Investigator Experiences with the Ethics Review Process of Cluster Randomized Trials: *An International Survey*

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Introduction

- **Ethics Guidelines:**
  - Used by ethics committees to formulate ethical standards
  - Developed primarily for individually randomized trials
- **Ethical Challenges posed by CRTs:**
  - Ethical foundation of cluster (as opposed to individual) randomization
  - Issues around the need for informed consent
  - Challenges not yet systematically explored →Differing views
    - Ethics committee <-> Investigator
    - Ethics committee <-> Ethics committee
- **Comprehensive International ethics guidelines for CRTs:**
  - to help investigators in the design and conduct of their CRTs
  - to guide ethics committees in their review of CRTs

Survey of CRT Investigators: Objectives

- **Purpose:**
  - To understand 'ethical landscape' in the conduct of CRTs in health research

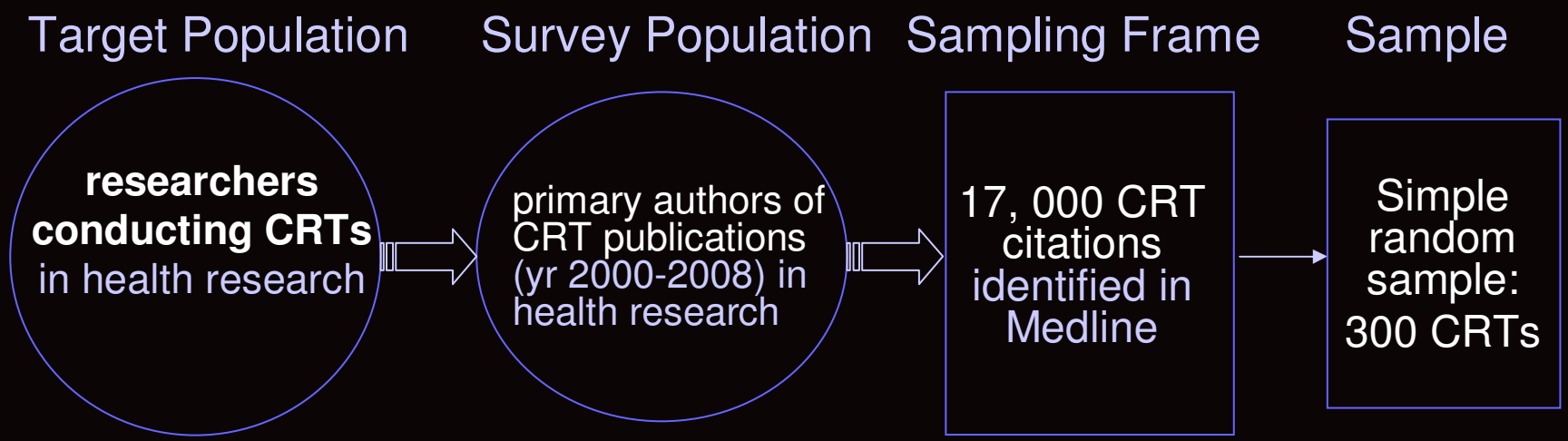
- **Objective 1)** Describe the ethics *review* process of CRTs from the experience of researchers seeking ethics approval.

  Questions

  - What factors are associated with seeking ethics approval for CRTs?
  - Do investigators experience variability among multiple ethics committees reviewing CRTs?
  - Do investigators experience positive or negative impacts of the ethics review process on various aspects of their CRTs?
  - Do investigators support a need for ethics guidelines for CRTs?

