Defining the Clinical Trial Question

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CYP-C Research Champion Educational Series

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CANCER IN YOUNG PEOPLE IN CANADA PROGRAM
PROGRAMME CANCER CHEZ LES JEUNES AU CANADA

Healthier Children. A Better World.

SickKids
THE HOSPITAL FOR SICK CHILDREN

Disclosures

- No financial

- Not a health services researcher

Outline

- Introduction to CYP-C
- Starting Out
- How to Develop a Research Question
- Conclusions

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Introduction to CYP-C

- Population-based Canadian pediatric cancer surveillance system
- Quality higher, more detailed than CCR
- Rationale:
  - Resource allocation, planning
  - Evaluation of quality, outcomes
  - Facilitate clinical care
  - Research

CANCER IN YOUNG PEOPLE IN CANADA PROGRAM
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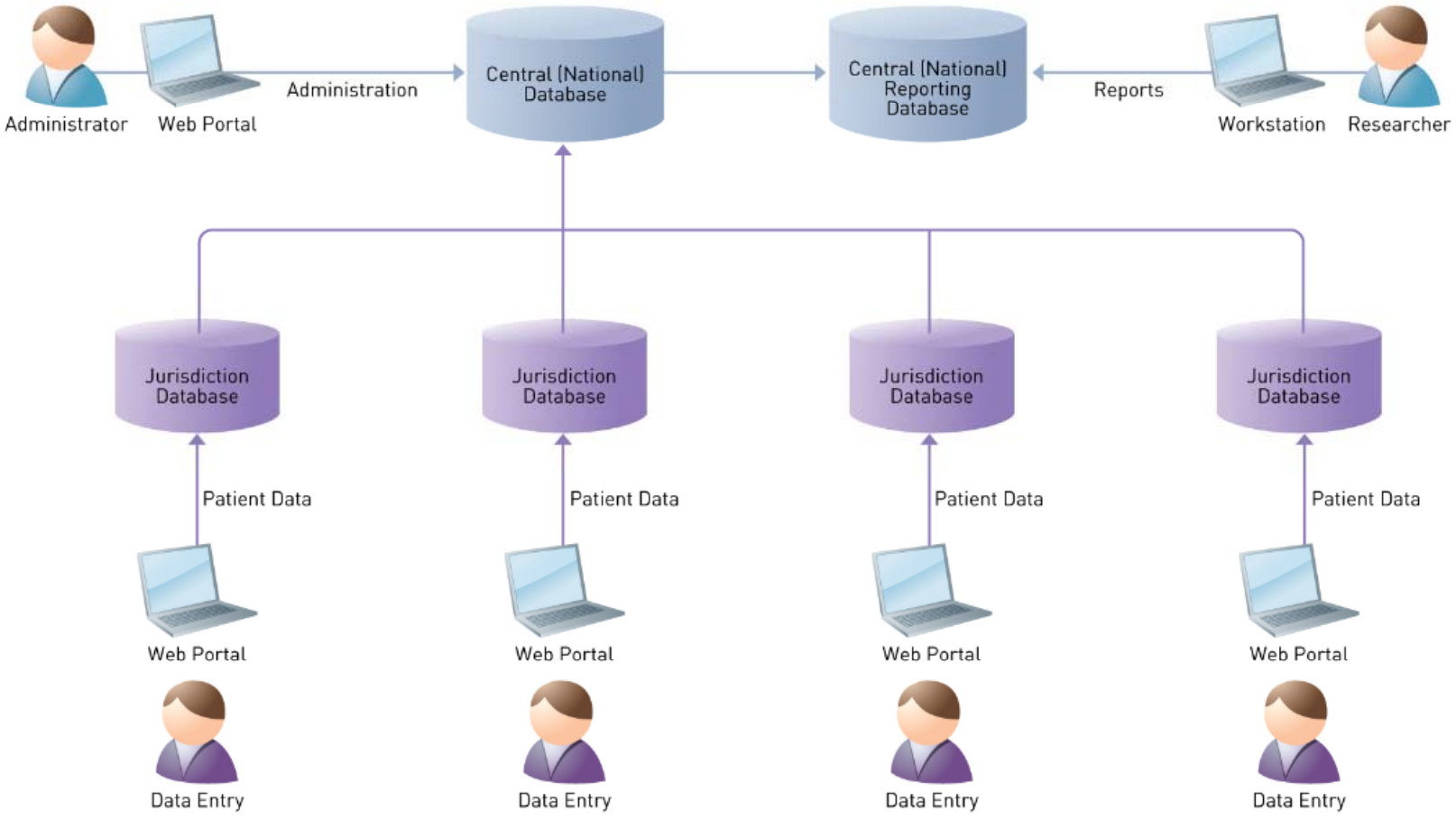
CYP-C Overview

