Conducting Cluster Randomized Controlled Trials in Hospitals: Barriers and enablers assessment and strategies to facilitate delivery

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Abstract

Background: Cluster randomized control trials (cRCTs) are useful for asking about system-level interventions compared to other types of clinical research design, however they present unique challenges with conduct and delivery. Numerous cRCTs in hospitals have encountered challenges and time delays in enrolling hospitals and launching the trials which contributes to research waste. While each cRCT has unique barriers and enablers to their conduct, it is important to understand and explore these factors at the general level of the cRCT itself. Previous literature has documented factors associated with successful cRCTs, however, these studies focused primarily on the statistical aspect, while neglecting to evaluate the delivery of the trial.

Objectives: The goal of this dissertation was to explore barriers and enablers to conducting cRCTs in hospitals, and to identify potential strategies that facilitate their delivery. This research was conducted to identify evidence and generate guidance for researchers aiming to conduct these trials. Specifically, the objectives were: 1) To explore the current knowledge and evidence surrounding the implementation of cRCTs in hospitals; 2) To explore from the perspective of the coordinating site, what influenced the delivery and hospital engagement of an ongoing cRCT, and what challenges were encountered; 3) To identify strategies to facilitate delivery of cRCTs in hospitals; 4) To systematically review reported recruitment strategies of healthcare facilities in cRCTs.

Methods: The dissertation employed multiple research methods. To address the first objective, a scoping review was performed of current literature related to hospitals in cRCTs. The second objective was addressed with a qualitative case study. Semi-structured interviews were carried out with six key members of the team to understand their perceptions of the delivery of the trial. For the third objective, a tool matching two implementation concepts (the Consolidated Framework for Implementation Research (CFIR)- Expert Recommendations for Implementing Change (ERIC) matching tool) was used to identify strategies targeted to address barriers and enablers to cRCT conduct identified in the first two studies. Lastly, a systematic review was performed to address the fourth objective, to identify reported strategies used for hospital engagement in cRCTs. The thesis was guided and analyzed using an over-arching implementation framework, CFIR, and an implementation strategies list, the ERIC compilation. This was done to allow comparability and synthesis of results between methodologies from the dissertation, and between the results from the studies and previous literature.

Results: Several key CFIR domains were identified in the literature in the scoping review that were determined to being influential for conducting the cRCTs in hospitals: the *adaptability* to tailor the trial to each site; the *engagement of opinion leaders*, *champions* and *formally appointed implementation leaders* in the cRCT process as facilitators to conducting the trial; the lack of a site perceiving a *relative priority* for the trial or *tension for change* for the clinical field presenting barriers to conducting the cRCT; and limited *available resources* can present barriers to conducting the cRCT. The qualitative case study identified similar CFIR domains and constructs as potentially influential for cRCT conduct, including the emphasis on *adaptability* of trial, the importance of *tension for change* in the sites for accepting inclusion in the trial, the *availability of resources,* and the *engagement* of leaders.

The CFIR-ERIC matching study identified strategies that may be used to overcome barriers and target enablers for cRCT delivery from CFIR domains and constructs identified in the first two studies. A list of strategies was generated, ranked by the number of many determinants for which the strategy was listed as a Level 1 strategy, then by how many determinants for which the strategy was listed as a Level 2 strategy. The top ERIC strategies that were endorsed as a Level 1 strategy for any or multiple CFIR domains were: 1) Identify and prepare champions, 2) Conduct local needs assessment, 3) Conduct educational meetings, 4) Inform local opinion leaders, 5) Build a coalition, 6) Promote adaptability, 7) Develop a formal implementation blueprint, 8) Involve patients/consumers and family members, 9) Obtain and use patients/consumers and family feedback, 10) Develop educational materials, 11) Promote network weaving, 12) Distribute educational materials, 13) Access new funding, and 14) Develop academic partnerships. The systematic review identified literature reporting on the recruitment of healthcare facility sites into cRCTs. Numerous strategies for cRCT site recruitment were identified, and these were coded to the ERIC compilation. Strategies that were commonly cited were: involve executive boards, promote network weaving, conduct educational meetings, inform local opinion leaders, and centralize technical assistance.

Conclusions: The results from the dissertation can contribute to the knowledge for facilitating cRCT delivery in hospitals while recognizing the critical limitations in the studies. Key concepts and strategies to facilitate the conduct and delivery of cRCTs in hospitals were identified. Future research should aim to empirically evaluate the identified strategies. Researchers should aim to address the reporting gap for cRCT delivery identified by this dissertation.

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Chapter 1 – Introduction

Thesis Rationale:

The research agenda for my dissertation was developed in collaboration with the principal investigator of an ongoing cluster randomized trial (cRCT)[1]. This trial, along with numerous other cRCTs in hospitals identified in the literature[2–8], encountered many challenges and time delays in enrolling hospitals and launching the trial. We wanted to address the following questions: 1) "what did the literature have to say to inform us about enrolling hospitals and launching the trial", and 2) "could we have chosen and enrolled the sites differently". The aim of the dissertation is therefore to explore barriers and enablers to conducting (meaning organizing and carrying out) cRCTs in hospitals and to identify potential strategies that facilitate their delivery (meaning engaging and enrolling sites).

I specifically focused this dissertation on cRCTs conducted in hospitals. cRCTs can often have hospitals as the clustered unit[9], however, we did not identify literature that systematically explored the conduct and delivery of cRCTs specifically within the context of hospitals. There are often multiple competing priorities and administrative policies in hospitals, which presents challenges in launching a trial in these settings. To reduce potential variability from exploring sites that were not hospitals (for example, community centres, dentist offices, or schools) we kept the scope of the dissertation to hospitals.

The rationale for the use of frameworks: I used theories and frameworks in this dissertation to inform the methods and analysis. I did this to facilitate comparison of results between studies Using implementation theory in research is beneficial to allow for the investigation of the external generalizability of results, the systematic evaluation of strategies, and the understanding of the underlying concepts of the implementation[10,11].

Background:

Randomized control trials (RCT) are often deemed the "gold" standard of clinical research[12]. When properly designed and rigorously conducted, RCTs may offer more credible results than can be obtained from observational studies or non-randomized trials. They allow for conclusions about the causality of the unit under investigation (mainly by avoiding selection bias but also if the sample size is large enough, potential confounders should be equally balanced between study arms, allowing for the intervention to be the "sole" variable affecting the outcome[13])[14]. RCTs can be conducted by either individual randomization (which can include multi-site trials), or by cluster randomization[14].

Cluster RCTs (cRCTs), also known as group-randomized trials, are trials where groups (clusters) are randomized rather than individual participants[14,15]. cRCTs are often used to investigate complex or multifaceted interventions targeted at the cluster, professionals, or individual cluster members, and outcomes can then be evaluated at the cluster level of the individual-level within the clusters[16,17]. Three commonly used methods for randomizing clusters are 1) completely random (no stratification or matching), 2) matched pairs in which one of two clusters in a

stratum is randomly assigned to each of two interventions, or 3) stratified, in which the random assignment of two or more clusters involves the combination of interventions and stratification factors[18]. Examples of clustered units could be schools, clinics, communities, worksites, or an individual physician, with all that physician's patients being treated as the cluster. cRCTs are frequently conducted with health facilities as the unit of randomization[15].

Randomization by clusters rather than individuals is an option to overcome issues when individual randomization is not feasible, for example, to avoid contamination of the intervention. There are no explicit rules for when cluster randomization should be performed rather than individual randomization, but commonly cited justifications include: 1) intervention must be delivered at the cluster level (i.e. the intervention is unavoidable for individuals; for example, if offering a certain community health service, whereby the entire community would need to be randomized as a whole); 2) intervention is targeted at healthcare professionals within a cluster; 3) to simplify the organization and logistics of conducting the trial; 4) to reduce costs associated with the trial; 5) for herd immunity (in the case of infectious diseases); 6) to investigate the indirect effects of the intervention; 7) to improve compliance of intervention uptake; and 8) to enable recruitment[17].

In addition to mitigating issues concerning the feasibility of individual randomization, cRCTs can have other advantages over non-cluster RCTs[15]. They may offer more widespread and diverse population access, with the potential for broader external generalizability of results than single-site RCT. In single-site non-cluster RCTs, the recruited population may be less representative of the external population that the intervention may be planned for in healthcare practice. Furthermore, cRCTs can allow for a quicker recruitment rate to reach a larger sample size for participants than a single site RCT can offer, while recognizing that sample size requirements are also larger in cRCTs to account for intra-cluster correlations.

While cRCTs offer advantages over non-cluster randomized controlled trials[15], they also present some challenges to the organization and conduct of the trials[9]. Some key challenges for conducting cRCTs include 1) Clusters in a cRCT are often randomized before individuals are identified and recruited for informed consent. 2) cRCTs often use organizations as the unit of randomization but understanding of groups and gatekeepers is limited. 3) Members of a cluster are not considered as statistically independent. 4) These trials have the potential for the units of allocation, invention, and outcome measurement to all be different, which may differ from how trials are conducted in single trials). 5) The intervention can be administered at the cluster level, which could lead to direct or indirect effects of many individuals associated with the trial. 6) It may be difficult for individuals to avoid cluster-level interventions, and therefore it can be challenging for an individual to refuse participation. 7) Risks to the group or subgroups of a cluster can be difficult to identify and can be underestimated[16,18].

Additionally, challenges can arise when considering the statistical analysis aspects of cRCTs[18]. Due to the intra-cluster correlation, cRCTs have less power to detect differences than what could be obtained from trials in which individuals are randomized. Greater power gains can be obtained when the number of clusters in a trial is increased, as opposed to increasing the size of the clusters themselves.

In line with the difficulties of conducting cRCTs identified above, and with particular focus on challenges 1 and 2, challenges in the delivery of trials can arise before patient recruitment and/or intervention launch[19,20]. Engagement and recruitment of the cluster sites themselves can prove difficult, with poor response and participation from the intended sites[2]. Variability between sites in the fidelity of an intervention can make it difficult to launch the full trial, as well as to assess the effectiveness of an intervention[21]. In part due to the randomization of entire clusters rather than individuals, the loss of individual sites and an inability to recruit the required sample size (whether by refusing to participate in the study or failing to launch the trial at the site) can prove more detrimental to ensuring the trial is adequately powered to detect intervention effects than the effect of the loss of a non-cluster randomized site (including multi-site, individual randomization trials) would lead to[14]. The inability to recruit an adequate number of sites or the loss of a site post-randomization can pose threats to the statistical analysis, especially related to powering the study for comparisons between trial arms. This can, therefore, pose large threats to the conduct of the trial and the interpretation of the trial results[9,14]. Furthermore, challenges in delivery of cRCTs, such as the inability to recruit an adequate number of sites or the loss of a site, have the potential to lead to research waste[22].

In 2010, global funding in biomedical research was estimated to be $240 billion USD[22]. This funding has allowed for important scientific discoveries in health sciences[22,23]. However, despite scientific advancements, much of the financial investment and research supported by these funds do not lead to published and disseminated findings. This lack of discernible progress can be due to the original study hypothesis being incorrect, or the study not having the anticipated results. In this case, while it can be beneficial for other researchers to be aware of these results to further conduct alternative lines of research, often these results go unpublished (leading to publication bias)[24]. Alternatively, this lack of disseminated results can be due to methodological failure (for example improper planning, research design, or lack of an effective research team), leading to what is known as research waste[22].

Research waste is a significant concern in biomedical research[22]. In 2014, the Lancet produced a five-paper series outlining the sources and providing recommendations on how to reduce this ongoing problem[22,25–28]. This series outlined various stages of the research process in which waste can occur, including setting priorities, design, and conduct, regulation and management, accessibility, and reporting. One of the key concerns leading to potential research waste is inefficient management of research[26]. The research team is crucial in the organization of the study[9]. A team must be able to communicate and navigate these levels to ensure the study is effectively conducted[29,30]. To reduce research waste, research teams need to have guidance in methods to facilitate the research.

Evaluation of Barriers and Enablers to cRCTs Implementation and Conduct

Implementation of Interventions:

A goal of healthcare research is to investigate and develop evidence-based medicine (EBM), which is crucial in ensuring patients receive the ideal care for their case[31]. EBM is defined as the "conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients"[32], and is performed using best available research knowledge at the time, combined with expertise of the healthcare practitioners from past experience for the

specific situation[31,32]. This emphasizes that healthcare providers should be providing the best care, informed by evidence, and not base their practice solely on intuition.

Despite ever-evolving health research, the translation of research findings is slow to be integrated into current practice to allow for EBM, and attempts to bring about changes to healthcare practices are frequently unsuccessful[10,33,34]. It takes an average of 17 years for new evidence to be incorporated into health care practice[35], which may be due to either the interventions being ineffective, or the implementation of the interventions themselves being ineffective. Patients frequently do not receive optimal care, with one study reporting only 55% of adults in the United States were receiving optimal care for their health condition[34,36]. Furthermore, not only do patients often not receive optimal care, it has been reported that 20 to 25% of provided care can be harmful to the patients[36]. The discrepancy between EBM and current practice is known as the knowledge to action (KTA) gap[33]. With a large increase in the number of research articles being published daily, it is unrealistic to expect end-users (healthcare providers in this case) to be able to read all relevant articles, and relying on this method of passive diffusion will inevitably result in large rates of failure of new evidence incorporation into practice [35,37]. A proposed solution to the ineffective translation of EBM into practice is to use targeted strategies of implementation[34].

Implementation science is the systematic study of how to optimize and facilitate uptake of research into healthcare[38]. Within the field, the terms knowledge translation, knowledge exchange, knowledge transfer, and research utilization are used to describe the process of putting the research evidence to use. Knowledge translation, the most commonly used term, is defined by the Canadian Institute of Health Research as "a dynamic and iterative process that includes the synthesis, dissemination, exchange and ethically sound application of knowledge to improve health, provide more effective health services and products and strengthen the healthcare system''[39]. Traditionally, studies have been conducted as a one-way flow of information (i.e from researcher to practitioners), in a step-by-step method[40,41]. The first step is typically efficacy studies, in which the intervention is studied in ideal and controlled environments, ensuring internal validity. This is followed by effectiveness studies, in which the intervention is studied in a more "real-life" environment with attempts to ensure external validity. Finally, implementation studies are performed in which the intervention is rolled out in a general setting to study the adoption of the initiative and maximize the effect of the research. This unilateral flow of information is likely to contribute to the slow uptake of information.

Evaluation of Intervention Implementation and Conduct:

Increased focus is being placed on the evaluation of the implementation of interventions in RCTs, in addition to the evaluation of the clinical intervention itself[42]. This differs from traditional evaluation of the trial, whereby the effect of the intervention itself is measured, and the outcomes are focused on the effectiveness of the clinical or behavioural intervention[43].

In evaluating implementation, the fidelity of the intervention, elements of implementation, and barriers/enablers to implementation can all be evaluated[43]. The evaluation of intervention implementation can offer insights into whether outcomes of the clinical/behavioural intervention can be attributed to the actual intervention or issues with the implementation of the trial. For example, if an intervention is shown to have no effect, the lack of effect may be in part due to

failure to properly implement the intervention into practice. Evaluations of the RCT implementation can be done alongside the conduct of the trial, or during the pilot of the trial to determine strategies to maximize the efficiency of the implementation[41,43]. Evaluation studies can be quantitative, qualitative, or a combination of both in a mixed-methods fashion[44].

Theories, Models, and Frameworks in Implementation Science:

Various definitions of terms are used in implementation science[33,38]. The terms theory, model, and framework are frequently used interchangeably, often erroneously[38]. Theories are often described as explanations of how principles work and relate, and are based on a collection of generalizations[38,45,46]. Models are used to simplify concepts, often by narrowly describing only certain aspects of a larger theory. They are largely descriptive. Finally, frameworks are used as a structure or plan and do not attempt to explain the phenomena on which they were built[11,47,48]. They can relate various variables within theories and models for ease of use[38]. Theories can also be subdivided into distinct types[49]. Motivational theories explain the reasons and thoughts behind the behaviours. Action theories describe how intent to perform a behaviour changes the actual performance of the behaviour. Stage theories focus on the different steps through which behaviour change occurs.

A review by Nilsen et al. (2015) identified three major aims of theories, models, and frameworks in implementation science: describing the process of implementation, understanding the factors of implementation, and evaluating the process[38]. These aims can be broken down into the following five categories: 1) process models; 2) determinant frameworks; 3) classical theories; 4) implementation theories; 5) evaluation frameworks. Several of the implementation theories, models, and frameworks in use have overlap between the categories, allowing for sections of each to be used to accomplish the different goals.

The conceptual framework adopted by the Canadian Institute of Health Research (CIHR) is known as the KTA Cycle (Figure 1.1) [33,39]. This overarching model of knowledge translation includes two separate, yet interacting, sections known as knowledge creation and action cycle. The KTA Cycle emphasizes a dynamic and cyclical process for efficient implementation, whereby the evidence is funneled into the action cycle, with the potential for a dynamic and fluid movement forward and back between the steps. Evaluation of the process can be undertaken at various steps in the cycle. Further theories have been designed to target and complement each stage of the process as well[50].

