Adolescents and Young Adults (AYA): The Forgotten Age Group in Cancer Clinical Trials

ARCS Annual Conference 2019
Victorian Comprehensive Cancer Centre (VCCC) **Steering Committee on Increasing AYA Access to Clinical Trials Program**

- Alexandra Robertson (Chair)
- Jeremy Lewin (Deputy Chair)
- Natasha Morello (Consumer)
• Do you work in oncology?

• Are you a:
  – Clinician researcher?
  – Pharma rep?
  – Regulator?
  – Consumer?
Session outline

- Clinical Trial Gap for AYA
- Consumer perspective
- VCCCC Increasing AYA Access to Clinical Trials Program
  - AYA Research Ethics & Governance Awareness
  - Hospital-based Access to clinical trials for AYA
  - Improving AYA cancer care and clinical trial Availability through paediatric-adult oncology collaboration

- Panel Discussion: sponsor, clinician, consumer, ethics & governance and <insert your name here>
Clinical trial gap for AYA

Jeremy Lewin
Medical Oncologist, Peter MacCallum Cancer Centre
Medical Director ONTrac at Peter Mac Victorian Adolescent & Young Adult Cancer Service
Cancer in the AYA population

- Cancer is the leading cause of non accidental death and follows: accidents, homicides, and suicides\(^1\)
- Incidence of cancer is 1.5 times higher in young people, compared to children less than 15 years\(^2\)
- AYA with particular cancer subtypes have inferior survival compared to children & older adults with the same diseases\(^3,4\)
- Overall improvements in AYA cancer survival rates lag well behind those achieved in both children or older adults\(^1\)

Clinical trial gap for AYA

Among AYA, lack of survival improvement compared to children and older adults\(^1\)

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\(^1\) Veal, G. J., Hartford, C. M., & Stewart, C. F. (2010). Journal of Clinical Oncology, 28(32), 4790
Survival gap contributors

Nature
- Tumour diversity
- Tumour biology
- Host biology

Nurture
- Delays in diagnosis
- Poor clinical trial enrolment
- Referral pathways
- Access to AYA oncology expertise
- Paediatric-adult divide
Clinical trial gap for AYA

- There is a clear *divide* between paediatric and adult clinical care in Australia
- AYA (15-25 years) may have paediatric- or adult-type cancers
- Also experience rare cancers relatively unique to their age group.
Clinical trial gap for AYA

Bleyer (2007). Adolescent and Young Adult (AYA) Oncology: The First A. Pediatric Hematology and Oncology 24:325-336

~315 Victorian AYA cancer diagnoses annually
Mean number of diagnoses 2015-2017, Victorian Cancer Registry, Cancer Council Victoria
Internationally, AYA enrolments to clinical trials are very low:

**USA**

**Victoria, Australia**

**Participation in Clinical Trials by Age 1992-1996 (Vic)** All 10-24yo leukaemias, lymphomas, brain tumours, germ cell tumours, bone tumours, soft tissue sarcomas identified from Victorian Cancer Registry

Bleyer et al, *Cancer* 2006

US National Treatment Trial Accruals, 1990-1998
US National Cancer Mortality Reduction, 2000 - 2006

Cancer Council Victoria – Victorian Cancer Trials Link (VCTL)

- In November 2018, of 183 listed cancer trials relevant to the 10 most common AYA cancers by incidence and mortality:
  - Only 11.5% of trials had an age eligibility both above and below the age of 18 years
  - Only 1.1% of trials were open at both a paediatric and an adult hospital

AYA **Availability** of relevant clinical trials (based on age eligibility) is *low*

AYA **Access** to clinical trials is *restricted* based on location of care
## Causes of clinical trial gap

### Institutional factors
- Caseload per institution, and proportion of caseload
- Research capacity of institution, and priorities
- Clinical interest
- Funding
- Access, location of care

### Trial factors
- Numbers
- Phase
- Age group and eligibility
- Funding
- IRB/HREC

### Co-operative group factors
- Restrictive membership (COG)
- Discipline vs age group approaches
- Group structure
- Trials strategies

### Patient factors
- Adherence
- Enrolment/consent
- Psychosocial concerns
Importance of trial access: consumer perspective

Natasha Morello
The VCCC
Strategic Research Plan 2017 – 2020:

What’s needed to turn research discoveries into better outcomes for Victorian cancer patients?