- Diagnosed with cancer in Canada
  ≥ 2001, < 15 years at diagnosis

- 17 pediatric oncology centers
  - Direct entry n=12
  - Data transfer from POGO n=5

- Diagnosis, treatment, outcomes for
  5 years after diagnosis

CYP-C Data Approach



Data Collected

Demographics	Diagnostic Details	Time to Treatment	Treatment	Other
Sex	Date of diagnosis Diagnosis	First health care professional contacted	Treatment plan and start date	Organ transplant
Date of birth	ICDO-M, ICDO-T and ICCC codes	Date first health care professional contacted	Treatment completion details	Complications
Age at diagnosis	Stage at diagnosis Risk	Dates first seen by: oncologist, surgeon, and/or specialist	Chemotherapy and dose	Hospitalizations
Province postal code	Grade Chromosomal testing Metastases and site(s)		Surgery details	Relapse
Ethnicity			Radiation (intent, type, site)	Vital status

Identifiers

- Full 6 digit postal code (3 digits in BC) – allows geospatial and socio-demographic (via census) analyses
- Full name – retained by center
- Health card number – retained by center

Potential for linkages with administrative databases

Need strong justification in request

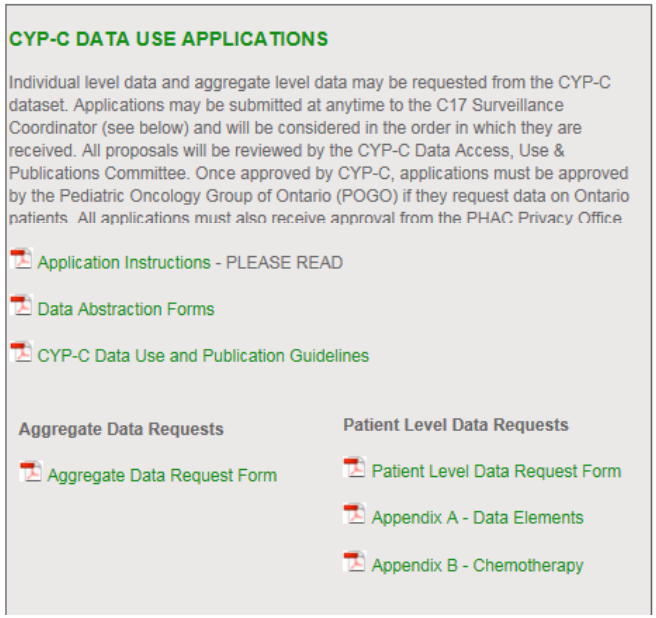
Quality Control

- High
- Community of practice
- Annual CRA face-to-face training
- Site audits (all sites audited at least once)
- Integrating better quality checking procedures

How to Access Data

- http://www.c17.ca/index.php?cID=70

  (www.c17.ca>>Committees Tab>>CYP-C/CCJC



- Randy.Barber@ahs.ca
- More coming March 20, 2017 CYP-C RC Webinar

Research Champion Webinar Series

- Objective to provide broad understanding of how to access and utilize CYP-C data for research
- Includes overview of how to:
  - Develop an appropriate research question
  - Complete the data access process
  - Perform basic data manipulation and analysis using SAS and Microsoft Access
- Webinars delivered 1-2 times per month
- Series developed/organized – Jason Pole PhD

Outline

- Why do Clinical Research
- Starting Out
- How to Develop a Research Question
- Conclusions

Starting Out

Early steps important in establishing a successful career

- Research training
- Writing and publishing
- Mentors
- Establishing your niche

Research Training

- Best time to “practice”
- Excellent understanding of methods
- Advantages of gaining through degree
  - MSc
  - PhD
- Every opportunity to learn outside of course work
  - Projects under best mentors
  - Different methodologies
- Identify mentors early

Writing and Publishing

- Key
- Learned skill – comes with practice

Career Timeline

Heterogeneous topics
First author
Case reports/series
Lower IF journal
Emphasis any publications