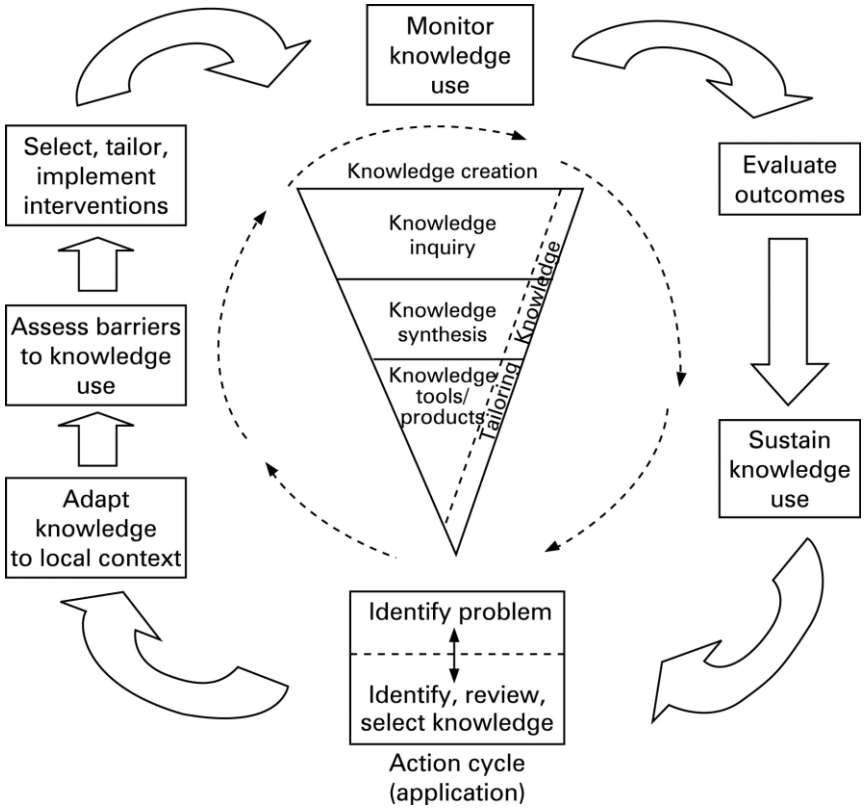

Figure 1.1 Knowledge-to-action cycle [33]

Within the KTA cycle is a step on the assessment of barriers and enablers to knowledge use[33]. This step can allow researchers to determine what factors can impede or aid the planned change[33,39]. These factors can be found at multiple levels, including at the individual level (for example the physician or the patient), at the organizational level (for example the clinic, or hospital), and at the system level (for example the healthcare system)[10,34,51].

The use of theories and frameworks from the field of implementation science, and specifically in barriers and enablers assessments, can be of great benefit to the implementation of evidence-based research[52] by facilitating the investigation of the external generalizability of results, the systematic evaluation of strategies, and the understanding of the underlying concepts of the implementation[10,11]. They allow for the more rigorous design of interventions, comparisons of results between studies, and identification of success factors in an intervention by enabling the comparison between studies[53–55]. When no framework is used, there is difficulty in comparing studies, and uncertainty as to whether comprehensive methods were used to identify all relevant aspects.

Goal and Objectives of the Dissertation

The goals of this dissertation were to explore barriers and enablers to conducting cRCTs in hospitals and to identify potential strategies to facilitate their delivery. This research aimed to generate knowledge to inform researchers aiming to conduct cRCTs in hospitals.

I specifically focused this dissertation on cRCTs conducted in hospitals to reduce potential variability from exploring sites that were not hospitals.

The specific objectives of the dissertation were:

Objective 1: To explore the current knowledge and evidence surrounding the conduct of cRCTs in hospitals.

Objective 2: To explore from the perspective of a coordinating site, what influenced the delivery and hospital engagement of an ongoing cRCT, and what challenges were encountered.

Objective 3: To identify strategies to facilitate the delivery of cRCTs in hospitals.

Objective 4: To systematically review recruitment strategies for healthcare facilities in cRCTs.

I used concepts from implementation science to address these objectives and to facilitate the design and analysis of the studies included in this dissertation. Using the concepts to analyze the conduct and the delivery of cRCTs is unique, as previously these frameworks have been used almost exclusively to guide and analyze the implementation of a trial.

Methods Used in the Dissertation

Reviewing the literature

Scoping reviews: Scoping reviews are a research methodology that can determine the coverage and breadth of literature in a certain field[56]. As they can be used to identify and incorporate data from a broad range of study designs and literature types[57], scoping reviews are beneficial for exploratory topics where there is uncertainty about the breadth and heterogeneity of the literature that will be identified[58]. This type of review can be used to inform and explore a research agenda, including identifying objectives and questions for systematic reviews (discussed further below) and other research methodologies, as well as to identify knowledge gaps[56].

Arksey & O'Malley (2002)[59] has published steps to conducting a scoping review. This methodology involves five steps: 1) *Identifying the research question.* The first step of conducting a scoping review is to determine the question that will be addressed by the review. This question is often broad in scoping reviews. 2) *Identifying relevant studies.* In the second step, a search is conducted of various sources to identify relevant literature and study that will address the research question. 3) *Study selection.* This step involves identifying studies and literature identified in the search that meet the inclusion criteria developed to address the research question. 4) *Charting the data.* Data from the selected studies must then be extracted and all relevant information should be collected. 5) *Collating, summarizing, and reporting results.* Finally, the data extracted from the selected studies are summarized to produce an overview of the information. The results can be charted to frameworks to allow for comparability of the data extracted from the various literature sources. Unlike in systematic reviews (further described below), scoping reviews do not generally include quality appraisals of the identified literature, as their goal is to provide an overview of the evidence, rather than to provide critically appraised evidence to address a research question[56].

A protocol for the scoping review in this dissertation was written *a priori* (including the rationale for the review, the inclusion and exclusion criteria, and a pilot data extraction). The Preferred

Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Scoping Review extension checklist was followed throughout the write-up of the review to ensure methodological rigour and reporting of key elements of a scoping review according to accepted standards[60].

Systematic Reviews: Systematic reviews are a research methodology that follows a structured and pre-defined methodology to identify and synthesize data for a specific research question in an accountable and explicit method[56,58]. While historically used to collect and analyze data from trials to conduct statistical analyses to estimate treatment effects, the methodology of systematic reviews has expanded to the production of qualitative or mixed-methods data.

Reporting standards suggest and encourage transparent conduct and reporting of systematic reviews[61]. Five key steps should be included in a systematic review[62]: 1) *Framing questions for a review*. In this step, an explicit question will be developed, along with the corresponding inclusion and exclusion criteria for what will be included in the review to answer the question. 2) *Identifying relevant work*. The search methods for identifying relevant literature should be extensive to ensure that literature which may address the proposed research questions is not missed. 3) *Assessing the quality of studies*. The quality of the studies must be assessed using methodologies appropriate to the study design (for example the Cochrane Risk of Bias tool for RCTs). 4) *Summarizing the evidence.* The evidence identified in the relevant literature must be summarized and integrated where appropriate. In the case of discrepancies between the results of various studies, explanations for the different results can be explored. 5) *Interpreting the results.* Finally, when feasible and appropriate, the results of the summarized and integrated evidence should be interpreted relative to the research question.

Qualitative Case Studies

Case studies can be used to intensively explore a single unit, using multiple data sources, in their natural setting[63,64]. Case studies allow for the investigation of a complex phenomenon in a manageable way. Data can be collected quantitatively, qualitatively, or a combination of both. Conceptual frameworks can be used to guide the study, as well as to analyze the data collected. Several types of case studies exist[64]. Explanatory cases can be used to investigate causal links. Exploratory cases can be used when there is no clear outcome. Descriptive cases can be used to describe a phenomenon. Instrumental cases are often used to provide insight into a specific context. Sampling strategies for cases depend on what type of research question that is being investigated[65]. The two principle sampling methods are random sampling, and information-oriented sampling. Random sampling can be further divided into simple random sampling and stratified sampling. Information oriented sampling can be further divided into extreme/deviant cases, maximum variation cases, critical cases and paradigmatic cases.

In this dissertation, a case study design was used. To ensure all members of the coordinating staff were identified and included, some interviewees were selected for inclusion via targeted snowball sampling[66], whereby the principal investigator of the BEACON study suggested further interviewees and so forth until no new relevant participants were suggested. Sampling of key group members has been suggested as appropriate to maximize variation in responses and to allow for all relevant perceptions to be included [67,68].

Implementation Science Frameworks

The Consolidated Framework for Implementation Research: The Consolidated Framework for Implementation Research (CFIR) is a framework for use in implementation science and barriers and enablers to implementation assessments[47]. This is a meta-theoretical framework, developed using previously published research to provide a guide for the implementation of interventions. It is touted as a comprehensive framework that organizes commonalities and overlapping themes from various theories and concepts of implementation science. The framework organizes 39 constructs into five domains [Appendix A for full descriptions of the constructs]: 1) characteristics of the intervention, 2) outer settings (for example economic, social and political context of an organization), 3) inner settings (for example structural, political and cultural context of the implementation), 4) individuals involved with the process, and 5) the implementation process. Within each of the CFIR domains, barriers and enablers can be investigated[69].

The CFIR can be used as a guiding framework for the development of an implementation strategy, as well as for the evaluation of the implementation[47]. It is beneficial in guiding the larger process of an implementation study. While it does provide details on barriers and enablers at multiple levels, the CFIR has been used and tested more systematically with an organization being the unit of study rather than the individual[69–71].

The CFIR has frequently been cited for use in qualitative research, often in a retrospective study design. The CFIR research team has created the "Interview Guide Tool", where a customized questionnaire based on the domains of the CFIR can be created online for use in semi-structured interviews[69]. Responses to the interviews and additional information collected by observations and meeting notes can then be coded for analysis in a pre-populated template, followed by a rating of the constructs. While the CFIR can be used as a guiding framework for implementation and for barrier and facilitator assessments, it does not provide explicit strategies for use.

The Expert Recommendations for Implementing Change compilation: In response to a lack of clarity on implementation strategies, the Expert Recommendations for Implementing Change (ERIC) compilation was developed[72]. The research group behind this compilation sought to develop a list of implementation strategies due to their identification of two key concerns for the state of the field at the time. Firstly, they identified inconsistencies in definitions of implementation strategies, and secondly, they described the lack of detail in published definitions of strategies which would not allow for the strategies to be replicated in the research or clinical settings.

The ERIC compilation is a list of 73 discrete implementation strategies that can be used as building blocks to plan the implementation of an intervention [Appendix B for the list of strategies and their definitions][72,73]. The development of the list involved conducting several rounds of a modified-Delphi process with a panel of stakeholders with implementation science and clinical practice to generate expert consensus on strategies and their definitions.

The implementation plan with the included strategies can be based on anticipated barriers identified in a barriers and enablers to implementation assessment. A recently designed tool has been developed to match ERIC strategies to CFIR domains[73], allowing the capacity to build the implementation strategy with reference to identified barriers from the CFIR domains.

CFIR-ERIC matching tool: To allow for the capacity to build an implementation plan using the ERIC compilation strategies matched to specific determinants from CFIR, the CFIR-ERIC matching tool was developed [73,74]. This tool was developed by having experts in the field of implementation science rank the top seven ERIC strategies that, in their opinion, would address barriers categorized by each of the CFIR constructs[73]. Strategies that were endorsed by ≥ 50% of the experts were deemed as "Level 1" strategies, and strategies that were endorsed by 20-49.9% of the experts were deemed as "Level 2" strategies. Based on the results of this study, the CFIR-ERIC matching tool was created, and made available as an Excel download online at www.cfirguide.com[69]. This tool allows users to select whether the determinant was deemed as relevant to the implementation under question (yes/no) and generates an output table with the CFIR construct matched to the ERIC strategies with a percentage. This percentage indicates what percent of the experts queried in the tool development endorsed the strategy for the construct.

BEACON Study:

The BEACON study is an ongoing Canadian Institute for Health Research funded study that aims to investigate a clinical intervention involving a smartphone-assisted face-to-face therapy in men presenting to the emergency department for self-harm[1]. The intervention consists of problem-solving therapy assisted by a smartphone application. The objective of the study is to determine whether this intervention reduces suicidality in the year following enrollment. This study is being conducted in a multi-hospital cRCT, with ten hospitals across Ontario randomized to be included in the intervention arm. Pilot studies of this intervention have been performed in a small set of men presenting to the emergency department at The Ottawa Hospital. At the time of this dissertation, the study was in the process of rolling out to sites randomly assigned to the intervention arm. This trial has encountered more challenges and time delays in enrolling hospitals and launching the trial than expected.

Organization of the dissertation

The organization, methodologies, and objectives for the studies in this dissertation are summarized in Table 1.1. The studies were conceived in an iterative manner, whereby the results of the first study (*Chapter 2 – Scoping review: To identify current literature in implementation of cluster RCTs in hospitals*) drove the subsequent study (*Chapter 3: Qualitative case study - To evaluate from the perspective of the coordinating site, what is influencing the delivery and hospital engagement of an ongoing cRCT, and what challenges are being encountered).* Findings from the scoping review and coordinating site study identified an evidence gap in reported conduct and delivery strategies for cRCTs, which then drove the final two studies study (*Chapter 4: Intervention Mapping Study - To identify reported strategies that can be used by future researchers to facilitate the delivery of cRCTs in hospitals* and *Chapter 5 – Systematic Review: To systematically review recruitment strategies for healthcare facilities in cRCTs)*.

Table 1.1 - Organization, methodologies, and objectives for the studies in this dissertation

Study	Methodology	Objectives
Chapter 2, Scoping review of the conduct of cRCTs in hospitals	Scoping review	To explore what is the current knowledge surrounding the conduct of cRCTs in hospitals.

Chapter 3, Qualitative case study of the coordinating site staff of the BEACON cRCT	Qualitative case study	To explore from the perspective of the coordinating site, what is influencing the delivery and hospital engagement of an ongoing cRCT, and what challenges are being encountered for trial delivery
Chapter 4, CFIR-ERIC matching study of strategies to facilitate cRCT delivery	CFIR-ERIC matching tool	To identify strategies to facilitate the delivery of cRCTs in hospitals
Chapter 5, Systematic review of reported site recruitments strategies for healthcare facilities in cRCTs	Systematic review	To systematically review reported recruitment strategies for healthcare facilities in cRCTs

Overview of the Chapters

Scoping review (Chapter 2):

A scoping review on the conduct of cRCTs in hospitals was performed to address Objective 1 - *To explore the current knowledge surrounding the implementation of cRCTs in hospitals.*

Following a preliminary hand search of the literature, it was determined that the literature was limited and heterogeneous, and there existed a lack of information or guidelines to assist research teams in identifying and circumventing these challenges. Due to the limited exploration of this topic, the selection of a scoping review methodology was deemed appropriate. To chart the data, constructs from CFIR were used as a coding book. The scoping review led to an identification of a gap in reporting of the strategies for site recruitment and for the delivery of cRCTs in hospitals.

Qualitative Case Study (Chapter 3):

Following the scoping review, a qualitative case study using semi-structured interviews was performed to address Objective 2 - *To explore from the perspective of the coordinating site, what is influencing the delivery and hospital engagement of an ongoing cRCT, and what challenges are being encountered.*

Case studies allow for the investigation of a complex phenomenon within their context in a manageable way[75], therefore the selection of this methodology to explore the perspectives of the coordinating centre staff of a cRCT was deemed appropriate. The results of analyses of the scoping review informed the content of the interview guide. CFIR constructs identified in the scoping review that were deemed as potentially relevant to the conduct of cRCTs were further explored in the interviews. Additionally, constructs that were not identified in the scoping review were included in the interview questions to further explore whether they were not deemed as relevant to cRCT conduct, or whether they were not reported in the literature identified in the scoping review.

The qualitative case study identified CFIR domains and constructs similar to those identified in the scoping review as potentially influential for cRCT conduct. Additionally, the case study

reinforced the reporting and knowledge gap in reporting of strategies for site recruitment strategies and for the delivery of cRCTs in hospitals

CFIR-ERIC matching (Chapter 4):

Next, a study was undertaken using the CFIR-ERIC matching tool to address Objective 3: *To identify strategies to facilitate the delivery of cRCTs in hospitals.*

The previous studies in the thesis demonstrated a knowledge and reporting gap in methodology to facilitate the delivery of cRCTs in hospitals. This provided a direction for a study aimed at identifying strategies to facilitate cRCT delivery. The scoping review identified a large gap in reporting of recruitment of hospitals and implementation and delivery strategies in cRCTs. The qualitative case study explored the perceptions of the coordinating staff of potential barriers and enablers to the delivery of the cRCT. The results of the CFIR domain analysis in the scoping review and the qualitative case study informed the identification of determinants to cRCT delivery, which were then mapped to strategies from the ERIC compilation using the CFIR-ERIC matching tool.

The CFIR-ERIC matching tool was selected for use in this study due to the previous studies in this dissertation being guided by CFIR. This tool allows for the capacity to build an implementation plan using the ERIC compilation strategies matched to specific determinants from CFIR[73,74]. A list of strategies was generated in this study using the CFIR-ERIC matching tool.

Systematic Review (Chapter 5):

Finally, a systematic review was conducted to address Objective 4: *To systematically review reported recruitment strategies for healthcare facilities in cRCTs.*

The research question arose primarily from the results of the scoping review and the qualitative study case study. The first two studies of the dissertation provided a clear direction to identify strategies to facilitate cRCT delivery in hospitals. The CFIR-ERIC matching study (Chapter 4) identified potential strategies to facilitate cRCT delivery, however, the results of this study were aimed at the delivery of these trials in general, and not at a specific task within the process, such as site recruitment. As a theme that frequently emerged in the scoping review and the qualitative case study was the difficulty in recruiting the hospital sites to participate in the trial, a need was determined to identify strategies specifically for site recruitment.