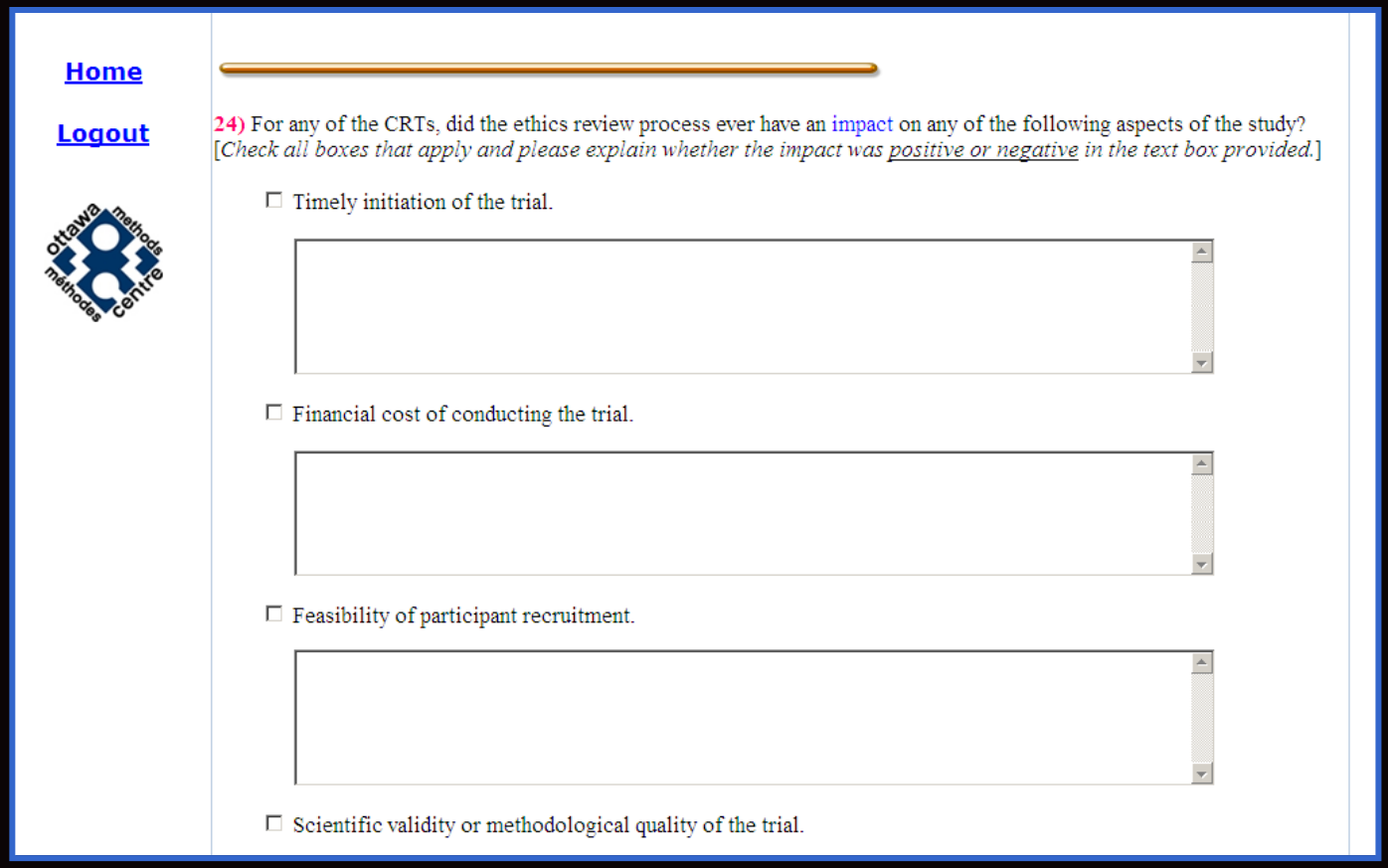
Survey of CRT Investigators: Methodology (1)

- **Survey Questionnaire**
  - **Content:** Literature review, key informant interviews, review of CRT publications
  - **Personalization of each questionnaire**: by type of cluster, type of cluster member, ethics review terminology
  - **Pre-testing:** Expert reviews & Cognitive interviewing
- **Sampling Strategy**



Survey of CRT Investigators: Methodology (2)