Narrower focus
Senior author, co-senior
More complex
Higher IF journal
Emphasis good publications

Mentors

- One size does not fit all
- Team mentors
- International mentors
- Trust, motivation
- Change as needed
- Learn how to mentor

Establishing Your Niche

- Critically important to success
- Likely will be clinical topic
  - Eg. infectious complications in leukemia
- Be wary of being too diffuse
  - World is too big

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Choose Questions Carefully

- Infinite research questions available
- Limited energy, resources, time
- Invest your efforts wisely

How to Develop a Good Research Questions

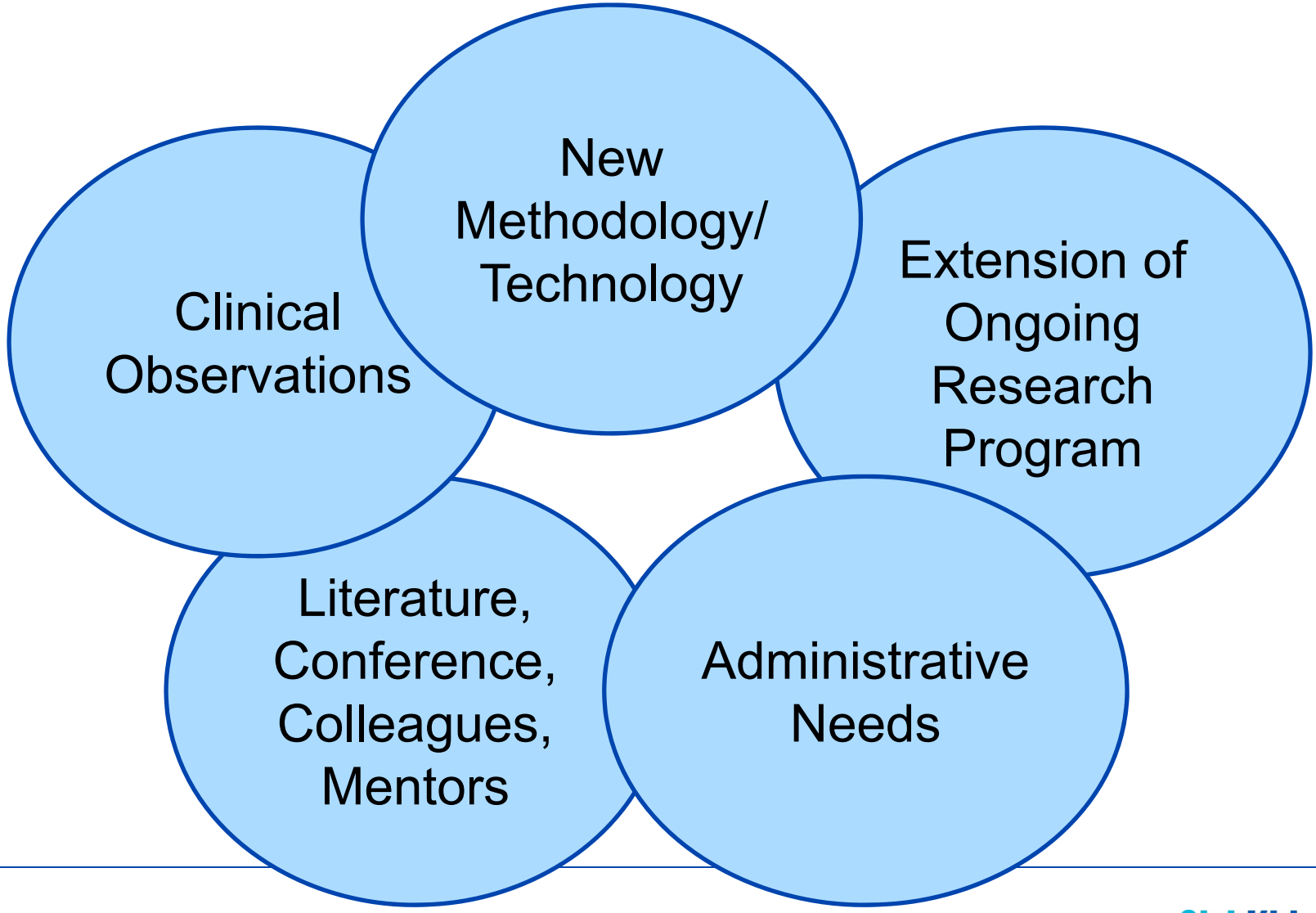
Good research questions foundational

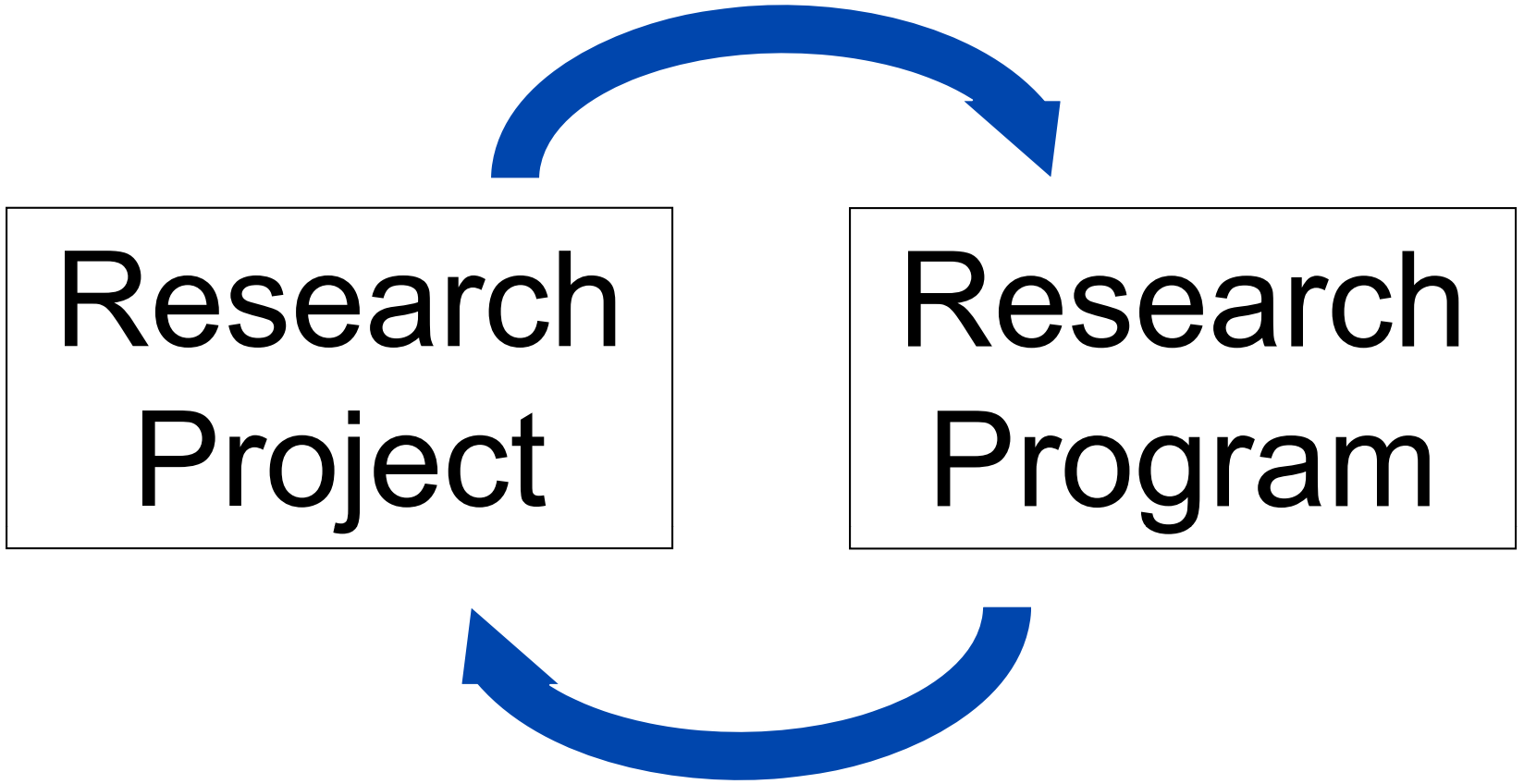
Attributes of Good Research Questions

FINER

- Feasible given resources and skill set available
- Interesting
- Novel – provides new knowledge goals
- Ethical – IRB approval
- Relevant (so what test)

Where Research Questions Come From?




Research Project
Research Program

What do you Need to Develop a Good Question?