Systematic reviews aim to provide critically appraised evidence to address a research question[56]. As the aim of this study was to produce a list of implementation strategies used in previous cRCTs and determine their success in recruiting sites into the trials, this methodology was deemed appropriate to address the research question. While the previous studies in our research agenda have focused specifically on hospitals, this review included any type of healthcare facility as sites randomized in a cRCT. This was due to the limited literature identified in the narrow scope of hospitals, as well as the assumed potential similarity in strategies that would be used in different healthcare facility types. Numerous strategies were used to recruit healthcare facility sites into cRCTs. While the articles described the strategies used, they rarely evaluated whether the strategies had any effect on site recruitment.

Author contributions

Four manuscripts were prepared as part of this thesis (presented in Chapters 2–5), of which one has been accepted for publication (Chapter 2), one is under review for publication (Chapter 3), and two are prepared for submission for publication (Chapters 4 and 5). All manuscripts were led by Arielle Weir and were co-authored by the thesis supervisor (Dr. Simon Hatcher) and members of the thesis advisory committee (Drs. Simon Kitto, Justin Presseau, and Ian Colman). Arielle is or will be the first author on all publications, having been responsible for study design, data collection, analysis, and writing of the manuscripts. All studies were designed in consultation and discussion with members of the thesis advisory committee.

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Chapter 2 - Barriers and enablers to conducting cluster randomized control trials in hospitals: *A theory-informed scoping review*

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Abstract

Background: Cluster randomized control trials (cRCTs) have unique challenges compared to single site trials with regards to conduct of the trial, and it is important to understand these barriers. The aim of this scoping review was to describe the current literature surrounding the implementation of the cRCTs in hospitals.

Methods: The search strategy was designed to identify literature relevant to conduct of cRCTs, with hospitals as the unit of randomization. Data was extracted and was mapped using the Consolidated Framework for Implementation Research (CFIR) as a codebook, which contains 39 constructs organized into five domains.

Results: Twenty-two articles met inclusion criteria and were included. 18 of 39 constructs of the CFIR were identified in coding, spanning four of the five domains. Barriers to the conduct of the trial were rarely reported as the main outcome of the study, and few details were included in the identified literature.

Conclusions: The review can provide guidance to future researchers planning cRCTs in hospitals. It also identified a large gap in reporting of conduct of these trials, demonstrating the need for a research agenda that further explores the barriers and facilitators, with the aim of garnering knowledge for improved guidance in the implementation.

Keywords

cluster randomized control trial; consolidated framework for implementation research; hospitals; implementation; conduct

Introduction

Randomized control trials (RCT) are often deemed the "gold" standard of clinical research[1]. Multi-site cluster RCTs (cRCTs) are frequently conducted as a study design [2]. cRCTs may offer more widespread population access, the potential for wider external generalizability of results, and quicker recruitment rates for participants than what may be possible from a single-site randomized trial.

Multiple research and administrative committees are often required in order to facilitate the cRCT[2,3]. cRCTs require detailed administration and documentation to ensure that the trials are properly conducted[3]. Coordination of these trials is generally conducted through the central trial personnel, who oversee the overall study management, including randomization, monitoring of sites, and centralized data management. This centre ensures the trial is initiated and the protocol is followed at the sites. While cRCTs offer advantages, they also present some challenges to organization of the trials[2]. These trials tend to be more complex and involve more personnel than what would be required for a single-site trial.

In order to evaluate barriers to conduct and implementation of trials, theoretical frameworks can be used [4]. They can allow for the more rigorous design of interventions and identification of successful factors in an intervention and enable the comparison between studies [5–7]. When no framework is used, there is difficulty in comparing studies, and uncertainty as to whether comprehensive methods were used to identify all relevant aspects. Therefore, they can be useful in retrospective reviews of studies, by allowing comparison and organization of the information extracted[8].

Due to its versatility in evaluating and guiding implementation of interventions, the Consolidated Framework for Implementation Research (CFIR) is commonly used for the investigation of barriers and facilitators to clinical trial implementation. CFIR is a comprehensive, meta-theoretical framework that organizes commonalities and overlapping themes from various theories and concepts of implementation science[8]. Using previously published research to provide a guide for effective implementation, the framework organizes 39 constructs into five domains: 1) intervention characteristics, 2) outer settings (for example the economic, social and political context of an organization), 3) inner settings (for example the structural, political and cultural context of the implementation), 4) characteristics of individuals, and 5) process. The CFIR may be used as a guiding framework for development of an implementation strategy, as well as for evaluation of the implementation[8]. Barriers and facilitators to implementation may be evaluated within each of the five domains[9].

As far as we know, there has yet to be a scoping review performed regarding the literature surrounding implementation of cRCTs in hospitals. cRCTs frequently randomize hospitals as the clustered unit[2]. A systematic review has looked at the delivery of interventions within cRCTs in hospitals, and this review identified nine implementation components: leadership, barrier identification, tailoring to context, patient involvement, communication, education, supportive supervisor, provision of resources, and audit and feedback[10]. However, no reviews were identified to have investigated the implementation of a trial itself, specifically within the context of hospitals whereby there are often multiple competing priorities and administrative policies

which may present challenges to launching a trial in these settings. Limited literature about the conduct of cRCTs exists, and there is a paucity of information or guidelines to assist research

teams in identifying and circumventing these challenges. Therefore, we aimed to conduct a scoping review with the objective of answering the following research question: *What is the current knowledge and evidence surrounding the implementation of cRCTs in hospitals?*

Methods

Scoping reviews are beneficial for exploratory topics where there is uncertainty about the breadth of the literature that will be identified[11]. Scoping reviews can be used to further inform research questions for systematic reviews and other research. Following a preliminary hand search of the literature, it was determined that the literature would likely be too heterogenous and sparse to be identified through the rigid screening methods of a systematic review.

A protocol for rationale, inclusion/exclusion, and pilot data extraction was written *a priori* [Appendix C], however registries of scoping review protocols do not currently exist, and therefore this was not published. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Scoping Review extension checklist [Appendix D] was followed throughout the write-up of the review to ensure methodological rigour and reporting of key elements of a scoping review according to accepted standards[12].

The scoping review search methodology by Arksey & O'Malley (2002)[13] was used. This methodology involves five steps: 1) Identifying the research question; 2) Identifying relevant studies; 3) Study selection; 4) Charting the data; 5) Collating, summarizing, and reporting results.

Identifying the research question

The research question was developed in collaboration with the principal investigator on a cRCT[14]. This trial is encountering more challenges and time delays in enrolling hospitals and launching the trial than expected. While each clinical intervention may have unique barriers and facilitators to implementation, it is important to understand and evaluate these factors at the general level of the cRCT itself as this scenario may present unique challenges compared to implementation of an intervention into wide-spread clinical practice.

The eligibility criteria were designed according to the Johanna Briggs manual of scoping review methodology, consisting of Population, Concept, Context, and Study Design[15]. ***Population:*** The population of study was research groups and organizations conducting cRCTs in randomized hospitals, including administrators and decision-makers within the hospitals. ***Concept:*** The "intervention" of interest was the perceived barriers and facilitators related to conducting cRCTs in hospitals. The hospitals were the units that are randomized within the clinical intervention. Sites were considered hospitals if they were healthcare facilities available for acute and complex conditions[16]. For example, sites with emergency, surgical, maternity, or inpatient care were considered for inclusion into the review. Other healthcare facilities that did not meet the definition for a hospital were excluded (for example dental offices, physiotherapy clinics, and primary care offices). Unique to this review was the examination of the conduct of the cRCT itself, not of the intervention being assessed by the cRCT. ***Context:*** The context was hospitals randomized in a cRCT. ***Study design:*** Study and literature types for inclusion were review articles, abstracts, editorials, guidelines, RCTs, cohort studies, cross-sectional studies, and

qualitative research designs. Protocols were not included. No other restrictions were made on study settings, language, year, or publication status. Abstracts and articles were screened on the basis of whether they were describing the implementation of cRCTs, without being specific to a clinical intervention.

Identifying relevant studies

A rigorous literature search was conducted of MEDLINE, EMBASE, and PsycINFO. The search strategy [Appendix E] was developed, and Peer Review of Electronic Search Strategies (PRESS) reviewed with the guidance of the University of Ottawa Health Science library services [Appendix F]. The keywords and syntax were developed in MEDLINE and adapted to the EMBASE and PsycINFO. Medical subject headings (MeSH) terms were specified and supplemented as needed. Hand searching of the literature was conducted from the references of included articles. Grey literature was also searched in appropriate organization sites (including Clinical Trial Ontario[17] and the Strategy for Patient-Oriented Research[18]).

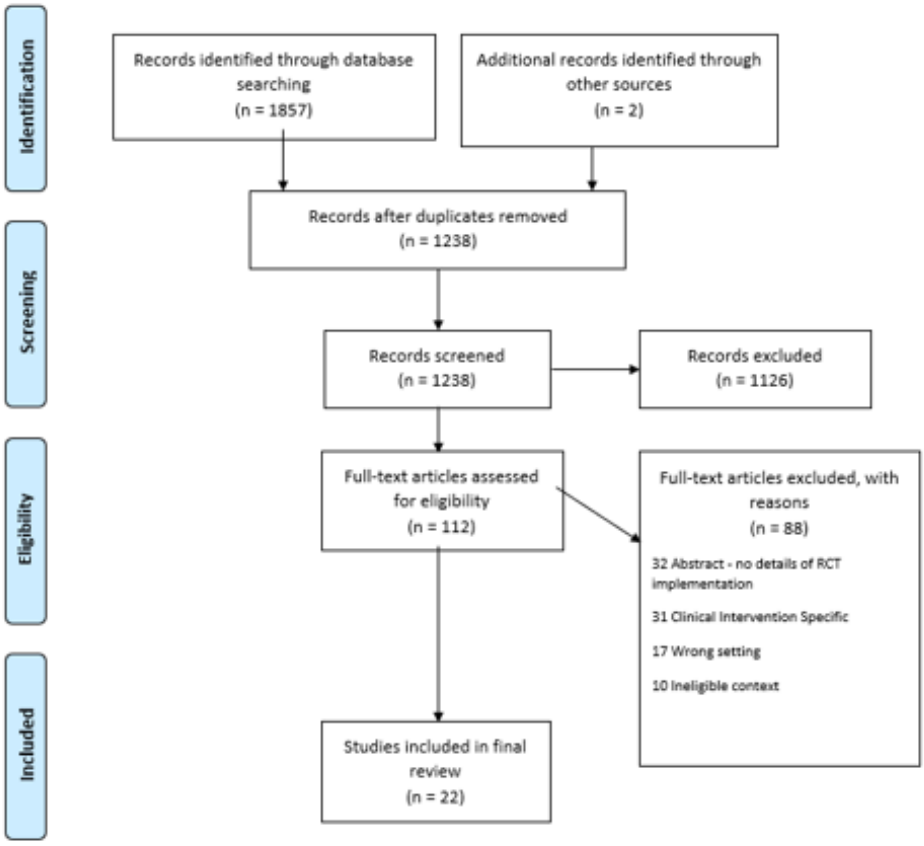
Study selection

Screening was performed at both the title/abstract level and full-text level. Two independent reviewers (AW and JS) screened a 20% random sample of studies at the title/abstract level, and as reviewer agreement was greater than 80% (i.e., there was agreement on over 80% of the sample as to whether they should be moved to full screen or rejected), one reviewer (AW) screened the remaining studies for selection. Uncertainties were resolved by discussion, and a third member (SH) was consulted when consensus between the two independent screeners could not be reached.

Two reviewers (AW and JS) independently reviewed each article in the second screening process. Inter-rater agreement was not calculated for the full-text screening due to the iterative nature of the review. Several face-to-face meetings were held throughout the screening process to resolve discrepancies through consensus.

Results of the screening are displayed in a PRISMA flow diagram[19] (Figure 2.1) with explanations for full-text exclusions.

Figure 2.1 - PRISMA flow diagram[19] of study selection for the scoping review



Charting the data

Identified studies were classified according to empirical papers, review papers, conference abstracts, and grey literature. A data extraction form was made to simplify the data collection process and to ensure that all relevant data was collected [Appendix G]. The form was tested independently by the two reviewers (AW and JS) on a random sample of five articles. Two independent reviewers (AW and JS) extracted from a 20% random sample of studies. A discussion was then held to have consensus on coding, and one reviewer (AW) extracted from the remaining studies. Uncertainties were resolved by discussion with, the other reviewer (JS), and a third member (SH) was consulted when consensus could not be reached.

Collating, summarizing and reporting results

Data was analyzed in an iterative process using the CFIR as a coding book. The primary author (AW) coded themes into constructs. Themes with multiple constructs were cross-coded. When there was uncertainty regarding coding, a second author (JS) was consulted as she was familiar with the CFIR codes. Upon first completion of coding, the coding was double-checked by the same coder. This was done to ensure consistency and ensure that there was uniformity across the coding process, as perceptions and understandings of the codes could have shifted. A codebook

template and guidelines for qualitative data were generated directly from the CFIR website[9]. The CFIR website provides guidelines and a codebook templated for qualitative data coding.

Ethics

Ethics approval was not required.

Results

Search results

The database search identified 1857 potentially relevant references. Two additional articles were identified from the references (hand search). The results of the database and hand search are displayed in Figure 2.1. No additional content was identified in the grey literature search. Following de-duplication, 1238 abstracts were screened. Of these, 112 references were selected for full-text review, from which 22 references were selected as meeting inclusion criteria. Reasons for exclusion of the full text are the following: 32 abstracts only with no implementation details, 31 articles intervention specific, 17 ineligible settings, and 10 ineligible contexts.

Characteristics of included references

General study characteristics of the literature are displayed in Table 2.1. Of the included references, 4 were conference abstracts, and 18 were full article publications. The full-text articles included various publication types including methodology focused (n=6), primary publications of a cRCT (n=9), review of cRCTs (n=2), and a process evaluation (n=1). The studies spanned 15 different countries, and 5 studies included multiple countries. Dates of publication ranged from 2001-2018. Two of the included articles described the same primary study, but with different methodological focus. For simplicity, all included references, both full studies and abstracts, will be referred to as articles.

An implementation framework was stated or described in 12 of 22 articles, including Campbell et al. framework for development and evaluation of RCTs in complex interventions, the theory of planned behaviour as a theoretical framework, the PRECEDE-PROCEED model, normalization process theory, Plan-Do-Study-Act, PARIHS framework, Diffusion of Innovation framework, CFIR, principles of social marketing. Of the articles that did explicitly state an implementation framework, the majority were not explicitly clear on how the framework was used, at which point in the implementation, or to how the framework was selected. Three articles[20–22] justified the use of the frameworks in the analysis of their results only, and do not mention using them as guidance in design. Three studies clearly used frameworks in study design[23–25]. One study's main objective was to evaluate three implementation strategies, including two frameworks that have been used in implementation science[26].

Table 2.1 - Characteristics of the studies included in the scoping review

First Author	Year	Literature Type	Location	Settings	Study period	Implementation Framework used?
Allanson, E[10]	2017	Systematic Review of cRCTs	United States	All cluster RCTs where the healthcare facility was	n/a	Mention of unclear frameworks consulted and cross tabulated with World Health

				the unit of randomization 46 studies		Organization quality of care framework for pregnant woman and newborns
Anderson, D[27]	2018	Methodology of a pragmatic cRCT	United States	9 hospitals in Southeastern US	Apr 2012 - Jul 2014	Not described
Ayieko, P[28]	2011	cRCT	Kenya	8 hospitals	Sept 2006 - Apr 2008	Unclear, references broad implementation articles
Bosch, M[23]	2016	Methodology of a cRCT	Australia	ED staff within 13 hospitals	Nov 2010 - May 2011	Vague organizational level theories (no mention of specific theories or how they were used in the research); model of diffusion in service organizations
Bouwsma, E[20]	2018	Step-wedge cRCT	Netherlands	9 secondary care hospitals	2011-2014	Theory of Planned Behaviour used as a theoretical framework for determinants of behaviour regarding recovery and return to work
Brown, B[24]	2018	Step-wedge cRCT	Australia	9 hospital sites in New South Wales (NSW), Australia with urology network	Dec 2013 - Aug 2014	PRECEDE-PROCEED model
Butrick, E[29]	2012	Abstract on a cRCT	Zambia and Zimbabwe	5 referral hospitals (RHs) and 38 primary health care clinics (PHCs)	2007 and 2012	Not described
Clack, L[30]	2018	Methodology of a cRCT	Europe	6 intensive care units of hospitals (of 14 in larger study)	Jan 2011 - Jun 2013	Diffusion of Innovation' framework, Consolidated Framework for Implementation Research
Clarke, D[21]	2014	Process evaluation of a pragmatic cRCT	England (Yorkshire, North West, South East	10 of the 36 stroke units participating in the TRACS trial in four	Feb 2008 - Feb 2010	Normalization Process Theory (for intervention explanation implementation)

			and South West, Peninsula)	regions in England		
Coury, J[25]	2017	Pragmatic cRCT	United States	26 clinics operated by 8 Federally Qualified health centers in Oregon and California	Jan 2015 - Jan 2016	Plan-Do-Study-Act Referenced CFIR in discussion
Coville, H[31]	2016	Abstract on a Step-wedge cRCT	Transcontinental	46 hospitals in 20 countries approached (38 now with IRB approval)	n/a	Not described
Doig, G[32]	2008	cRCT	Australia and New Zealand	ICUs of 27 community and tertiary hospitals	Nov 2003 to May 2004	Not described
English, M[22]	2011	Methodology of a cRCT	Kenya	8 hospitals	Sept 2006 - Apr 2008	Diffusion of innovation, organizational culture and transforming systems, clinical microsystems, Theory of Planned Behaviour, motivation and worker performance and barriers to guideline uptake
Gülmezoglu, A[33]	2004	Methodology of a cRCT	Mexico and Thailand	Maternity units of hospitals with (>1000 deliveries year) 22 hospitals in Mexico 18 hospitals in Thailand	Baseline Oct 2003	Vague mention of Campbell et al. framework for development and evaluation of RCTs in complex interventions (no details provided as to how the framework was used).
Johnson, A[34]	2018	Methodology of a pragmatic cRCT	United States	Analysis of hospital recruitment in a pragmatic cluster RCT 41 of those eligible participated	Sept 2015 - Sept 2016	Not described

Kaseba, C[35]	2009	Abstract on a cRCT	Zambia	25 district clinics and 3 referral facilities	Oct 2007 - Jan 2009	Not described
Koller, A[36]	2018	Abstract on a Step-wedge cRCT	Austria	17 wards in 3 hospitals	Recruitment Jan 2017 - May 2018	Not described
Labarere, J[37]	2007	cRCT	France	25 hospital-based post-acute care departments	2001 - 2004	Not described
Rycroft-Malone, J[26]	2012	Pragmatic cRCT	United Kingdom	19 acute National Health Service hospitals 2 hospitals lost in access process	2006-2009	PARIHS framework Plan-Do-Study-Act as part of one of the intervention arms
Weinfurt, K[38]	2017	Review of pragmatic RCTs	n/a	n/a	n/a	Not described
Wong, C[39]	2007	cRCT	Canada	30 hospitals performing primary THJA were randomly assigned to implement the algorithm or to continue with usual care	Oct 2002 - Feb 2005	Not described
Wright, F[40]	2006	cRCT	Canada	42 hospitals	Jan 2004 - Jun 2004	Principles of social marketing

Analysis using the CFIR domains

Of the five CFIR domains, four were coded from literature identified in this scoping review. Of the 39 constructs of the CFIR, 18 were identified within the included articles as having relevance to implementation of cRCTs in hospitals. 14 of 22 articles included more than one construct, with 10 being the maximum number of constructs included in one article. Table 2.2 describes the spread of domains across included studies. Domains from the CFIR are listed in ***bold italics,*** and constructs within the domains are in *italics.* Direct quote examples from the studies are provided, along with the construct in which they were classified, and whether they are examples of barriers or facilitators to conducting the cRCT.