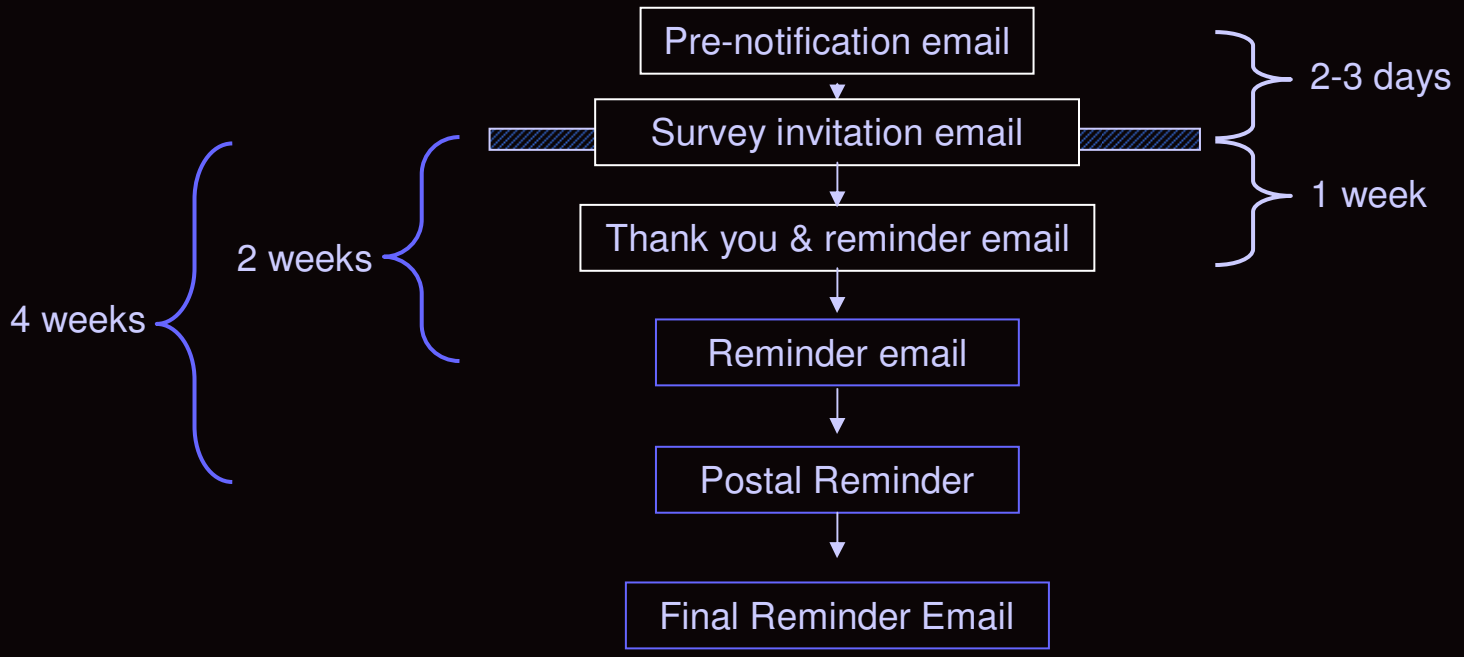
- **Data collection mode:**
  - Self-administered web survey



Survey of CRT Investigators: Methodology (3)

- **Incentive:** complimentary book offer;
  - *Design and Analysis of Cluster Randomization Trials in Health Research* (2000). By A. Donner and N. Klar