- Excellent understanding of what is known
  - Systematic review
- Ability to recognize what is clinically important
  - "So what"
- Ability to determine what is feasible
- Methodological guidance
- Colleagues/mentors who will listen to your ideas and provide critical input

Why is a Systematic Review Required?

- Question may have already been answered
- To know what instruments to use if using patient-reported outcomes
- Understand adverse events if drugs
- Learn about different ways the question has been studied
- Identify potential confounders
- Estimate treatment effect and variability - help with sample size calculation

Purpose	Design That Yields Most Valid Information
Benefits and/or harms of an intervention	Randomized controlled trials
Prognosis	Cohort studies
Diagnostic test	Cross-sectional studies
Is a trial feasible	Pilot/feasibility study
Initial understanding	Qualitative

How to Create a Good Research Question

P Population/patient

I Intervention

C Control/comparison

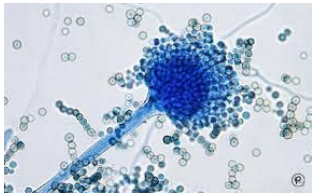
O Outcome

T Timing

After reading the question, should know:

- What is the design
- What is the hypothesis
- What is the primary outcome
- What is the primary analysis
- What is sample size based upon

Example



- Children's Oncology Group - RCT comparing caspofungin and fluconazole prophylaxis for children with AML

- 12% of children with AML have invasive fungal infections – both yeasts and molds

- Standard prophylaxis most institutions
  - Fluconazole - only has activity against yeasts

Example Research Question

Is caspofungin better than fluconazole?

- Don’t know the population
- Don’t know much about intervention and control groups
- Don’t know the outcome
- Don’t know timing

Thus, don’t know the design

Example Research Question

Is prophylaxis with caspofungin administered during periods of neutropenia following chemotherapy for children with acute myeloid leukemia (AML) associated with a lower incidence of proven or probable invasive fungal infections (IFI) compared with fluconazole?

Population/patient

Is prophylaxis with caspofungin administered during periods of neutropenia following chemotherapy for children with acute myeloid leukemia (AML) associated with a lower incidence of proven or probable invasive fungal infections (IFI) compared with fluconazole?

Intervention

Is prophylaxis with caspofungin administered during periods of neutropenia following chemotherapy for children with acute myeloid leukemia (AML) associated with a lower incidence of proven or probable invasive fungal infections (IFI) compared with fluconazole?

Control/comparison

Is prophylaxis with caspofungin administered during periods of neutropenia following chemotherapy for children with acute myeloid leukemia (AML) associated with a lower incidence of proven or probable invasive fungal infections (IFI) compared with fluconazole?

Outcome

Is prophylaxis with caspofungin administered during periods of neutropenia following chemotherapy for children with acute myeloid leukemia (AML) associated with a lower incidence of proven or probable invasive fungal infections (IFI) compared with fluconazole?

Timing

Is prophylaxis with caspofungin administered during periods of neutropenia following chemotherapy for children with acute myeloid leukemia (AML) associated with a lower incidence of proven or probable invasive fungal infections (IFI) compared with fluconazole?

Hypothesis

Must mirror research question

Hypothesis

Question: Is prophylaxis with caspofungin administered during periods of neutropenia following chemotherapy for children with AML associated with a lower incidence of proven or probable IFI compared with fluconazole?

Hypothesis: Prophylaxis with caspofungin administered during periods of neutropenia following chemotherapy for children with AML will be associated with a lower incidence of proven or probable IFI compared with fluconazole.

Once I Read Question, I Know…

- Type of research question
- Setting
- Comparison
- Primary endpoint
- Primary analysis
- What power calculation will be based upon

Developing Question is Really Hard

- Identify question meets FINER
- Select intervention
- Identify appropriate control group
- Select primary endpoint
- Select time frame

Pitfalls of Not Spending Enough Time on the Research Question

- If you do not know what you are asking, you won't know what data to collect
- If you do not know what question you are asking, you may expose patients to risk without likelihood of benefit
- A unanswerable question wastes resources
- A poorly designed question contributes to research failure

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Conclusions

- CYP-C resource available to all of you
- Webinar series – enable you to conduct research using this type of data
- Invest time in developing excellent research questions
- Importance of mentorship

Acknowledgement

- My mentors – too many to list….
- Jason Pole – leading RC educational series
- Randy Barber and CYP-C Management Committee
- C17 Council
- Public Health Agency Canada