Intervention Characteristics. This domain considers key attributes of an intervention that may influence the success of its implementation.[9] This domain was coded in 13 of 22 articles. *Intervention source* and *relative advantage* were each coded in 3 of 22 articles. *Adaptability* of the cRCT was coded as relevant in 10 of 22 articles. *Trialability* was mentioned in 1 of 22 articles. The articles included quotes such as:

"…doubts regarding the additive value of participation…"[34] [lack of *relative advantage*; barrier]

"Subsequently, the implementation team worked with the appropriate site personnel to collaboratively develop a site-specific implementation plan. For each institution, appropriate educational materials were generated to meet local needs."[39] [*adaptability*; facilitator]

Intervention characteristics were frequently represented in the articles. It was noted that increased engagement from the hospitals was facilitated if the trial was deemed to be at least partially internally sourced[30,34]. This can include aspects such as having hospital staff contribute to the design of the project. Additionally, the trials' adaptability was mentioned multiple times as being a facilitator for the hospitals for participation in the cRCT[10,24–26,36,38,39,41]. If a trial was perceived as having little flexibility to allow for tailoring to the sites, the implementation was thought to be more challenging, thus presenting a barrier to conducting the trial[36]. Several articles specifically mentioned they made appropriate modifications to address the unique factors at sites to facilitate the study implementation[10,24,34,39]. Additionally, one study described that while some modifications were planned in advance for each site, they also valued the ability to make further adjustments as challenges arose in the implementation phase[38]. This focus on the importance of adaptability may be due to the nature of cRCTs having to be implemented in various unique hospitals, all with their own systems and organization. It appears the perception of the ability to tailor and adapt the study to each individual hospital is a facilitator to trial conduct. Furthermore, there was noted importance of the sites' focus on the relative advantage of the intended trial[21,25,34]. Lack of perceiving that the intended trial would be advantageous over current practice and programs was cited as a barrier to the sites participating and as a reason for a site refusing to participate in the trial[34]. It is possible that this may lead to a site's refusal to commit to entering a trial if they do not anticipate there may be benefit from participating. The trialability of a study was only mentioned in one of the included articles, in which the sites expressed it would be a facilitator to trial participation to have an intervention that they could try before full implementation in order to avoid wasting time, energy and other resources if it was not a good fit for that site[25].

Outer settings. This domain considers factors that are external to the intervention which may influence its implementation. This domain was coded in 3 of 22 articles. *Cosmopolitanism* was coded in 2 of 22 articles. 1 of 22 included *external policy & incentives* as playing a part in implementation of cRCTs. This included quotes such as:

"…leveraged relationships built through a previous collaborative…"[34] [*cosmopolitanism*, facilitator].

"A number of barriers to successful PCTs are associated with how incentives align with health systems, clinicians, and potential sponsors…"[38] [*external policy and incentives*, facilitator]

The domain of ***outer settings*** was described in several of the included studies. Cosmopolitanism, which is how much an organization is networked with other external organizations, refers to the environment external to the hospitals and can include the larger organizations in which a site is a member, as well as healthcare and governmental policies and priorities[42]. Two of the articles explicitly described engaging their site through pre-established collaborations and networks, and this was determined to be a facilitator to trial conduct and site recruitment[32,34]. Johnson et al.

(2018) described first reaching out to hospitals within a previous collaborative before reaching out to other sites and noted there was a larger participation rate from those within the collaborative[34]. In terms of external policy & incentives, one study described their experiences with a barrier they had faced to conducting their trial being the priorities and incentives of the health systems which were not aligned with the objectives of the trial[38]. These constructs may speak to the importance of establishing hospital networks that allow for the potential to align priorities and establish common goals in order to facilitate conducting the trial.

Inner settings. This domain considers aspects associated from within the organization that may influence the implementation of the intervention.[42] This domain was coded in 8 of 22 articles. *Relative priority* was coded in 2 of 22 articles. *Compatibility, tension for change,* and *organizational incentives & rewards* were each included in 1 of 22 articles. *Leadership engagement* and *available resources* were each coded in 4 of 22 articles, and *access to knowledge & information* was coded in 1 of 22 articles. This included quotes such as:

"…low priority placed on improving post-acute stroke care…"[34] [lack of *relative priority*, barrier]

"lack of leadership support …to overcome these barriers we implemented different strategies including engaging leadership support…"[31] [*leadership engagement*, facilitator (overcoming the barrier)]

"Limited resources—both material and human—were mentioned in all hospitals, although the level of impact was different. The distribution of limited resources reflected the organization's relative priorities, sometimes shifting over time, particularly driven by change agents and disruptive events."[30] [*relative priority* and *available resources*, barrier]

Multiple constructs within the domain of ***inner settings*** were identified in the included articles. As inner settings address challenges associated with the different levels within an organization[42], they can include factors that are related to the individual sites. This may therefore assess the site's factors associated with the cRCT implementation. One study noted that while they did not uncover any differences in the demographics of hospitals that agreed or not to participate in their trial, they assumed that those that did agree prioritized a need for the intervention, which presented as a facilitator to the site participating in the trial[26]. Additionally, two studies noted that agendas of some hospitals may not have aligned with the aims of the research trial, presenting a barrier to acceptance into a trial[30,34]. One of these studies went on to state that successful implementation was facilitated when they were able to align their priorities with those of the hospitals[30]. Therefore, the current tension for change and alignment with the hospitals' priorities may be facilitating factors for a site's agreement to participate and actively engage in a cRCT. If there are pre-established needs and desires to bring about change, in an area that is under investigation by the study, this could help facilitate the process. Additionally, as noted by one study, if the culture of the organization prioritizes the research, the process may be facilitated and more easily implemented[38].

Regardless of the overall climate for implementation, the readiness for implementation may need to be evaluated and addressed. Organizational support was sought by some studies early in the planning stage[31,41] or proposed for future studies as a way to address barriers they had encountered while planning the cRCT[35]. Additionally, the limited availability of resources, including time, personnel, finances, information was seen as a barrier for

implementation[30,31,34,37]. Participation in a trial could be challenging without the appropriate staff, knowledge, and/or funds to be able to appropriately carry out the trial. One study did note that the availability of resources could also shift depending on the organization's current priorities, which could either present a barrier or a facilitator to conducting the trial depending on how the priorities shift[30].

Characteristics of individuals. This domain considers associated with the individuals within an organization that can influence the implementation of an intervention. This domain was not coded from any articles. The limited identification within this domain may be in line with the focus of the review being on the implementation of the cRCT itself, and not on the clinical intervention. The clinical intervention itself may be more strongly influenced by individuals; however, the cRCT may be thought as more of an organization-dependent initiative.

Process. This domain considers plans and procedures for implementation. This domain was coded in 17 of 22 articles. *Planning* was mentioned in 11 of 22 articles. *Opinion leaders formally appointed internal implementation leaders,* and *champions* were included in 9 of 22, 5 of 22, and 3 of 22 articles respectively. *Reflecting and evaluation* was coded in 1 of 22 articles.

"…met with hospital directors before intervention for their consent and support to ensure organizational buy in…"[41] [*planning* and *opinion leaders*, facilitator]

"…working with the project leads from each health center, we identified and recruited via email key staff involved in implementing…" [25] [*formally appointed internal implementation leaders*, facilitator]

"…a number of key stakeholders took a leadership role in championing the issue, and the key contact led on multiple implementation related activities."[26] [*champions*, facilitator]

Process factors for the trial were coded in the majority of the included studies[10,22–26,28–30,34,35,38–41,43]. Studies reported that they spent considerable effort into planning the study in advance, in order to identify and overcome some of the expected barriers[29,38]. This was often cited in terms of meeting with the key stakeholders (for example directors, physicians, administrators, patients) to seek their prior engagement [22,23,25,38,40,41,44,45], as well as to assess their current experiences and infrastructure to determine whether they should be considered for inclusion in the study[25,28].

Furthermore, the engagement of multiple groups and individuals was described. Engaging the opinion leaders, champions, and implementation leaders from the start was seen as a strength to the study development and a facilitator for successful implementation[30,45] and was also proposed as a solution to overcoming some of the barriers that were encountered[35]. These influencers may be able to facilitate conducting the trial by offering insight into the hospitals in which the trial is intended in order to tailor the trial to the sites for more success in implementation. One study noted that 1/5 of hospitals who declined the study cited a lack of support from the hospital or system decision-makers as being a barrier to participation[34]. The review of implementation by Allanson et al. (2017) [10] concluded that engaged and solid leadership is often seen in successful implementation efforts, however, it is challenging to decipher causality. Some studies stated that they engaged champions in the planning phase to facilitate the trial, however, a description of who the champions were identified was not explicitly clear[23,26,40,44].

Table 2.2 - Mapping of implementation factors identified in the scoping review to CFIR

DOMAIN	Construct	Sub Construct	Allansonn, E[10]	Anderson, D[27]	Ayieko, P[28]	Bosch, M[23]	Bouwsma, E[20]	Brown, B[24]	Butrick, E[29]
Intervention Characteristics	Intervention Source								
	Evidence Strength & Quality								
	Relative Advantage								
	Adaptability		x				x	x	
	Trialability								
	Complexity								
	Design Quality & Packaging								
	Cost								
Outer Settings	Patient Needs & Resources								
	Cosmopolitanism								
	Peer Pressure								
	External Policy & Incentives								
Inner Settings	Structural Characteristics								
	Networks & Communications								
	Culture								
	Implementation Climate	Tension for Change							
		Compatibility							
		Relative Priority							
		Organizational Incentives & Rewards							
		Goals and Feedback							
		Learning Climate							
	Readiness for Implementation	Leadership Engagement							
		Available Resources							
		Access to Knowledge & Information							
Characteristics of individuals	Knowledge & Beliefs about the Intervention								
	Self-efficacy								
	Individual Stage of Change								
	Individual Identification with Organization								
	Other Personal Attributes								
Process	Planning		x		x		x	x	x
	Engaging	Opinion Leaders			x	x	x	x	
		Formally Appointed Internal Implementation Leaders	x						
		Champions		x					
		External Change Agents							
	Executing								
	Reflecting & Evaluating		x						

Table 2.2. Continued

DOMAIN	Construct	Sub Construct	Clack, L[30]	Clarke, D[21]	Coury, J[25]	Coville, H[31]	Doig, G[32]	English, M[22]	Gülmezoglu, A[33]	Johnson, A[34]
Intervention Characteristics	Intervention Source		x							x
	Evidence Strength & Quality									
	Relative Advantage			x	x					x
	Adaptability				x				x	x
	Trialability				x					
	Complexity									
	Design Quality & Packaging									
	Cost									
Outer Settings	Patient Needs & Resources									
	Cosmopolitanism						x			x
	Peer Pressure									
	External Policy & Incentives									
Inner Settings	Structural Characteristics									
	Networks & Communications									
	Culture									
	Implementation Climate	Tension for Change								
		Compatibility								
		Relative Priority	x							x
		Organizational Incentives & Rewards								
		Goals and Feedback								
		Learning Climate								
	Readiness for Implementation	Leadership Engagement				x			x	x
		Available Resources	x			x				x
		Access to Knowledge & Information								x
Characteristics of individuals	Knowledge & Beliefs about the Intervention									
	Self-efficacy									
	Individual Stage of Change									
	Individual Identification with Organization									
	Other Personal Attributes									
Process	Planning				x				x	x
	Engaging	Opinion Leaders							x	
		Formally Appointed Internal Implementation Leaders			x			x		x
		Champions	x							
		External Change Agents								
	Executing									
	Reflecting & Evaluating									

Table 2.2. Continued

DOMAIN	Construct	Sub Construct	Kaseba, C[35]	Koller, A[36]	Labarere, J[37]	Rycroft-Malone,	Weinfurt, K[38]	Wong, C[39]	Wright, F[40]
Intervention Characteristics	Intervention Source								x
	Evidence Strength & Quality								
	Relative Advantage								
	Adaptability			x		x	x	x	
	Trialability								
	Complexity								
	Design Quality & Packaging								
	Cost								
Outer Settings	Patient Needs & Resources								
	Cosmopolitanism								
	Peer Pressure								
	External Policy & Incentives						x		
Inner Settings	Structural Characteristics								
	Networks & Communications								
	Culture								
	Implementation Climate	Tension for Change				x			
		Compatibility	x						
		Relative Priority							
		Organizational Incentives & Rewards					x		
		Goals and Feedback							
		Learning Climate							
	Readiness for Implementation	Leadership Engagement	x						
		Available Resources			x				
		Access to Knowledge & Information							
Characteristics of individuals	Knowledge & Beliefs about the Intervention								
	Self-efficacy								
	Individual Stage of Change								
	Individual Identification with Organization								
	Other Personal Attributes								
Process	Planning		x				x	x	
	Engaging	Opinion Leaders				x	x	x	x
		Formally Appointed Internal Implementation Leaders					x		
		Champions				x			
		External Change Agents							
	Executing								
	Reflecting & Evaluating								

Discussion

To our knowledge, this is the first scoping review that has examined the overall barriers to conducting cRCTs in hospitals. This review is intended as a multi-phase study investigating and describing the challenges of conducting cRCTs in hospitals, with the intention of facilitating future studies by recognizing and circumventing the barriers in the planning process. This review attempted to explore the literature surrounding the conduct and implementation of cRCTs in a hospital setting, with factors that were not specific to the clinical interventions and were important for the development and initiation of the trial. Many challenges in trial launch do not appear to be specific to the clinical intervention, establishing a need to better understand the implementation of cRCTs to determine generalizable strategies to facilitate the process. Although the CFIR has yet to be used in the context of identifying barriers and facilitators to trial implementation in cRCTs, all aspects of the identified concepts were able to be coded within the domains. The review coded four of the five CFIR domains in the included studies which were: ***intervention characteristics, outer settings, inner settings, and process***. The constructs within the identified domains represented either barriers or facilitators to conducting the cRCTs in hospitals.

The identified references contained a large percentage of conference abstracts (4 of 22 included references) with no full study publications linked. Abstracts were included in the analysis if they contained details regarding cRCT implementation. This large number of abstracts identified is potentially due to implementation details and challenges encountered in cRCT initiation rarely being the main objectives of trials and publications and are therefore frequently only discussed in preliminary reports and conference presentations. This low representation of cRCT initiation as the study focus can be highlighted by only one article identified in our review as having the primary goal of describing the pre-launch cRCT implementation strategies[34]. Due to identifying challenges in hospital recruitment and engagement before they were even able to commence recruiting patients, Johnson et al. (2018) conducted an analysis to describe factors related to the implementation of the cRCT.

Additionally, it is important to note that there is not always a clear distinction between what is specific to conduct of the cRCT, separate from the clinical intervention itself. In fact, this is more often true than not, and aspects that are related to cRCT start-up and launch are also embedded in the strategies for implementation of the clinical intervention. With the emergence of a more frequent use of pragmatic design of trials, whereby the trial is intended to be embedded into real-world practice as part of the implementation[46], it may make it difficult to differentiate between the aspects that are specific to implementation of the cRCT separate from the implementation of the specific intervention, as they are more intertwined.