➢ 19 SRP programs supported by $30M from the Victorian Government
The VCCC AYA Program

Increasing AYA Access to Clinical Trials Program:

• 2018 – 2020

• VISION: to ameliorate barriers to AYA cancer clinical trial access in our local Victorian setting

• Expert Steering Committee encompassing:
  – VCCC Partner Organisation clinicians
    • Adult and paediatrics
    • Doctors and nurses
  – Research Ethics & Governance expertise
  – Consumer representation
  – Pharmaceutical representation
  – Regional representation
The VCCC AYA Program

Mapping Local Processes and Barriers

Working Group 1: Ethics & Governance Awareness
- No streamlined processes b/w adult and paed centres
- Lack of resources to open trials across multiple sites
- Reviewing ethics committees specific to paeds or adults
- Parent vs participant consent across the age range
- Trial PIs are usually adult or paediatric, not both

Working Group 2: Availability
- Age eligibility criteria
  - Institutional & regulatory barriers for inclusion of adolescents in adult trials & young adults in paediatric trials
  - Traditional separation of paediatric and adult clinical care
    - Lack of trials for rare AYA cancer types
    - Lack of local data on current AYA trial participation

Working Group 3: Access
- Paediatric trial access in adult/regional centres
- Trial governance at regional centres
- Access to adult trials in paediatric setting, and to paediatric trials in adult setting
The VCCC AYA Program

Working Group 1: Ethics & Governance **Awareness**

**Aims:**
Increase awareness of ethics and governance processes that support the establishment of clinical trials with an age eligibility encompassing both children and adults
- Consenting child participants
- National Mutual Acceptance HREC review

**Deliverable:**
Communication strategy and guidelines for ethics & governance processes to establish an AYA clinical trial

Working Group 2: AYA Clinical Trial **Availability**

**Aims:**
Better understand availability of AYA-relevant cancer clinical trials in the Victorian setting
- Cancer Council Victoria VCR and CTMS data
  - How many AYAs and their diagnosis?
  - Where are the AYAs?
  - What relevant trials are open?
  - What is the trial age eligibility?
  - Where are the trials open?

Improve communication and collaboration between adult and paediatric oncology
- AYA Craft Groups within relevant tumour streams

**Deliverable:**
Develop and implement a viable paediatric-adult “craft group” model to ensure ongoing availability of AYA clinical trials

Working Group 3: AYA Clinical Trial **Access**

**Aims:**
Work with key stakeholders to identify a process that improves access for young adults to paediatric trials, and adolescents to adult trials
- Trials to AYAs?
  (open paed trials at adult sites)
- AYAs to trials?
  (formalised procedure for young adult access to paediatric hospital)
- Recommended care pathways based on age and cancer type?

**Deliverable:**
Guidelines for the referral of AYAs across sites in order to access open clinical trials
VCCC Survey of IIT Investigators and Research Ethics Offices revealed:

- Few HRECs query the justification for age eligibility in trial protocols
  - Biologically based, or a carry-over from old protocols?
- Lack of Investigator understanding of National Mutual Acceptance HREC system
  - Belief that trial must be reviewed by the HREC associated with the lead site, rather than the most appropriate HREC
  - Belief that a trial enrolling adults and adolescents/children needs to be reviewed by both an adult and a paediatric HREC
- Adult Investigator fear of/extra workload for consenting paediatric research participants

Solution: Produce a Guideline document addressing these *perceived* barriers to AYA trial establishment
ESTABLISHING A CANCER CLINICAL TRIAL WITH AGE ELIGIBILITY ENCOMPASSING ADOLESCENTS AND YOUNG ADULTS (AYA)

(AYA Cancer Clinical Trials)

Research Ethics and Governance Guidelines

These guidelines are based on standard operating procedures observed by research ethics and governance offices of the Royal Children's Hospital and Melbourne Health in Victoria, Australia. As such, some processes may not be broadly applicable in all settings.
Research Ethics and Governance Guidelines

