

**Importance index: sum of all responses, higher score indicates greater importance**

<table>
<thead>
<tr>
<th></th>
<th>Pediatric centres</th>
<th>Adult centres</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Index Score (max score =64)</td>
<td>Order</td>
</tr>
<tr>
<td>Lack of experience of oncologist</td>
<td>55</td>
<td>1</td>
</tr>
<tr>
<td>Limited access to appropriate specialist for consultation</td>
<td>28</td>
<td>4</td>
</tr>
<tr>
<td>Lack of experience of pathologists</td>
<td>28</td>
<td>4</td>
</tr>
<tr>
<td>Lack of experience of surgeons</td>
<td>33</td>
<td>2</td>
</tr>
<tr>
<td>Lack of experience of radiologists</td>
<td>30</td>
<td>3</td>
</tr>
<tr>
<td>Lack of experience of pharmacists</td>
<td>26</td>
<td>5</td>
</tr>
<tr>
<td>Limited availability of appropriate drugs</td>
<td>28</td>
<td>4</td>
</tr>
</tbody>
</table>
Workshop on
Adolescents and Young Adults with Cancer:
Towards Better Outcomes in Canada

March 11 – 13, 2010
Novotel Toronto Centre • 45 The Esplanade • Toronto, Ontario, Canada • M5E 1W2

Workshop Programme

Organized by the Task Force on Adolescent and Young Adult Cancer, an initiative of the Canadian Partnership Against Cancer, and C17 Council, the national network of Canadian Pediatric Hematology/Oncology Programs.
Principles and Recommendations for the Provision of Healthcare in Canada to Adolescent and Young Adult-Aged Cancer Patients and Survivors

Canadian AYA Task Force

Journal of Adolescent and Young Adult Oncology
Volume 1, Number 1, 2011
Recommendations

1. Active Therapy and Supportive Care
   • Services must be provided to address the unique needs of AYAs with cancer and survivors of cancer in childhood, adolescence and young adulthood in order to redress inequities in the care provided to this group relative to both younger and older cancer patients.
Recommendations

2. Psychosocial Needs
   - AYA with cancer have unique psychosocial needs that must be met to enable each one to reach their full potential as productive functioning members of society
3. Palliation and Symptom Management
   - The challenge of providing palliative care to AYA patients, who have unique needs related to their developmental stage, must be addressed
Recommendations

4. Survivorship
   - Implementation of life-long monitoring and follow-up of survivors of cancer in childhood, adolescence and young adulthood will provide economic and other societal benefits and help mitigate late and long-term treatment effects.
5. Research and Metrics

- Research and establishment of outcome metrics are required to investigate issues critical to AYA with cancer and survivors of cancer in childhood, adolescence and young adulthood in order to target interventions and health care policy to improve all phases of the cancer journey.
6. Awareness and Advocacy

- Awareness of issues specific to AYA with cancer must be improved and advocacy efforts to increase awareness and advocate for change must be nurtured.
Framework for Action on Recommendations for Care of AYA with Cancer

A Process for Change in the Care of Adolescents and Young Adults (AYAs) with Cancer in Canada. “Moving to Action”: the Second Canadian International Workshop. International Perspectives on AYAO,

JOURNAL OF ADOLESCENT AND YOUNG ADULT ONCOLOGY
Volume 2, Number 2, 2013
Framework for Action

Two common areas of focus across all recommendations:

- Creation of AYA multi-disciplinary teams
- Development of tools specific to AYA needs
to be implemented within a five-year period.
Multi-disciplinary teams

Goal:
Age-appropriate care should be delivered and/or supported by multi-disciplinary teams populated with age- and disease-specific medical and psychosocial experts able to communicate effectively and provide evidence-based care, including age-appropriate and developmentally appropriate supportive and psychosocial care.
AYA-specific tools

Goal:
Every AYA and their care team should have access to specific tools to help improve the quality of care and manage their cancer journey from diagnosis to palliation or survivorship.
Organization: Multi-disciplinary Team Structures

Three organizational structures will work in concert at the national and regional levels to implement the roadmap:

- National Task Force (NTF)
- NTF Working Groups
- Regional Action Partnerships (RAPs)
The RAPs are responsible for leading implementation of the roadmap in their provinces and territories and for communicating with others at the national and provincial levels.
What is needed in BC Provincial Strategy for AYA

- Risk Based Tier System of LTFU for AYA survivors
- Multidisciplinary AYA Consult Team for new patients
- Communication between sites and tumour groups
- Increase Clinical trial Availability
- Age appropriate Unit
- Awareness that this cohort requires a different approach
- Implementation of National Recommendations
Baboons