Knowledge gaps in reporting

The limited studies identified in this review highlights the reporting gap surrounding implementation of the cRCTs. While our search strategy was detailed, few studies were identified. This leads us to believe that the objective of a study is seldom the implementation of the cRCT, and therefore details are rarely included in the main results. While we included conference abstracts, these may not have provided full details of the described studies. There are currently no widespread guidelines or consensus on the necessity and details of the strategies used, and therefore little information makes its way to peer-reviewed journals and wider

circulation. Furthermore, much of the literature and reports in the studies is opinion-based interpretations, without empirical data.

While many constructs were identified frequently (for example *planning* in 11 articles and a*daptability* in 10 articles*)*, others were infrequently identified, or not identified at all (for example e*vidence strength & quality, cost, characteristics of the individuals* and *patient needs and resources).* Reasons for this are unclear, although it may be due to reporting patterns, whereby certain aspects are more frequently included in the publications of these trials. For example, the limited identification of *characteristics of individuals* may be due to the trial reporting aspects related to the overall trial, and not specific to individuals involved or participating in the trial.

It is possible that due to the nature of a cRCT or patterns in reporting, certain CFIR constructs are not represented in implementation of trials or described in the study publication. Clinical trials may be envisioned as being short term attempts to determine the effectiveness of an intervention, and aspects such as *evidence strength & quality* and *cost* may not be as important factors in implementation. This short-term view may have different influence when pragmatic trials are included as they are intended for longer-term infiltration with current clinical practice, but it did not come up as relevant in the articles described here.

Furthermore, *patient needs and resources* were not described in any of the included articles. This may be due to the nature of examining features related to implementation at the level of the cRCT, and therefore would exclude factors such as patient needs, which would be more specific to the actual clinical intervention studied within the cRCT. At the more macro level of the cRCT, it is the hospital factors (which may in themselves include patient needs) that could have a greater influence on the implementation of the cRCT. Further empirical investigation should attempt to decipher this further and to determine whether it is a case of lack of reporting or a true representation of limited perceived importance.

Limitations

Limitations in search strategy must be noted. The review limited included studies to English language only. Additionally, as previously stated, it was not always clear the separation between the elements related to the implementation of the cRCT, and elements related to the implementation of the clinical intervention, and therefore some overlap may be reported. Furthermore, while the coding was calibrated with the second reviewer, full coding was performed by a single reviewer.

Conclusion and Lessons Learned

This scoping review aimed to identify literature surrounding the conduct of cRCTs in hospitals and to map the literature to the CFIR in order to analyze the data. All factors identified in the literature were able to be mapped to the framework, and four of the five CFIR domains were identified (***intervention characteristic, outer settings, inner settings, and process)***.

This review can be informative for researchers planning and conducting future cRCTs in hospitals. Strategies for conducting the trial may be developed from the results drawn from this scoping study. Certain factors were identified in the literature as presenting either a barrier or a facilitator to conducting the trial. The adaptability to tailor the trial to each site and the early engagement of opinion leaders, champions, and implementation leaders in the cRCT process can

be facilitators to conducting the trial. A site not perceiving a relative priority for the trial or tension for change for the clinical field, as well as limited resources, can present barriers to conducting the cRCT. Future researchers should be conscious of recognizing and addressing these factors while planning the cRCT in order to facilitate the trial's conduct.

While the review identified many factors associated with conducting cRCTs in hospitals**,** a gap in reporting of recruitment and conduct techniques from studies also became apparent. While these aspects of the trial may be briefly described in study publications, they are rarely the focus of published articles, adding to a lack of guidance for future studies. The studies identified in this review described primarily the authors' personal experiences and lessons learned from the implementations of their studies, and little empirical data was identified in the literature. This highlights the need for further investigating the gap, by means of empirical studies with more directed methodology (for example, by interviewing relevant stakeholders of the cRCT process). There may also be a call to increase reporting of the implementation strategies.

As previously stated, this review was the first step in a multi-stage process to describe the challenges in the process of launching cRCTs in hospitals. The knowledge gap identified by this review highlights the need for a research agenda that focuses on further and more rigorous identification of the barriers and facilitators of these large-scale trials, to be able to determine strategies for future success and a reduction in wasted resources. Further studies are necessary to provide guidance for cRCTs in hospitals, and our intended sub-analysis of a cRCT in select Ontario hospitals will aim to contribute to this important understanding.

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Chapter 3 - Coordinating site staff perceptions on initiation and engagement of sites in a cluster randomized controlled trial: a qualitative study guided by the Consolidated Framework for Implementation Research

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Abstract

Background: Cluster randomized control trials (cRCTs) have unique challenges compared to non-clustered trials with regards to the conduct of the trial, and it is important to understand these barriers. The aim of this qualitative case study review was to explore from the perspective of the coordinating site, what is influencing the launch and conduct of an ongoing cRCT in hospitals.

Methods: The case was defined as the coordinating site team of the cRCT. The study was performed in a period of transition for the cRCT, whereby the first sites were nearing launch and commencement of active recruitment. Interview questions were open-ended and guided by themes from the Consolidated Framework for Implementation Research (CFIR). Data analysis was guided by CFIR as a codebook.

Results: Six individuals were interviewed. All themes were able to be mapped to CFIR constructs and domains. Several key domains were perceived as important to trial conduct.

Conclusions: The experiences of the coordinating staff for BEACON explored in this study using the CFIR framework can be informative in facilitating the launch of future cRCTs. Site recruitment and engagement strategies can be developed or tailored from the results drawn from this study.

Keywords

cluster randomized control trial; consolidated framework for implementation research; hospitals; implementation; conduct; qualitative

Introduction

Randomized controlled trials (RCT) are often deemed the "gold" standard of clinical research[1]. Multi-site cluster RCTs (cRCTs) are often being conducted as a study design [2]. These multi-site trials have the potential of better generalizability of results, as well as the possibility of larger recruitment than what is possible from a single site. While multi-site cRCTs offer advantages, they also present some challenges to the organization of the trials[2]. These tend to be more complex and involve more personnel than what would be required for a single-site trial.

Multiple committees can be required to conduct a cRCT[2,3]. This can include a steering committee to oversee design and conduct, a data safety monitoring board to monitor trial safety and effectiveness, and adjudication committees to review end data to ensure the objectives of the study are met. Multi-site trials also require detailed administration and documentation to ensure that the trials are properly conducted[3]. Coordination of this is generally conducted through the central trial personnel, who oversee the overall study management, including randomization, monitoring of sites, and centralized data management. This centre, the coordinating site, attempts to ensure the trial is initiated and the protocol is followed at all the sites.

The team chosen to design and initiate any study can have major influences on the success or failure of initiation of the research. Regardless of the actual effect of the intervention or the observed unit of study, an effective study team is necessary for the success of a research study[4]. Ineffective management of a study can increase the chances of the research being wasted[5]. Some key factors of study team experience are: 1) expertise in the field of study, 2) experience in unique study methods, 3) experience in working with regulating agencies, 4) critical thinking and problem-solving skills, 5) experience dealing with sites which may have never been involved in research, 6) team chemistry, and 7) confidence[6]. Basic recommendations have been published with various authors' experiences on what factors are crucial for a clinical research team[2–4], including ensuring that the team is engaged in the study and recommendations that the staff is devoted solely to research rather than having a position split between clinical and research tasks[4].

In addition, there has been a recent increase in focus on the evaluation of the delivery of interventions in RCTs, rather than solely on the evaluation of the intervention[7]. This differs from the traditional evaluation of the trial, where only the effect of the clinical or behavioural intervention itself is measured[8]. cRCTs offer a unique opportunity for implementation evaluation[8]. As each site can have slight variations in organization and services, cRCTs present the opportunity to study the implementation of the trial intervention between sites. Factors affecting implementation differences between the sites can be explored, providing an opportunity to generate and enhance existing empirically and conceptually transferable findings to inform cRCT implementation of best practice guidelines. This paper attempts to add to this body of literature through a study of a cRCT in Ontario.

The focus of this study concerns the implementation of the BEACON trial, which aims to investigate a clinical intervention involving a smartphone-assisted face-to-face therapy in men presenting to the emergency department for self-harm[9]. The intervention consists of problem-solving therapy delivered through a smartphone application. The aim of the BEACON trial is to determine whether this intervention can assist in reducing suicidality in the year following enrolment. The BEACON study is designed as a cRCT, whereby ten hospitals across Ontario

have been randomized to be included in the intervention arm. As of October 2019, the hospitals were each at various points along with the launch of the study, however, the roll-out phase encountered unexpected delays and challenges.

This qualitative study was designed as the second step of a multi-phase research agenda that aimed to investigate and describe the challenges of launching and conducting a cRCT trial. The first step in this agenda was to conduct a scoping review surrounding the conduct of cRCTs. This scoping review (Weir et al., under review) aimed to identify and describe the current literature, and to chart it to the domains of the Consolidated Framework for Implementation Research (CFIR) (framework described below).

The CFIR is a framework developed within implementation science this is used to identify barriers and facilitators to implementation of interventions[10]. CFIR is touted as a comprehensive, meta-theoretical framework that organizes commonalities and overlapping themes from various published frameworks and theories. The framework organizes 39 constructs into five domains [see Appendix A 1 for detailed definitions and constructs within the domains]: 1) *intervention characteristics* –design features of the trial, 2) *outer settings* –external political and network influences, 3) *inner settings* - inner political and organizational influences within the sites, 4) *process* –plans and procedures for implementation, and 5) *characteristics of individuals* – personal factors and experiences of the people involved in implementation and conduct (for clarity, domains from the CFIR are listed in ***bold underlined italics***, and constructs/subconstructs within the domains are in *underlined italics)*.

The scoping review identified 22 articles, from which 18 constructs spanned four of the five CFIR domains: ***intervention characteristics***, ***outer settings***, ***inner settings***, and ***process***. In terms of ***intervention characteristics***, the *adaptability* and perception of a *relative advantage* of the trial over current practice were frequently mentioned as being important to cRCT conduct. For ***outer settings***, current healthcare and governmental *policies and priorities* were deemed as potentially influential to implementation. The domain of ***inner settings*** included the importance of *tension for change*, whereby the hospitals have an agenda that prioritizes the need to fill a gap in current clinical care that the trial may address. As for the ***process***, the *engagement* of various individuals and groups at various time points in conducting the trial was described. The domain of ***characteristics of individuals*** was not coded from any of the included articles. While many constructs were identified frequently (for example *adaptability* in articles), others were infrequently identified, or not found at all (for example *evidence strength & quality, cost,* and *patient needs and resources*). Reasons for this are unclear, although it may be due to reporting patterns, whereby certain features and processes of the trial are more frequently included in the publications of these trials.

Overall, the scoping review identified a gap in reporting of site recruitment and implementation strategies for hospitals in cRCTs. It provided clear direction for a qualitative analysis of the identified gap within our research agenda that focuses on rigorous identification of the barriers and facilitators of cRCTs in hospitals.

Despite the importance of the coordinating site in conducting the cRCT[4], there is a paucity of published knowledge about the roles and experiences of these members in the design and conduct of the cRCT. Gaining an understanding of the coordinating site members' experiences and perceptions with the trial may prove beneficial to recognize the influences the members can

have for the successful initiation cRCTs. Therefore, this study aimed to explore from the perspective of the coordinating site, what is influencing the launch and conduct of an ongoing cRCT in hospitals.

Methods

Study design and approach:

The study was conducted using a qualitative case study approach. Case studies can be used to intensively explore a single unit, using multiple data sources, in their natural setting[11,12]. Case studies allow for investigation of a complex phenomenon within their context and in a manageable way[13]. This study was guided by the following research question: *What are the perceptions of the staff from the perspective of the coordinating site, what is influencing the launch and conduct of the BEACON cRCT?* The study was performed in a period of transition for BEACON, whereby the first sites were nearing launch and commencement of active recruitment. The study protocol and interview guide were approved by the Research Ethics Board of the Ottawa Hospital Research Institute [Appendix H].

Participants and Settings

The case of investigation was defined as the coordinating site research team of the BEACON cRCT. The goal of this study was to gain insights from the coordinating site research staff as to their perspectives on the launch of the trial, and therefore to gain multiple perspectives, individuals from multiple roles were interviewed. As the focus of this study was on the perspectives of the coordinating site to determine specifically what their thoughts were surrounding the launch of the trial, all members of the coordinating site staff were invited to participate in semi-structured interviews. We included the members of the coordinating staff due to the instrumental role this group plays in conducting and organizing the cRCT. They are involved in study design, acquiring ethics and approval, recruiting the individual sites, coordinating the study, and are the main source of communication with each site.

Data Collection

Semi-structured interviews with coordinating site members were performed. An invitation email was sent to participants either directly from the primary author (AW), or through the research coordinators of the BEACON study. Reminder emails were sent to non-responders up to three times. Interviews took place either face-to-face or via teleconference, and all interviews were conducted on a one-on-one basis by the primary author (AW). To ensure all members of the coordinating staff were identified and included, some interviewees were selected for inclusion via snowball sampling[14], whereby the principal investigator of the BEACON study suggested further interviewees and so forth until no new relevant participants were suggested. Sampling of key group members has been suggested as appropriate to maximize variation in responses and to allow for all relevant perceptions to be included [15,16].

Interview questions were open-ended and were guided by the themes from the CFIR. The interview guide [Appendix I] was further informed by findings from our scoping review which sought to describe literature surrounding the conduct of cRCTs in hospitals within CFIR domains and constructs. The interview questions consisted of identifying sections (for example, role in team, interactions within the team), and CFIR driven questions, organized by CFIR domain and construct within the domain.

Observations were made in weekly team meetings geared towards updating all members on the progress and challenges encountered. These meetings were held both face-to-face or via teleconference dependent on member availability and included the research coordinators and principle investigator. Minutes from meetings were analyzed as well as field notes collected during the meetings. The researcher remained a mostly passive observer in these meetings and did not actively participate in the discussion. The observations did not lead to data results which contributed to the research question of this paper, and therefore this data was not further reported.

Data Analysis

Interviews were recorded and transcribed verbatim. Interviews were read first without coding to gain familiarity with the content. Interview transcripts were explored using directed content analysis[17] and guided by a coding manual developed based on CFIR. CFIR was selected as the coding framework due to its versatility in evaluating and guiding the implementation of interventions, as well as its use in barrier and enabler investigation[10]. It was used to identify perceived factors associated with the launch of BEACON. These factors may have been perceived as barriers, facilitators, or general descriptions of their perceptions.

All data were entered and coded in NVivo (version 12.4.0). Data was coded based on relevance to the definitions for the domains provided by the CFIR framework. Data was permitted to be coded into multiple codes if it was deemed as fitting the description for more than one domain. Two independent researchers (AW, KC) coded all transcripts, and discussions were held to come to a consensus for final coding on any discrepancies. Following coding, the data was organized by CFIR constructs. Guided by this framework, the domains and constructs most frequently coded from the transcripts were identified as being relevant to understanding the launch of the BEACON cRCT. Samples of the coding process are included in Table 3.1.

Table 3.1 - Examples of extracted codes, domains, and constructs in the case study

Domain	**Construct**	**Code**	**Quote sample**
Inner Settings	Culture	Fits in values	"…but value-wise, I think it will fit in quite well with what these hospitals try to offer."
Intervention Characteristics	Adaptability	Allow to adapt program to local context	"But being cognizant of the location of the hospital, that patients of the hospital are from outside communities are generally flown in so that the intervention would have to be adapted for that site in particular"
Process	Engaging (Formally Appointed Internal Implementation Leaders)	Higher up the chain, the longer it takes	"…the further up the chain we have to go, the more parties need to be involved and the slower the submission process tends to have

			been”

Reflexivity and evaluative rigour

The primary researcher is a PhD candidate under the primary investigator of BEACON. She is not involved directly in the launch and implementation of BEACON and did not provide any input for design or recruitment. This position in the research teams allows for rich access to information and direct observations of the case, with integration unlikely to cause any changes in behaviour to the research teams as can be the case if an outsider were to conduct the study. The second coder was a newly assigned student to the lab with no involvement in BEACON and limited knowledge of the trial. To ensure that prior knowledge and beliefs about the participants did not cloud and bias the perception of meanings of statements in the transcripts, this coder was blinded to the identities of the participants in the transcripts, and all names and identifiers were removed before coding.

The Standards for Reporting Qualitative Research (SRQR)[18] was used to guide the reporting of findings [Appendix J].

Results

A total of seven individuals were selected and invited for participation, and all agreed to be interviewed over the period of January 2019 to May 2019. One individual (a patient investigator) did not reply to follow up emails to schedule a time and was therefore not included in the final sample. The participants included two principal investigators (one being the lead author’s supervisor), two research coordinators, one research manager, and one patient co-investigator (a patient with lived experience with the disease). The research coordinators, research manager, and one principal investigator work together in an academic hospital office, while the other principal investigator and patient researchers are remote and call in for team meetings. The research of the group focuses on clinical trials for mental health disorders in under-served populations and includes the use of technologies, service delivery, and non-pharmacological interventions. All members were directly involved in the conception of the BEACON study and continued to be actively involved at the time of the interviews. Brief summaries of their roles according to descriptions provided by participants about their tasks regarding the BEACON trial are listed in Table 3.2. Further participant demographics are not reported due to the small sample size allowing for the potential for identification of individuals. Interview time totalled 180m, 50s, with interviews ranging from 18m48s to 50m51s.