- Education and practical recommendations
- For both Trial Investigators and HRECs (Research Offices)
- Covering:
  - Age eligibility for a cancer clinical trial
  - PICFs and consent processes for participants and parents/guardians
  - Selecting an appropriate reviewing HREC
  - Protocol amendments to provide AYA access to already established trial protocols
<table>
<thead>
<tr>
<th>Working Group 1: Ethics &amp; Governance <strong>Awareness</strong></th>
<th>Working Group 2: AYA Clinical Trial <strong>Availability</strong></th>
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  - National Mutual Acceptance HREC review | **Aims:** Better understand availability of AYA-relevant cancer clinical trials in the Victorian setting  
  - Cancer Council Victoria VCR and CTMS data  
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  - AYA Craft Groups within relevant tumour streams | **Aims:** Work with key stakeholders to identify a process that improves access for young adults to paediatric trials, and adolescents to adult trials  
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  - Recommended care pathways based on age and cancer type? |
| **Deliverable:** Communication strategy and guidelines for ethics & governance processes to establish an AYA clinical trial | **Deliverable:** Develop and implement a viable paediatric-adult clinical liaison model to ensure ongoing availability of AYA clinical trials | **Deliverable:** Guidelines for the referral of AYAs across sites in order to access open clinical trials |
Access to AYA trials

Adolescents 15-17yrs

- **Adult Trial Available**
  - Yes
  - **Adult Trial Accessible**
    - NO
    - 3% Victorian trials with age eligibility <18yrs*
    - n=1 eligibility waiver?
  - Access to adult hospital permitted
  - **Trial Enrolment Possible**
    - YES

Young Adults 18-25yrs

- **Paediatric Trial Available**
  - YES
  - **Paediatric Trial Accessible**
    - No
    - Access to paediatric hospital restricted
  - **Trial Enrolment Possible**
    - Yes
    - NO

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*Therapeutic cancer trials relevant to AYA cancers, open for recruitment in Victoria in November 2018
Source: Cancer Council Victoria, Victorian Cancer Trials Link, manual search
1. Bring the patients to the trials
   - AYA treated at paediatric site on appropriate trial
   - Issues: appropriateness of space, agreement by Executive, scope of practice of clinicians

2. Bring the trials to the patients
   - Expand Children’s Oncology Group (COG) membership: allow trials to be opened at both paed & adult sites
   - Issues: duplicating resources, study coordinators, governance requirements

Por qué no los dos?
# The VCCC AYA Program

## Working Group 1: Ethics & Governance **Awareness**

**Aims:**
- Increase awareness of ethics and governance processes that support the establishment of clinical trials with an age eligibility encompassing both children and adults
- Consenting child participants
- National Mutual Acceptance HREC review

## Working Group 2: AYA Clinical Trial **Availability**

**Aims:**
- Better understand availability of AYA-relevant cancer clinical trials in the Victorian setting
  - Cancer Council Victoria VCR and CTMS data
    - How many AYAs and their diagnosis?
    - Where are the AYAs?
    - What relevant trials are open?
    - What is the trial age eligibility?
    - Where are the trials open?
- Improve communication and collaboration between adult and paediatric oncology
- AYA Craft Groups within relevant tumour streams

## Working Group 3: AYA Clinical Trial **Access**

**Aims:**
- Work with key stakeholders to identify a process that improves access for young adults to paediatric trials, and adolescents to adult trials
  - Trials to AYAs?
    - (open paed trials at adult sites)
  - AYAs to trials?
    - (formalised procedure for young adult access to paediatric hospital)
    - Recommended care pathways based on age and cancer type?

## Deliverables:

**Working Group 1: Ethics & Governance**
- **Awareness**
  - Communication strategy and guidelines for ethics & governance processes to establish an AYA clinical trial

**Working Group 2: AYA Clinical Trial**
- **Availability**
  - Develop and implement a viable paediatric-adult “craft group” model to ensure ongoing availability of AYA clinical trials

**Working Group 3: AYA Clinical Trial**
- **Access**
  - Guidelines for the referral of AYAs across sites in order to access open clinical trials
Jeremy Lewin
Medical Oncologist, Peter MacCallum Cancer Centre
Medical Director ONTrac at Peter Mac Victorian Adolescent & Young Adult Cancer Service
AYA clinical trial availability