- **Implementation Procedures:** Dillman's tailored design method



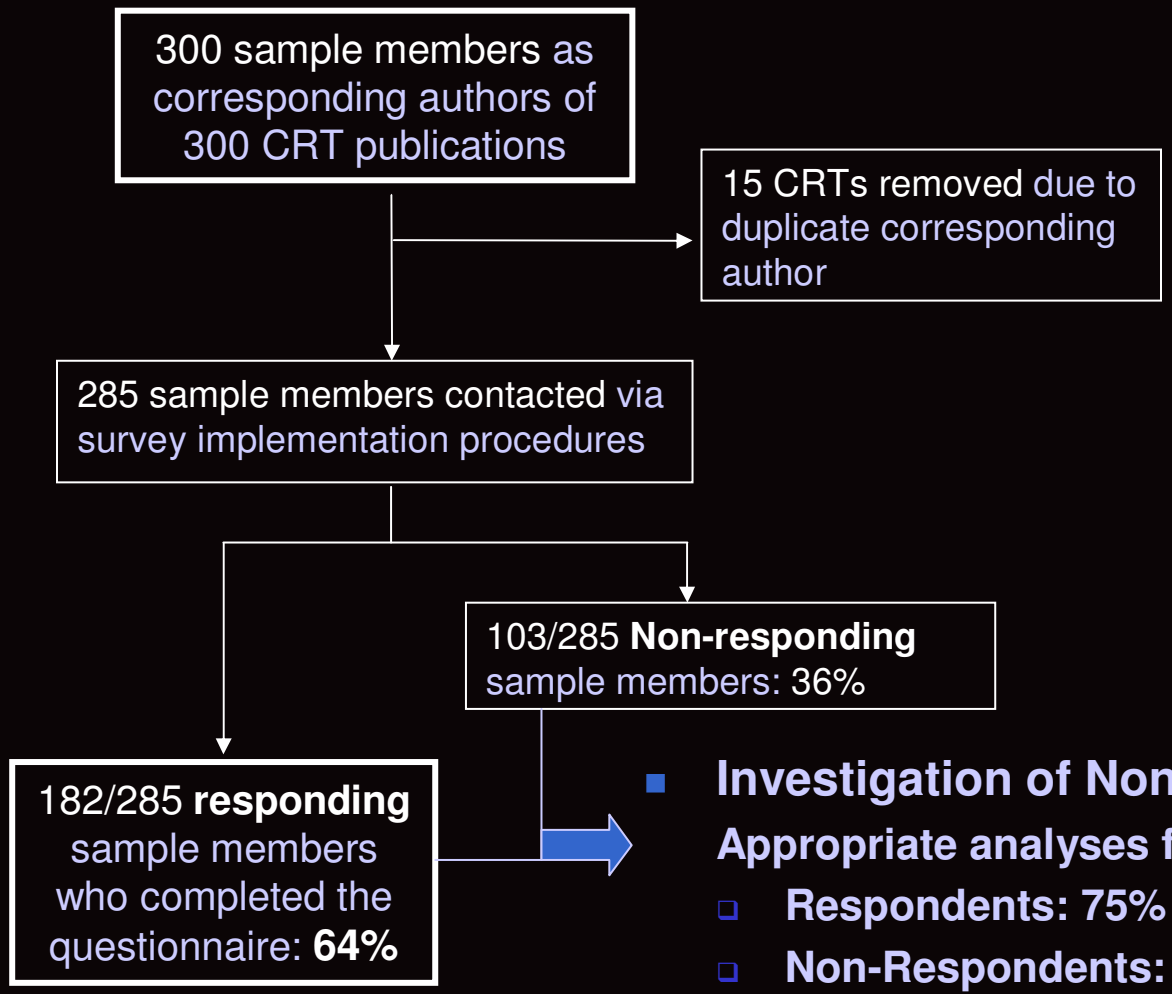
Ethics approval: Ottawa Hospital Research Ethics Board (OHREB); Protocol #2009693-01H

Survey of CRT Investigators: Survey sample

- **Table 1:** Sample Characteristics (N=285)

		Frequency %
Country of primary study author	Canada or USA	47% (135)
	UK or Ireland	19% (54)
	Australia or New Zealand	6% (16)
	Elsewhere in Europe	20% (58)
	Various low/middle income countries	8% (22)
Unit of randomization	Health care organization	57% (162)
	Non-health care	43% (123)
Appropriate analyses for CRT design	Yes, ICC accounted for / cluster level analyses	70% (119)
	No	30% (86)
Ethics approval reported	Yes, including exemption from review	74% (210)
	No, not reported	26% (75)

Survey of CRT Investigators: Response



- **Investigation of Non-response bias:**
  Appropriate analyses for the CRT design
  - **Respondents: 75%**
  - **Non-Respondents: 61% p=0.0166**

Results: Ethics approval of selected CRTs (1)

- **Table 2:** Ethics approval of the selected CRT publication:

	Frequency % (N=182)
Ethics approval sought	**91.2% (166)**
Number of ethics committees approached for approval	**(N=163)**
Median [25% quartile (Q1), 75% quartile (Q3)]	1 [1, 2]
Range [Min, Max]	90 [1, 91]
Time delay (years) from ethics approval until CRT publication	**(N=166)**
Median [Q1, Q3]	5 [3, 7]
Range [Min, Max]	16 [0, 16]
Ethics approval not sought	**8.8% (16)**

- Reasons ethics approval was not sought:
  - Quality improvement or service evaluation
  - Not required for the study
  - Lack of ethics guidance or review structure at the time
  - Ethics considered by a research committee

Results: Ethics approval of selected CRTs (2)

- **Table 3:** Characteristics associated with obtaining research ethics approval in CRTs

		Ethics Approval sought (N=182)	
		Yes (%)	p
Publication Year	2000-2002	94% (33)	0.2264
	2003-2005	94% (65)	
	2006-2008	87% (68)	
Country of primary study author	Middle/low income countries	94% (16)	**0.0272**
	Canada or USA	97% (82)	
	Other high income countries	85% (68)	
Unit of randomization	Health care organization	90% (95)	0.4355
	Other	93% (71)	
Target of planned interventions	Individual level only	97% (60)	**0.0245**
	Cluster level only	84% (56)	
	Cluster and individual level	94% (50)	
Types of data collection interventions	Routine data only	75% (18)	**0.0069**
	Individual level only	96% (110)	
	Cluster level only	85% (17)	
	Cluster and individual level	91% (21)	

Results: Experiences with ethics review (1)

- **Table 4:** Investigator experiences with the ethics review process of CRTs

	Frequency %	
Experiencing variability in the ethics review of a CRT undergoing review by more than one ethics committee=yes		
Yes, among all respondents	28%	(50)
Yes, excluding N/A: ethics review of a CRT did not involve multiple ethics committees	47%	(50)
Negative Impact of the ethics review process on aspects of a CRT=yes		
Timely initiation of a CRT	26%	(48)
Financial cost of conducting a trial	9%	(17)
Feasibility of participant recruitment	15%	(28)
Scientific validity or methodological quality of a trial.	9%	(16)
Other aspects of a trial.	5%	(9)
Positive Impact of the ethics review process on aspects of a CRT=yes		
Timely initiation of a CRT	1.6%	(3)
Financial cost of conducting a trial	1.1%	(2)
Feasibility of participant recruitment	4%	(7)
Scientific validity or methodological quality of a trial.	5%	(9)
Other aspects of a trial.	1.6%	(3)

Results: Investigator views on CRTs (1)

- **Table 5:** Investigator views on ethics guidelines and ethics committee review of CRTs

	Frequency %		95% CI for %
There is a need to develop ethics guidelines for CRTs			
Agree or strongly agree	73.5%	(133)	[67%, 80%]
Disagree or strongly disagree	16%	(29)	[11%, 21%]
No opinion	10.5%	(19)	[6%, 15%]
Ethics committees could be better informed about distinct ethical issues surrounding CRTs			
Agree or strongly agree	70%	(126)	[63%, 77%]
Disagree or strongly disagree	12%	(22)	[7%, 17%]
No opinion	18%	(32)	[12%, 23%]
Ethics committee application forms standardized for various study designs are hard to use in the context of the CRT design			
Agree or strongly agree	46%	(84)	[39%, 54%]
Disagree or strongly disagree	30%	(54)	[23%, 37%]
No opinion	24%	(43)	[18%, 30%]

Survey of CRT Investigators: Conclusion

- **Study Findings:**
  - **Ethics committees demonstrate variable standards as to the type of research requiring ethics approval**
  - **Investigators conducting CRTs are experiencing challenges with the ethics review process**
    - Variability in the ethics review of multijurisdictional CRTs
    - Negative impacts in greater proportion to positive impacts of the ethics review process on various aspects of the trials

- **Limitations:**
  - Exact contribution of CRT design to challenges is uncertain

- **Strengths:**
  - Surveyed investigators with varying levels of experience in conducting CRT
  - Many commented about challenges arising from the CRT design
  - Majority of respondents agreed that there is need for ethics guidelines for CRT, and that ethics committee could be better informed about distinct ethical issues arising from CRTs

Acknowledgements

Questions