Table 3.2 - Roles of participants in the case study in relation to BEACON cRCT

Participant	Role

Principal Investigator 1	- Take responsibility for trial throughout the stages - Provide leadership (everything from securing finance and approval from regulatory authorities to enrolling participants) - Write protocols, make relationships, sell the study and ensure consistency of vision - Provide clinical oversight and safety
Principal Investigator 2	- Meet with various key members and organizations - Contribute to protocols (reading, writing, editing for everything from methodology and outcomes to challenges) - Help organize the study team - Coordinate for meetings with other principal investigator and staff
Research Coordinator 1	- Oversee the sites - Ensure site operations (set up standard operating procedures, oversee the protocol, submit ethics forms, organize contracts and finances)
Research Coordinator 2	- Coordinate the sites to keep them up and running - Identify key personnel at each site, connect with them to assess interest in the study, work with to get the trial running - Provide administrative support - Submit research ethics and contracts
Research Manager	- Provide managerial support - Supervise other staff members - Sit on publications committees and other committees - Provide oversight of study and additional insight on working with sites in a trial - Budget study finances and contracts
Patient Investigator	- Provide general input in terms of study design and patient perspectives - Act as a mental health and health promotion advocate - Communicate insights during meetings - Edit study protocol

The study investigated the perception of the initiation of the BEACON cRCT from the perspective of the coordinating team and to determine whether themes were apparent in relation to factors of the implementation, guided by the CFIR. All data collection was performed during the pre-launch phase of the trial, whereby participants were not being enrolled in BEACON. The results section is organized by the five domains in the following order: ***intervention characteristics***, ***outer settings***, ***inner settings***, ***process,*** and ***characteristics of individuals***. The most frequently coded constructs within the domains are reported. Table 3.3 details the individual codes within each domain.

Table 3.3 - Frequency of codes in the case study by domains of CFIR

Construct		Description of Theme	Number of individuals (of 6)	Frequency of code
I. INTERVENTION CHARACTERISTICS				
A	Intervention Source	Grant funded project	1	1

		Initial suspicion from hospitals of outside source	1	1
		Study team devised protocol	4	11
B	Evidence Strength & Quality	Front line users may want evidence	1	2
		Little evidence needed by sites	3	3
		Pilot project presented - uncertain if influenced	3	3
C	Relative Advantage	Need to show there's an advantage over current programs	2	3
		Nothing similar currently	6	7
		Similar program but issues	2	2
		Similar program in the works so no perceived benefit of this	1	1
		Will fill a gap over current clinical care	4	11
D	Adaptability	Adaptations possible with site collaboration	3	5
		Adaptations done at discretion of PI	2	2
		Allow to adapt program to local context	5	10
		Allow to tailor study population	3	2
		Need allow continuous adaptability	3	5
		Must ensure similarity in core safety concepts	1	1
E	Trialability	-	0	0
F	Complexity	-	0	0
G	Design Quality & Packaging	-	0	0
H	Cost	-	0	0
II. OUTER SETTING				
A	Patient Needs & Resources	Need to consider the patients' needs	6	10
		Need for any program in gap for these patients	1	1
		Patient inclusion on study team helpful	5	7
B	Cosmopolitanism	-	-	-
C	Peer Pressure	-	-	-
D	External Policy & Incentives	Financial compensation provided for sites	2	2
		No financial gain for coordinating team	1	1
		No financial gain for anyone, just interest	3	3
III. INNER SETTING				
A	Structural Characteristics	Similarity between sites ensured through protocol	1	2
		Structure will affect, large site variability	4	6
B	Networks & Communications	-	0	0
C	Culture	Cultural differences between sites	2	2
		Fits in values of the sites	3	3
D	Implementation Climate	-	-	-
1	Tension for Change	Need for any program	4	8
		These patients aren't a priority	1	1
2	Compatibility	Make fit with current practice	3	3
		Need time to adjust to changes	1	2
		Unsure how will fit with current practice	2	4
3	Relative Priority	Competing priorities that may not allow time	3	6
		Too much going on to be a priority	1	1

4	Organizational Incentives & Rewards	Putting money into system	1	1
5	Goals and Feedback	Informal feedback received helpful	3	3
		Would like more feedback	2	3
6	Learning Climate	Academic learning centre supportive	1	1
		Some sites not set up for learning (eg. smaller sites)	1	1
E	Readiness for Implementation	-	-	-
1	Leadership Engagement	Turnover in staff - adjust and reengage new people	2	4
		Differential engagement across sites	4	6
		Perceived engagement from leaders	7	7
		Unable to engage leaders	2	2
2	Available Resources	Competition for limited resources	5	8
		Leaders concerned for their hospitals' resources	1	1
		Sufficient resources at coordinating site	3	3
		Sufficient resources at hospital sites	4	5
		Will add resources as needed	1	1
3	Access to Knowledge & Information	Need to ensure adequate training or support	4	5
		People are accessible for questions	5	6
		Hard to access people for questions	1	3
IV. CHARACTERISTICS OF INDIVIDUALS				
A	Knowledge & Beliefs about the Intervention	Little experience with research	3	4
		Perceived enthusiasm	3	6
		Uncertainty about the project	3	8
B	Self-efficacy	-	0	0
C	Individual Stage of Change	-	0	0
D	Individual Identification with Organization	-	0	0
E	Other Personal Attributes	-	0	0
V. PROCESS				
A	Planning	Multi-disciplinary team was involved in planning process	1	1
B	Engaging	-	-	-
1	Opinion Leaders	Lack of approaching specific key groups	1	1
		Need to get key people on board so no barrier	6	11
		Some key members are already overwhelmed	2	2
2	Formally Appointed Internal Implementation Leaders	Higher up the chain of command, longer it takes to access	1	1
		Formal leaders already identified at each site	2	3
		Need to ensure include people with experience and pull in the organization	4	7
		Keep their engagement and stick with it attitude throughout	4	10
		Make sure people feel like part of the study	2	2

3	Champions	Champions driving the success of the trial	1	2
		Champions will be further identified throughout the trial	1	2
		Engaged those with experience and methodology expertise	2	3
4	External Change Agents	All necessary people are currently on board	2	2
C	Executing	Progress tracked by if enrolling patients	1	1
D	Reflecting & Evaluating	-	-	-

Note: Codes are organized by constructs or sub-construct within each domain. The number of individuals refers to how many participants from which the topic was coded. Frequency refers to how many times the topic was coded across all transcripts.

Intervention Characteristics:

The domain of ***intervention characteristics*** was frequently mentioned by participants as having a perceived influence on the launch of the trial. This domain was represented by multiple constructs.

The *adaptability* ("The degree to which an intervention can be adapted, tailored, refined, or reinvented to meet local needs."[19]) of the study for each site was emphasized by all participants, and this was thought to be a strength of the study. Each site was thought to have its unique infrastructure and organizational makeup, and the coordinating staff believed that there was enough flexibility in the design of the project to be able to allow the project to fit in with the current practice. This included changes that could be made at the level of administrations (whether that be in budgetary management), staffing (combining roles), and/or study populations:

"*So, we want to implement an intervention that can be easily implemented into the current clinical pathways and that's also why it's taking so long to launch because we want to take into account the unique kind of circumstances at each site."* - research coordinator 2

Additionally, the ability to tailor the program to the study population and allow continuous adaptations as the study unfolded was mentioned throughout the interviews. One site was noted by multiple participants as requiring more adaptations than others due to the unique population serviced in the hospital. It was noted by participants that although adaptations were allowable and ideal to be able to suit the needs of the sites, there was a need to ensure that the core safety principles remained the same throughout the sites. There was the recognition that a level of comparability must remain between sites for cross-site analyses and to be able to generalize results:

"*Yeah, I do think there has been enough flexibility and I do think the core components around patient safety and patient privacy are similar enough across sites that we haven't had to change really had to change any drastic aspects of the protocol for that reason."* - research coordinator 1

There was also mention of who would be able to approve the adaptations. While all adaptations were left to the PI for final approval, they were developed in collaboration with the coordinating site and the hospitals to produce changes that would be acceptable and beneficial to each site individually.

Prior *evidence strength and quality* ("Stakeholders' perceptions of the quality and validity of evidence supporting the belief that the intervention will have desired outcomes."[19]) from previous studies was not noted as being of great importance to the hospitals in their decision as to whether to accept participation in the trial. While the results of the pilot study were presented, it was unclear whether this was necessary to have the sites join, and the coordinating site team did not see a large need to emphasize these results to the sites. It was viewed as predominantly unnecessary in the process, as hospitals were often concerned with filling a practice gap, regardless of whether it was currently evidence-based:

"*No for the most part, for the hospitals, I mean this sounds a bit jaded, but evidence is not really something they're concerned about to be quite honest."* - principal investigator 2

Furthermore, as mentioned by one of the participants, the sites may have been less concerned with ensuring there is supporting evidence for the trial's success due to the perceived need to fill a clinical gap (as previously stated), and that any potential to fill this gap would be accepted to ease the tension:

"*Not a lot to be honest [in response to evidence requirements]. I mean we did a pilot study once we got the money, which has been useful in selling it to the different sites, but what I think sold it to the different sites was that people see this as a problem."* - principal investigator 1

There was however some expression of a need to demonstrate whether the trial had been piloted to those who may be directly involved in administering the project, such as the physicians in the emergency department:

"And speaking just a week ago about the physicians in our emergency department, and researchers committee in our emergency department, they wanted to know, has it been piloted? And part to know because these are physicians on the front line, who wanted to know is someone going to be sitting there? Who's going to be recruiting?" - principal investigator 2

This perception of a need to demonstrate there was a *relative advantage* ("Stakeholders' perception of the advantage of implementing the intervention versus an alternative solution."[19]) to participating in this study was discussed by all participants. There was the perception that the program in BEACON was superior to current clinical care, and that no current similar programs existed:

"We just don't have good public health surveillance system for self-harm, self-injury, suicide attempts in Ontario… So we know that that's one huge challenge to delivering good mental health care, to getting people quickly connected up with service providers and services that can help improve their lives and help save their lives and that being able to offer essentially a new program through an emergency department, it can help actually create cost savings, time savings in the system." - principal investigator 2

Additionally, the need to demonstrate that there would be an advantage in BEACON for continued use was stated. There was uncertainly noted as to whether the program would be successful in filling the existing care gap:

"I was just saying that that's where I see potentially it filling that gap. Of course, we wouldn't know for certain until the study has been completed and we're looking at the results." - research manager

Outer settings:

The perception of the influence of the domain ***Outer Settings*** on the launch of the trial was represented by two constructs.

Firstly, *patient needs, and resources* ("The extent to which patient needs, as well as barriers and facilitators to meet those needs, are accurately known and prioritized by the organization."[19]) were perceived as a crucial aspect of this trial. As the primary funder of BEACON came from an agency representing patient-oriented research, there was a drive for patient inclusion on the relevant committees. Patient investigators sat on various committees of the study to be able to inform, critique, and assess feasibility and acceptability by the intended end-users of the intervention (patients). One participant suggested that increasing patient involvement by having patient committee members at each site may be beneficial to encourage engagement and trial participation:

"*One thing that I don't know necessarily that we've done, I'm just thinking about this now, is to engage either patient liaison officers, or quite frankly, consumers of the mental health systems within each of the cities, within each of the sites for obvious reasons it can be hard to do. There are people who are on the steering committee who have been involved in the project from the start with lived experience who are helping to develop, revising, giving feedback on the protocol at various steps throughout the way*." – principal investigator 2

Additionally, there was mention of ensuring that the program would be viewed as acceptable to the patients and that it would meet their needs in providing care to the target population.

"So that was really, really valuable and then we did also somewhat talk about the BEACON study with our service users and caregivers research interest group in suicide prevention, although we had predominantly women on that committee, we did have men who would come in and out. We really tried to get both perspectives, but particularly the male perspective and from the people with lived experience too and who they would access it, how they would find it, and just really if you're looking at the acceptability, the feasibility elements as well." – research manager

The *external policies and incentives* ("A broad construct that includes external strategies to spread interventions, including policy and regulations (governmental or other central entity), external mandates, recommendations and guidelines, pay-for-performance, collaboratives, and public or benchmark reporting."[19]) did not appear to be perceived as influential for the sites to participate in the trial. Financial incentives were not offered for the sites participating in the trial. It was perceived that the participation from the sites in the trial was more from an interest in the study than monetary gains:

"Yeah so there has been money available, but I don't think it was in any way that would have actually been a financial incentive. There has really not been any way for sites to make money off of participating in the trial. So I think it's genuinely been an interest for patient good rather than for any financial incentive." – research coordinator 1

Inner Settings:

The domain of ***inner settings*** was represented by several constructs.

The current *culture* (" Norms, values, and basic assumptions of a given organization."[19]) was mentioned by multiple participants, and there was the recognition that each site may have unique values and priorities. It was perceived as important to understand and work with the culture of the hospitals, and to ensure that the BEACON project aligned with the values in each region. Furthermore, one site was stated to be more of a unique outlier than the other sites due to its northern location and it primarily servicing an indigenous population. There was also an apparent understanding of the differences between the sites that would be encountered:

"*I think the biggest challenge for integrating it into hospitals will be the lack of manpower to actually deliver the face to face therapy, but value-wise, I think it will fit in quite well with what these hospitals try to offer*." – research coordinator 1

The *implementation climate* ("The absorptive capacity for change, shared receptivity of involved individuals to an intervention, and the extent to which use of that intervention will be rewarded, supported, and expected within their organization."[19]) was frequently coded from transcripts, and it was represented by several of its subcategories. The *compatibility* ("The degree of tangible fit between meaning and values attached to the intervention by involved individuals, how those align with individuals' norms, values, and perceived risks and needs, and how the intervention fits with existing workflows and systems."[19]) of BEACON, whereby the study launch would be facilitated by fitting well into current practice was noted. There was some hesitation on how the program would fit however, with some sites declining participation due to the inability to fit the program in with usual care and programs.

"There's been 2 or 3 sites where they haven't been supportive, where they think that they're very different and wouldn't fit in and have got existing work underway." – principal investigator 1

The *relative priorities* ("Individuals' shared perception of the importance of the implementation within the organization."[19]) of the sites' agendas were noted as a potential barrier for the trial if the sites did not prioritize mental health or research. It was also mentioned that priorities may change over time, and although the trial may be deemed as necessary at the current moment, this could change over time:

"*But that, you know I think priorities within hospitals sometimes change and that's a change almost from day to day, but certainly from year to year, and I think that's one of the huge challenges to implementing studies like this, where you do require a certain degree of buy-in and a certain amount of consistency or agreement to stick with it."* – research coordinator 2

Furthermore, the *tension for change* ("The degree to which stakeholders perceive the current situation as intolerable or needing change."[19]) and lack of current programs in place to service

the intended study population was seen as an enabler to hospital engagement. The coordinating staff discussed the absence of a specific program targeted at improving the outcomes for men who present with self-harm. Usual care and discharge may not be enough to help these people, and any study or program aimed at these people may be viewed as a positive change. The participants noted that there were no current programs similar to BEACON's intervention, and therefore it was possible the hospitals may have been more likely to accept inclusion into the trial as they perceive this as an area that needs improvement, and they prioritized an agenda addressing this gap. It was however noted that this tension to bring in a program must be undertaken cautiously, however, if the sites were to accept any study to attempt to fill the gap, regardless of evidence supporting the decision:

"…they do kind of have that on their back, where they're blaming you for what's happening and you're just trying to find a way so people aren't hounding you as much necessarily. They'll just pretty much do anything, without trying to think critically, they're just trying to get rid of the issue." – patient investigator

The sites' *readiness for implementation* ("Tangible and immediate indicators of organizational commitment to its decision to implement an intervention."[19]) was also frequently mentioned by participants. A site's perceived state of preparation for the trial was represented by two of the construct's subdomains. *Available resources* ("The level of resources dedicated for implementation and on-going operations, including money, training, education, physical space, and time."[19]) were viewed as having a major impact on the trial, primarily at the level of the local sites. It was noted that these resources were not solely financial resources, but time and personnel as well. The participants expressed the need to ensure that resources were available both to the coordinating centre and to the individual sites and that resources remained available throughout the study, despite the time length of the trial. There was a general perception from the participants that there would be enough financial and time resources provided and available for the trial to be conducted at the sites. The availability of resources was however perceived as a potential barrier to the initial agreement for participation of the sites if the leaders deemed that it would burden their hospitals, and they wished to guard what was already limitedly available (for example, time and money). The perceived lack of resources by the sites was thought to be the reason they declined to participate, as well as it being a concern from leaders in the hospitals:

"The biggest concern is always that their staff are already stretched pretty thin and they don't want this to be an additional burden on their staff. Financial concerns are always there as well. Leaders don't want this study to actually cost their site any money." – research coordinator 1

Leadership engagement ("Commitment, involvement, and accountability of leaders and managers with the implementation."[19]) was noted as variable across the sites. Some hospital leaders showing little interest in the details of the trial, while others were wanting to be more directly involved. Other sites had leaders that were strongly committed to the trial, while some others appeared to be less enthusiastic. In addition, some concerns were expressed by the coordinating site members regarding the challenges that had been encountered where there was a change in the leadership at the sites that necessitated a new engagement during the turnover:

"So, the director I spoke to maybe a month ago who's happy to support this is […leaving...] *and there's going to be someone else and this is probably about the sixth director since we started this study. So, I think those are some of the challenges."* - principal investigator 2

The sites' unique *structural characteristics* ("The social architecture, age, maturity, and size of an organization."[19]) were also recognized by the participants. There was the recognition that the study may need to be tailored to the sites. However, the variation in the structure of the hospitals was limited by the inclusion criteria for the study, to be able to allow comparability across the sites. Regardless, some sites were seen to be less able to conduct research projects such as the BEACON trial.