**Adolescents 15-17yrs**

- **Adult Trial Available**: Yes → **Adult Trial Accessible**: Access to adult hospital permitted
  - 3% Victorian trials with age eligibility <18yrs*
  - n=1 eligibility waiver?
  - YES → **Trial Enrolment Possible**

**Young Adults 18-25yrs**

- **Paediatric Trial Available**: YES → **Paediatric Trial Accessible**: Access to paediatric hospital restricted
  - 58% Victorian trials with age eligibility ≥18yrs*
  - No
  - YES → **Trial Enrolment Possible**

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*Therapeutic cancer trials relevant to AYA cancers, open for recruitment in Victoria in November 2018
Source: Cancer Council Victoria, Victorian Cancer Trials Link, manual search
• Apparent that there is no established mechanism for communication and collaboration between paediatric and adult oncology

• Facilitate regular and deliberate paediatric-adult oncology knowledge

• Framework works at a systems level (not patient level)
Objectives:

- Improved awareness of AYA treatment standards across the oncology sector
- Collaborative decision making around appropriate AYA care pathways
- Improved awareness of AYA clinical trials open across paediatric and adult oncology centres
- Improved availability of clinical trials open for AYA via collaborative trial development
- Reduced duplication of research efforts between paediatric and adult oncology
- Improvements to AYA treatment standards over time
AYA Craft Group Logic

Participants/Inputs

- Adult oncology
- Paediatric oncology
  - Tumour streams: Sarcoma, Brain, Leukaemia, Lymphoma, Germ Cell, EDD/molecular sequencing
  - VCCC AYA and R&E Leads Programs

Activities

- Regular tumour stream AYA craft group meetings
  - Discuss: Treatment standards, Trial availability, New IIT ideas, Trial access, etc.

Products

- Bridge between paediatric and adult oncology

Short term outcomes

- Improved communication between adult and paediatric oncology
- Increased awareness of available clinical trials and how to access them
- More AYA cancer patients offered clinical trial participation
- Increased AYA clinical trial participation within the tumour stream
- Increased research collaboration between adult and paediatric centres

Long term outcomes

- Strengthened paeds-adult oncology relationships
- Collaborative location of care decisions
- Increase in cancer clinical trials availability
- Advancements in AYA standard of care
- Increases in AYA cancer survival

Assumptions

Craft group participants are motivated to improve standard care for AYAs with cancer
AYAs will enrol in trials made available to them

External factors

Relevant clinical trials are open and accessible
Funding and resources are available to ensure ongoing craft group sustainability
For each tumour stream within which an AYA Craft Group is established, membership should include the following:

- Paediatric oncologist
- Adult oncologist
- Tumour Stream Champion

Membership might additionally include:

- AYA oncology representation
- Clinical trial pathway navigator
- Program Manager
• Information on availability of clinical trials relevant to AYA
• Will aid in future research directions focussed on improvements to AYA standards of care
• Encourage the inclusion of broader age eligibilities that encompass the AYA age range of 15-25 years in future trial protocols
• Harmonization of clinical trial pipelines relevant to AYA
• Avoidance of trial duplication for rare cancer subtypes
• To perform a basic audit of the patient population including clinical trial recruitment 15-25yo within the craft group on an annual basis
• Young people deserve **equity of access** to clinical trials, irrespective of where they are being treated.
• In the Victorian landscape there are **no ethics and governance barriers** to this equity of access - the barriers are perceived in nature.
• Deliberate **paediatric-adult relationship building** through ‘craft-groups’ is aimed at improving future trial opportunities.
• Creating **access procedures** for adolescents to be treated at adult sites (15-18yo) and young adults (18-25yo) to be treated at paediatric sites for clinical trials is currently in development.
• Although our program is Victorian based, the AYA equity issue should be on the **national agenda**.
• We urge others to translate our learnings and modify to their local health environment.
VCCC Increasing AYA Access to Clinical Trials Steering Committee:

Alexandra Robertson (Chair)  Jeremy Lewin (Deputy Chair)
Christie Allan  Natasha Morello
Nicholas Ball  Robyn Strong
Peter Choong  Leanne Super
Rachel Conyers  Angela Watt
Ryan Hehir  Chris Williams

Program Management:  Anne Woollett (Head, Clinical Trials Programs VCCC)
                      Justine Ellis (Program Manager)

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