"I'm concerned that smaller hospitals, for instance, non-academic hospitals who might not have crisis management staff or support institutionally that they may have issues implementing this into correct pathways." – research coordinator 2

Process:

At the time of the interviews, most of the ***process*** of the trials were still primarily under the authority of the coordinating staff, however, there was some input and collaboration with the sites to tailor the intervention.

Engagement ("Attracting and involving appropriate individuals in the implementation and use of the intervention through a combined strategy of social marketing, education, role modeling, training, and other similar activities."[19]) of the sites and the relevant individuals within the hospitals in the process was stated as being crucial for the process. It was perceived as important to ensure that individuals at the sites with potential influence on trial conduct were on-board and enthusiastic about the project while maintaining their enthusiasm throughout the process. The coordinating site members all stated the importance of engaging members of the sites, whether that be *internal implementation leaders*, *opinion leaders*, *champions*, and *external change agents*. The site leaders had been involved throughout the launch of the study, and attempts had been made to keep them informed and up to date on trial progress. A key concern was the several-year process of launching the trial presenting a challenge to the continued engagement. Additionally, there was some uncertainty of who was best within the sites to engage, whether that be formal leaders or those with interest. It was noted that those with both influence and appropriate skills were crucial in addressing. Furthermore, the more people that needed to be engaged, and the more senior involvement was required, the more delay there could be:

"Yeah so certainly the further up the chain we have to go, the more parties need to be involved and the slower the submission process tends to have been." – research coordinator 1

There was also the recognition that if the program were to become more widespread, additional hospital personnel would need to be engaged:

"If we were moving to implement this, kind of as a program, we would need to involve more hospital staff, more hospital administration leadership, but right now because it's kind of targeted in ED in each site, we have not had to involve them to date. As well as if it was going to be funded, we would need to involve others." – research coordinator 2

Characteristics of the individual:

The only construct coded in the domain of ***characteristic of the individuals*** was *knowledge and beliefs about the intervention* ("Individuals' attitudes toward and value placed on the intervention as well as familiarity with facts, truths, and principles related to the intervention."[19]). The coordinating staff spoke of their perceptions of the project, and while mostly enthusiasm and positivity about the benefit of the trial were expressed, some hesitation and concern were noted about the feasibility:

"Um, I mean both. I'm really excited about it. I think it's a good intervention, however, I worry about how long it has taken to launch, I worry about the extent to which people in crisis will be able to use it. I mean that's the point of doing this study. But I worry." – research coordinator 2

Some participants spoke as well about the apparent perception from sites that this would be a worthwhile trial, however, some skepticism about the enthusiasm from the sites was mentioned. There was also concern expressed surrounding the knowledge of the hospitals in undergoing large research projects, with some having little experience:

"And a lot of them talk about doing research. Very few of them actually do clinical trials, especially in psychiatry. There's very few people in Canada who are actually doing clinical trials." – principal investigator 1

Discussion

The purpose of this study was to explore the perceptions of the coordinating site staff about the launch phase of the BEACON cRCT, whereby the sites themselves were being recruited. As this phase of the trial involved the conduct and implementation of the project into hospitals, the interviews were guided by the CFIR, an implementation framework. The responses were tabulated using a codebook designed using the CFIR to enable analysis and comparison of results with the literature identified in the scoping review.

This current qualitative study identified CFIR domains and constructs similar to those from the scoping review as potentially influential for cRCT conduct, including the emphasis on the *adaptability* of trial, the importance of *tension for change* in accepting inclusion in the trial, the *availability of resources* and the *engagement* of leaders. The interviews reported in this paper further explored the domains and constructs that were not reported in the scoping review, such as ***characteristics of the individuals*** and *evidence strength and quality*. Their responses built upon what was uncovered in our scoping review. The scoping review had identified several relevant constructs and domains of the CFIR to be useful in better understanding the barriers and enablers involved in conducting cRCTs in hospitals. The key findings of the review were: the *adaptability* of the trial to each site and perception of a *relative advantage* of the trial over current practice were deemed important to conduct cRCTs in hospitals; the *policies and priorities* of the sites and government were potentially influential on cRCT implementation, and the *tension for change* within the hospital sites was identified as being important to the *engagement* of the sites to participate in the cRCT.

Furthermore, the scoping review also highlighted a reporting gap surrounding the implementation of the cRCTs, indicating a need for further evaluation and standardization in

reporting, as well as a need to explore whether the gap was due to primarily to a lack of reporting, or a true representation of limited perceived importance of other domains. This current qualitative study expanded upon this gap by exploring how the process is perceived from the coordinating staff and what factors are thought to be important in trial conduct. The following sections discuss the findings of this study in more detail organized within the framework of the CFIR constructs identified.

Intervention characteristics:

Adaptability was mentioned by all participants as being an enabler to engaging the sites. All participants emphasized that the trial's ability to be tailored to the sites was advantageous in getting the sites recruited to the study. Perceived lack of flexibility has been shown to be a barrier to hospitals participating in cRCTs[20], and therefore the ability to tailor the trial to the hospitals may have led to increased acceptance of inclusion into the trial by the sites. The findings from this qualitative study are in line with findings from previous literature, whereby trial adaptability and flexibility to tailor the program for a site's unique aspects were deemed as facilitators to initiating trials in hospitals[7,20–26].

Furthermore, previous literature investigating implementation strategies and hospital recruitment into pragmatic cRCTs have emphasized the importance of demonstrating the *relative advantage* of the study[24,27,28]. This was corroborated by statements from the coordinating site members, whereby they expressed the importance of the sites perceiving that the BEACON trial would be advantageous over current programs and practice. Not perceiving an advantage to participating in a clinical trial has been stated by hospitals as a reason for non-participation[27]. Responses in this study supported that the perceived advantage of the BEACON intervention was seen as a potential facilitator to engagement if the sites viewed there was a benefit over current programs or regular clinical practice.

Consistent with the limited identification of *evidence strength and quality* in the scoping review, the coordinating staff participants stated that they did not feel that previous evidence from a pilot trial had much influence on engaging the sites. As the scoping review identified literature that had limited focus on the conduct of cRCTs (most literature focused on the efficacy results from the intervention of the trial), it was difficult to determine whether this construct was not reported, or truly not viewed as necessary for conducting the trial. Results from this qualitative study indicate that the latter may be true, as perceptions from the coordinating study staff indicated that the sites did not place much importance on the evidence. This has relevant implications for how a trial may be pitched to a site, when evidence may be perceived as of higher importance to the trial team.

Outer settings:

The importance perceived by the coordinating staff of *patient needs and resources* in the development of BEACON, whereby they emphasize the positive influence of involving patients in designing the study, contrasts with the scoping review. The scoping review did not identify literature in which the benefit of addressing patient needs was mentioned. This lack of identification of this construct may be due to an absence of reporting it in the literature. The BEACON study received funding from an organization focusing on patient-oriented research, potentially influencing the emphasis and discussions of the construct[29].

Inner settings:

An organization's *culture* that prioritizes and values research may be more likely to engage in a trial than one in which there is less priority for research[26]. Previous literature investigating an organizational culture's effect on evidence-based practice for mental health interventions stressed the importance of assessing the organization's current values as this is correlated with success in implementation[30]. Agendas that do not align between a study and the intended sites can present a barrier to participation[27,31]. The interview participants in this study expressed their belief that the sites felt a necessity for change to fill the service gap to the intended population of the BEACON trial, and that this may have been beneficial to hospital engagement. Additionally, engagement may have been facilitated by the study being compatible with the current site structure, as fewer changes to practice are associated with a more successful implementation[32,33].

The responses of the participants about the *availability of resources* focused mostly on the resources for the sites, and not for the coordinating team. The participants did however mention that they perceived that there were enough resources available for both the coordinating site and the hospital sites to run the BEACON cRCT. The coordinating staff mentioned a need to ensure sufficient resources to keep the sites engaged throughout the trial. This is in accordance with literature concluding that limited resources of time, personnel, finances, and information are a barrier to participation by sites in cRCTs[27,31,34,35].

Additionally, the *leadership engagement* across the sites was perceived as variable, with participants stating that they were seeing different degrees of engagement from the leaders across the sites. While limited literature has investigated whether the turnover of leaders affects site engagement and local trial implementation, change in leadership personnel has been stated as a barrier to implementing change in healthcare[36].

Process:

The ***process*** of implementation was still in the pre-launch phase of the study at the time of the interviews and was primarily controlled by the coordinating staff, however, the *engagement* of the sites and the individuals within the hospitals were frequently mentioned. All participants mentioned the importance of communicating and engaging people at the sites throughout the setup of the trial. The early engagement of the sites has been seen as a strength in studies for successful implementation[31,37,38], partially due to the ability to identify challenges within the organizations early in the process to be able to determine strategies to overcome them in advance[26,39]. The early involvement of sites in the BEACON trial was however a concern noted by interview participants, whereby such early engagement, coupled with a long pre-launch phase may have led to a decline in the initial enthusiasm and engagement.

Characteristics of individuals:

Participants spoke about their personal *knowledge and beliefs about the intervention*, as well as about the impressions they were getting by the sites about the study. The participants mentioned they were not clear if the enthusiasm for the trial by the sites truly represented their beliefs about the study, or whether the sites expressed this positivity only when the coordinating staff was present. There is limited previous evidence surrounding the influence of the coordinating site's

beliefs about a trial, and it is difficult to determine how and to what extend their positivity has influenced site engagement and implementation progress. While limited empirical evidence about how the staff affects the trial conduct exists, recommendations have been made that it should be ensured that the coordinating site team should be engaged in the research[2–4].

Implications for future cRCTs

The experiences of the coordinating staff for BEACON analyzed in this study using the CFIR framework could be informative in facilitating the launch of future cRCTs. Site recruitment and engagement strategies can be developed or tailored from the results drawn from this study.

The *adaptability* of a trial was perceived as an enabler to engaging the sites, and future trials should ensure that the intervention can be tailored to each site, while still maintaining validity and comparability of the effectiveness of the intervention between sites. Furthermore, assessing the *tension for change* in a clinical gap of a potential site and demonstrating to the sites that there is a *relative advantage* of the trial over current care may be important to engage the sites. *Engagement* with the sites should be initiated early in the design of the trial, and efforts should be made to identify key personnel (including *internal implementation leaders*, *opinion leaders*, *champions*, and *external change agents*).

Limitations

This study intended to explore perceptions of coordinating staff for the BEACON cRCT about the launch of the trial. Limitations associated with a single case sample with a small sample size must be recognized. The case of investigation in this study was of one coordinating site only, and the experiences and perceptions uncovered may not be generalizable to other coordinating sites. The BEACON trial has encountered more challenges and time delays in enrolling hospitals and launching the trial than expected, and therefore the coordinating staff may have bad opinions that reflected potential frustrations with the conduct of the trial. Additionally, as the coordinating site was composed of a small number of people who work in close relation to each other, there may have been an overlap in their perceptions. A further stage of this study aimed to conduct similar interviews for members of the trial sites, however, there were limited replies from the site members who were willing to participate in the interview, which made the study not feasible to continue. Gaining an understanding of what the sites perceive as barriers and enablers to the trial would allow for unique insight that could benefit the design of targeted strategies for trial conduct. Future studies of other coordinating sites would help determine if the results of this study are generalizable to other cRCTs in hospitals.

Furthermore, while participants were ensured confidentiality and anonymity, there is a possibility that that was some sense of hesitation in expressing frustrations or perceived negative feelings towards the study or about other team members. The identification of a relatively small number of constructs may be due to the interview design, whereby certain constructs may have been more directly explored by the questions.

Conclusion and Lessons Learned

To the best of our knowledge, this is the first study conducted to gather and analyze the perceptions of the coordinating staff of a cRCT to investigate their perspectives as to what is

influencing the launch of the trial at the sites. Staff should be aware and knowledgeable about the length of time required to launch these trials, to be able to prepare and plan accordingly, and ensure adequate resources. Certain key features of a cRCT should be planned for while designing the trial, and the manifestation of these features will differ in the sites. As this study investigated perceptions, without evaluating the influence on trial conduct of differences in the investigated features, studies may be necessary to test various strategies to determine their effects on-site engagement and trial launch. Additionally, coordinating staff of other cRCTs should also be interviewed to determine whether the results of this case study of a single coordinating site are generalizable.

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Chapter 4 - Strategies for facilitating the delivery of cluster randomized controlled trials in hospitals – a study informed by the CFIR-ERIC matching tool

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Abstract

Background: Recruitment and engagement of clusters in a cluster randomized controlled trial (cRCT) can sometimes prove challenging. Identification of successful or unsuccessful strategies can be beneficial in guiding future researchers in conducting their cRCT. This study aimed to identify strategies that could be used to facilitate the delivery of cRCTs in hospitals.

Methods: The study employed the Consolidated Framework for Implementation Research (CFIR) - Expert Recommendations for Implementing Change (ERIC) matching tool. The barriers and enablers to cRCT conduct identified in our previously conducted studies served as a means of determinant identification for the conduct of cRCTs. These determinants were mapped to CFIR constructs and then matched to ERIC compilation strategies using the CFIR-ERIC matching tool.

Results: The ERIC strategies matched to at least one determinant CFIR construct were: 1) Identify and prepare champions, 2) Conduct local needs assessment, 3) Conduct educational meetings, 4) Inform local opinion leaders, 5) Build a coalition, 6) Promote adaptability, 7) Develop a formal implementation blueprint, 8) Involve patients/consumers and family members, 9) Obtain and use patients/consumers and family feedback, 10) Develop educational materials, 11) Promote network weaving, 12) Distribute educational materials, 13) Access new funding, and 14) Develop academic partnerships.

Conclusions: This study was intended as a step in the research agenda aimed at facilitating cRCT delivery in hospitals and can act as a resource for future researchers when planning their cRCT, with the expectation that the strategies identified here will be tailored to each context.

Keywords

cluster randomized control trial; consolidated framework for implementation research; hospitals; implementation; CFIR-ERIC matching; Expert Recommendations for Implementing Change

Introduction

Cluster randomized controlled trials (cRCTs) offer advantages over non-cluster randomized controlled trials (RCTs)[1], however, they also present logistical challenges[2]. cRCTs tend to be more complex and involve more personnel than what would be required for a single-site RCT. Challenges in the delivery of trials can arise before patient recruitment and/or intervention launch[3,4]. Recruitment and continued engagement of the clusters as a whole can prove difficult, with poor response and participation from the intended sites often encountered by researchers attempting to run a cRCT[5]. Furthermore, variability between sites in the delivery fidelity of an intervention can make it difficult to assess the effectiveness of an intervention[6].

In part due to the randomization of entire clusters rather than individuals, the loss of individual sites and/or an inability to recruit the required sample size (whether by a site refusing to participate in the study or dropping out of the study for any reason after randomization) can prove more detrimental to adequately powering the trial than the loss of power that would be experienced when losing a non-cluster randomized site (including multi-site, individual randomization trials)[7]. There tend to be a smaller number of sites in a cRCT than there would be individuals in a non-clustered RCT. The inability to recruit an adequate number of sites or the loss of a site post randomized can pose threats to the statistical analysis, especially related to powering the study for comparisons between trial arms. This can, therefore, pose large threats to the conduct of the trial and the interpretation of the trial results[2,7].

To guide researchers planning trials, recent literature has emphasized the need to consider more empirical and generalizable research into the conduct of trials themselves[8]. The conduct of cRCTs is often relegated to the internal expertise of a trial team rather than from results reported on as part of trials, making these processes effectively a 'black box'[3]. While the identification of barriers to implementation and development of strategies to facilitate the delivery of trials is prioritized in implementation science research[9–12], there remains a lack of knowledge linking theory-informed barriers and enablers to implementation strategies best suited to address them. To select and operationalize intervention strategies, methods of intervention strategy mapping can be used[13], which aims to systematically develop strategies for interventions (most frequently used for health promotion interventions) through a combination of theory and evidence from the literature.

Previous studies by our group, which consisted of a scoping review[14] and a qualitative case study[15], demonstrated a reporting gap in methodology for delivering cRCTs in hospitals. The scoping review aimed to investigate the barriers and enablers to conducting cRCTs in hospitals. This review identified several barriers and enablers to delivering cRCTs reported in the literature, however, a reporting gap for the delivery of cRCTs in hospitals was also identified. The qualitative study consisted of semi-structured interviews of the coordinating site staff for an ongoing cRCT being conducted in Ontario hospitals. This study aimed to gain an in-depth understanding from a specific case of a cRCT[16], where there had been significant challenges in recruiting sites and launching the intervention in the hospitals. That study identified the coordinating site staffs' perceptions of potential barriers and enablers to launch of the cRCT.

Strategies to circumvent perceived barriers to cRCT conduct may be conceptually generalizable, and identification of successful or unsuccessful techniques as intervention strategies can be beneficial in guiding future researchers in conducting their cRCT. Barriers to conducting cRCTs

can have commonalities between studies, however, there is currently limited literature or guidelines to assist research teams in identifying and circumventing these challenges. Therefore, the objective of this study was to identify strategies that could be used to facilitate the delivery of cRCTs in hospitals.

Methods

This study was guided by the Consolidated Framework for Implementation Research (CFIR) - Expert Recommendations for Implementing Change (ERIC) matching tool[17] to identify strategies to address barriers and enablers to cRCT identified in our previously conducted scoping review[14] and a qualitative case study[15]. This tool and the methodological processes undertaken in this paper are described below.

CFIR-ERIC matching tool

CFIR is a determinant framework (defined as a theoretical framework designed to assess potential contextual determinants of implementation[17]) that organizes commonalities and overlapping themes from various theories and concepts of implementation science[17,18]. Using previously published research to provide a guide for effective implementation, the framework organizes 39 constructs into five domains (see Appendix A for detailed definitions and constructs within the domains): 1) *intervention characteristics* –design features of the trial, 2) *outer settings* –external political and network influences, 3) *inner settings* - inner political and organizational influences within the sites, 4) *process* –plans and procedures for implementation, and 5) *characteristics of individuals* –personal factors and experiences of the people involved in implementation and conduct. The CFIR can be used as a framework to guide the development and evaluation of an implementation strategy, as well as for the investigation of barriers and enablers to trial implementation[18]. Barriers and enablers to implementation can be evaluated within each of the five domains[19]. While CFIR can be used to assess potential determinants for implementation, it does not provide explicit implementation strategies for operationalized use[17,20].

The Expert Recommendations for Implementing Change (ERIC) compilation is a list of 73 discrete implementation strategies that can be used as building blocks to plan the implementation, and potentially address anticipated barriers[17,21] (see Appendix B for the strategies and their definitions). The development of the list involved conducting several rounds of a modified-Delphi process with a panel of stakeholders with implementation science and clinical practice to generate expert consensus on strategies and their definitions.

To allow for the capacity to build an implementation plan using the ERIC compilation strategies matched to specific determinants from CFIR, the CFIR-ERIC matching tool was developed [17,20]. This tool was developed by asking implementation science experts to rank the top seven ERIC strategies that, in their view, would address barriers categorized by each of the CFIR constructs[17]. Strategies that were endorsed by ≥ 50% of the experts were deemed as "Level 1" strategies, and strategies that were endorsed by 20-49.9% of the experts were deemed as "Level 2" strategies. Based on the results of this study, the CFIR-ERIC matching tool was created, and made available as an Excel download online at www.cfirguide.com[19]. This tool allows users to select whether the determinant was deemed as relevant to the implementation under question (yes/no) and generates an output table with the CFIR construct matched to the ERIC strategies

with a percentage. This percentage indicates what percent of the experts queried in the tool development endorsed the strategy for the construct.

Identification of determinants of cRCT delivery

Consistent with best practice recommended by several frameworks for intervention development[13,22,23], determinants of delivery of cRCTs in hospitals were first identified. Identification of these determinants consisted of an assessment of the barriers and enablers to delivery and conduct of cRCTs in hospitals from our previous studies in this research field. This assessment consisted of a scoping review[14] and a qualitative case study[15], which is consistent with numerous studies in intervention development that have used mixed methodology studies, including literature reviews, as a means of determinant identification[13,24–26]. The 'determinants' of cRCT delivery in hospitals were identified from the themes that emerged in the scoping review and qualitative case study. In these two previous studies, data that emerged were coded into the CFIR constructs they were determined to represent. This data, coded by the CFIR constructs, were identified as determinants of delivery of cRCTs in hospitals and were classified by whether they presented barriers or enablers to the delivery of the trials.

To select strategies to address the determinants identified from the scoping review and the qualitative case study, the CFIR – ERIC matching tool was used. The tool was used to generate an output that matched the CFIR constructs that had been identified as determinants of delivery of cRCTs in hospitals to ERIC compilation strategies. This matching was performed by one author (AW) with all the identified determinants, regardless of whether they were deemed as barriers or enablers for two reasons: 1) the determinants classified as enablers were generally framed in the way of methods that were used to overcome the perceived barriers; 2) the perceived benefit to providing implementation plans that not only addresses strategies to overcome barriers, but also provides strategies that would support the enablers. This paper focused on Level 1 strategies. Level 1 strategies are ERIC strategies that were endorsed by the highest percentage of the experts during development of the CFIR-ERIC matching tool (≥ 50% of the experts), and therefore, it can be reasoned that these strategies are most likely to be effective in addressing the corresponding CFIR domains (based on expert-consensus) compared to strategies that were not endorsed as Level 1 strategies.

Results

This study was conducted using the CFIR-ERIC matching tool to identify implementation strategies from the ERIC compilation that could be matched to CFIR constructs which had previously been identified as potential facilitators or enablers the delivery of cRCTs in hospitals. Throughout the rest of this paper, strategies from the ERIC compilation are <u>underlined</u>, and constructs from the CFIR are listed in *italics***.**

Our previously conducted scoping review[14] and a qualitative case study[15] informed this current study by allowing for the identification of determinants of cRCT delivery in hospitals. The determinants were identified from the CFIR coded results of the scoping review and the qualitative case study. These determinants are listed in Table 4.1, along with their classification as to whether they presented as barriers or enablers to delivering the trial.

Table 4.1 - Determinants of cRCT delivery identified from the scoping review and qualitative case study

CFIR			Determinant	
Domain	**Construct**	**Subconstruct**	**Barrier Details**	**Facilitator Details**
Intervention Characteristics	Intervention Source			Increased engagement from the hospitals if the trial was deemed to be at least partially internally sourced[5,27]
	Evidence Strength & Quality			
	Relative Advantage		Lack of perceiving that the intended trial would be advantageous over current practice and programs[5]	Demonstration of a relative advantage to participating in the trial[5,15,28,29]
	Adaptability		Perception of having little flexibility to allow for tailoring to the sites[30]	Adaptability of the trial being a facilitator for the hospitals' participation[8,15,29–35]
	Trialability			Ability to have an intervention that could be trialed try before full implementation to avoid wasting time, energy and other resources if it was not a good fit for that site[29]
	Complexity			
	Design Quality & Packaging			
	Cost			
Outer Settings	Patient Needs & Resources			Increase in patient involvement by having patient committee members at each site suggested as beneficial to encourage engagement and trial participation[15]
	Cosmopolitanism			Engagement of sites through pre-established collaborations and networks[5,36]
	Peer Pressure			
	External Policy & Incentives		Lack of alignment between the priorities and incentives of the health systems and the objectives of the trial[35]	
Inner Settings	Structural Characteristics			
	Networks & Communications			
	Culture			Organizational culture that prioritizes research and the specific research agenda of the trial[15,35]
	Implementation Climate	Tension for Change		Perceived need for change due to lack of current programs in place to service the intended study population[15]
		Compatibility	Inability to fit the program in with usual care and programs at the site[15]	

		Relative Priority	Lack of alignment between the agendas of the hospitals and the aims of the research trial[5,15,27]	Prioritization of a need for the intervention[27,37]
		Organizational Incentives & Rewards		
		Goals and Feedback		
		Learning Climate		
	Readiness for Implementation	Leadership Engagement	Lack of early organizational support was sought by some studies early in the planning stage of the cRCT[38]	Organizational support sought early in the planning stage[39,40]
		Available Resources	Limited availability of resources, including time, personnel, finances, and information[5,15,27,39,41] Shift of the availability of resources could also shift depending on the organization's current priorities (could either present a barrier or a facilitator)[27]	Shift of the availability of resources could also shift depending on the organization's current priorities (could either present a barrier or a facilitator)[27]
		Access to Knowledge & Information		Provision of detailed procedures and manuals for trial conduct[5]
Characteristics of Individuals	Knowledge & Beliefs about the Intervention		Potential limited knowledge and experience of the hospitals in undergoing large research projects[15]	
	Self-efficacy			
	Individual Stage of Change			
	Individual Identification with Organization			
	Other Personal Attributes			
Process	Planning			Considerable effort into planning in advance, to identify and overcome some of the expected barriers[35,42]
	Engaging	Opinion Leaders		Engagement of the opinion leaders, champions and implementation leaders from early in the trial[15,27,38,43]
		Formally Appointed Internal Implementation Leaders	Lack of support from the hospital or system decision makers[5]	Engagement of the opinion leaders, champions and implementation leaders from early in the trial[15,27,38,43]
		Champions		Engagement of the opinion leaders, champions and implementation leaders from early in the trial[15,27,34,38,43–46]

		External Change Agents		
	Executing			
	Reflecting & Evaluating			

In total, nineteen constructs from all five of the CFIR domains were identified as relevant determinants of cRCT delivery in hospitals in our previous work. Nine constructs, spanning all five of the CFIR domains were categorized as barriers to delivery, and sixteen constructs, spanning four of the CFIR domains were identified as enablers. Many of the constructs were categorized as both a barrier and an enabler to trial delivery.

The mapping of ERIC strategies to identified CFIR domains is displayed in Table 4.2. Strategies were listed in order of how many determinants for which the strategy was listed as a Level 1 strategy, then by how many determinants for which the strategy was listed as a Level 2 strategy. The ERIC strategies (as ranked by the ordering described above) for strategies that were endorsed as a Level 1 strategy for at least one identified CFIR construct were: 1) Identify and prepare champions, 2) Conduct local needs assessment, 3) Conduct educational meetings, 4) Inform local opinion leaders, 5) Build a coalition, 6) Promote adaptability, 7) Develop a formal implementation blueprint, 8) Involve patients/consumers and family members, 9) Obtain and use patients/consumers and family feedback, 10) Develop educational materials, 11) Promote network weaving, 12) Distribute educational materials, 13) Access new funding, and 14) Develop academic partnerships. The maximum number of determinants for which a strategy was listed as a Level 1 strategy was four (Identify and prepare champions). The CFIR constructs with the largest number of Level 1 endorsed strategies were *Patient Needs & Resources*, *Cosmopolitan,* and *Access to knowledge & information*, each with three Level 1 endorsed strategies.

Table 4.2 - ERIC-CFIR matching of strategies to the determinants

ERIC Strategy	Number of determinants where Level 1 strategy	Number of determinants where Level 2 strategy	Intervention Source	Relative advantage	Adaptability	Trialability	Patient Needs & Resources	Cosmopolitanism	External Policy & Incentives	Culture	Tension for Change	Compatibility	Relative Priority	Leadership Engagement	Available Resources	Access to knowledge & information	Knowledge & Beliefs about the Intervention	Planning	Opinion Leaders	Formally appointed internal implementation leaders	Champions
Identify and prepare champions	4	10																			
Conduct local needs assessment	2	7																			
Conduct educational meetings	2	4																			
Inform local opinion leaders	1	9																			
Build a coalition	1	5																			
Promote adaptability	1	5																			
Develop a formal implementation blueprint	1	2																			
Involve patients/consumers and family members	1	2																			
Obtain and use patients/consumers and family feedback	1	1																			
Develop educational materials	1	1																			
Promote network weaving	1	0																			
Distribute educational materials	1	0																			
Access new funding	1	0																			
Develop academic partnerships	1	0																			
Assess for readiness and identify barriers and facilitators	0	12																			
Conduct local consensus discussions	0	12																			
Capture and share local knowledge	0	9																			
Facilitation	0	7																			
Identify early adopters	0	5																			
Create a learning collaborative	0	4																			
Increase demand	0	4																			
Conduct cyclical small tests of change	0	4																			
Tailor strategies	0	4																			

Involve executive boards	0	3																			
Visit other sites	0	3																			
Conduct educational outreach visits	0	3																			
Use an implementation adviser	0	2																			
Organize clinician implementation team meetings	0	2																			
Obtain formal commitments	0	2																			
Stage implementation scale up	0	2																			
Conduct ongoing training	0	2																			
Develop resource sharing agreements	0	2																			
Prepare patients/consumers to be active participants	0	1																			
Purposely re-examine the implementation	0	1																			
Facilitate relay of clinical data to providers	0	1																			
Develop and implement tools for quality monitoring	0	1																			
Model and simulate change	0	1																			
Fund and contract for clinical innovation	0	1																			
Provide ongoing consultation	0	1																			
Mandate change	0	1																			
Provide local technical assistance	0	1																			
Shadow other experts	0	1																			
Intervene with patients/consumers to enhance uptake & adherence	0	1																			
Change physical structure and equipment	0	1																			
Develop disincentives	0	1																			
Use other payment schemes	0	1																			
Make billing easier	0	1																			
Alter patient/consumer fees	0	1																			
Audit and provide feedback	0	0																			
Use data experts	0	0																			
Develop and organize quality monitoring systems	0	0																			
Place innovation on fee for service lists/formularies	0	0																			
Work with educational institutions	0	0																			
Create or change credentialing and/or licensure standards	0	0																			
Revise professional roles	0	0																			
Use train the trainer strategies	0	0																			
Use mass media	0	0																			
Centralize technical assistance	0	0																			

Create new clinical teams	0	0																			
Provide clinical supervision	0	0																			
Change accreditation or membership reqs	0	0																			
Start a dissemination organization	0	0																			
Develop an implementation glossary	0	0																			
Make training dynamic	0	0																			
Change liability laws	0	0																			
Change record system	0	0																			
Use data warehousing techniques	0	0																			
Use capitated payments	0	0																			
Remind clinicians	0	0																			
Change service sites	0	0																			
Number of Level 1 strategies for the determinant	**-**	**-**	**1**	**0**	**3**	**3**	**0**	**1**	**0**	**0**	**0**	**0**	**1**	**3**	**1**	**2**	**2**	**1**	**1**	**0**	**0**
Number of Level 1 strategies for the determinant	-	-	**10**	**10**	**5**	**7**	**7**	**12**	**8**	**10**	**6**	**9**	**7**	**7**	**11**	**6**	**6**	**11**	**6**	**9**	**11**

Note:
Level 1 strategies (strategies endorsed by ≥ 50% of the experts) for each determinant are displayed in black.
Level 2 strategies (endorsed by 20-49.9% of the experts) for each determinant are displayed in grey.

Discussion

Main findings

To the best of our knowledge, this is the first study using the CFIR-ERIC matching tool to identify potential strategies that can help to facilitate the delivery of cRCTs in hospitals by addressing known barriers and enablers. The identification of these strategies was aimed towards future researchers using the strategies and tailoring it to their specific trial. The matching identified many strategies from the ERIC compilation that were endorsed for addressing determinants of cRCT delivery in hospitals, which were organized by CFIR constructs. The ERIC strategies were: 1) Identify and prepare champions, 2) Conduct local needs assessment, 3) Conduct educational meetings, 4) Inform local opinion leaders, 5) Build a coalition, 6) Promote adaptability, 7) Develop a formal implementation blueprint, 8) Involve patients/consumers and family members, 9) Obtain and use patients/consumers and family feedback, 10) Develop educational materials, 11) Promote network weaving, 12) Distribute educational materials, 13) Access new funding, and 14) Develop academic partnerships.

Some of the identified strategies emphasize the potential value of clear planning for cRCTs. The strategies Conduct local needs assessment and Develop a formal implementation blueprint. These two strategies, while different in their overall focus (the former is used to identify whether there is value to conducting a trial, and the latter is used to clearly outline and define the implementation of the trial), they both are potentially crucial strategies to be employed while planning the cRCT to ensure that there is value to the trial and transparent steps of the process.

Several of the identified strategies were similar in terms of their general focus. For example, three identified strategies were educational: Conduct educational meetings, Develop educational materials, and Distribute educational materials. Researchers planning for delivery of a cRCT

may be able to plan for all three strategies simultaneously, or in a way that the strategies complement each other (for example develop materials for the educational meetings, at which the materials are distributed). Guidelines for conducting educational meetings concluded that this strategy may offer a modest effect on changing clinical behaviour, but only when they are planned, implemented, and evaluated properly[47].

Additionally, several strategies involved engagement of people related to the intended sites: Identify and prepare champions, Inform local opinion leaders, Involve patients/consumers and family members, and Obtain and use patients/consumers and family feedback. The former two strategies involve engagement of relevant stakeholders early in planning for recruiting sites into cRCTs, which has been emphasized as important for cRCT conduct in previous studies[27,35,38,42,43,48]. Meanwhile, the latter two strategies can emphasize the importance of engaging the patients/consumers to facilitate cRCT delivery, as they may be able to offer unique insights when planning and delivering the trial.

The identified ERIC strategies were ranked in this paper in order of how many CFIR determinants for which the strategy was listed as a Level 1 strategy. They were ranked in this order due to the assumption that a strategy with a higher number of CFIR domain determinants for which the ERIC strategy was a Level 1 strategy would be best suited to simultaneously address multiple determinants. However, this assumption has not been evaluated, and caution should be taken when developing implementation plans using these strategies. Furthermore, while some of the strategies were ranked high according to the number determinants for which it was a Level 1 strategy, this may discount the value of Level 2 strategies. For example, two strategies that were not listed as Level 1 strategies for any CFIR domains but were each listed as Level 2 strategies for twelve CFIR domains were: Assess for readiness and identify barriers and facilitators and Conduct local consensus discussions. With the high number of CFIR domains for which these ERIC strategies are endorsed as a Level 2 strategy, it is possible these strategies may be more impactful for facilitating cRCT delivery than a strategy that is endorsed as a Level 1 strategy for a fewer number of CFIR domains.

Although the effects of the identified ERIC compilation strategies on cRCT delivery and conduct were not evaluated in this mapping study, systematic reviews from the Effective Practice and Organisation of Care (EPOC) Group[49] of the Cochrane Review Group have investigated the effects of various strategies for implementation of clinical trials and behaviour change in healthcare. While none of these reviews directly explored the effect of the strategies on cRCT delivery and conduct, they can offer some insight and conceptual generalizability about whether some of these strategies can be effectively used in this context. These are further discussed below.

Identified strategies in relation to Effective Practice and Organisation of Care Group[49] Reviews

A strategy identified in this mapping study was Inform local opinion leaders. A review by the Cochrane EPOC Group concluded that the strategy of recruiting local opinion leaders when used alone or in combination with other strategies can be effective to promote practice change, however, the effectiveness of this strategy varied within and between included studies in the review[50]. In this review, interventions that involved leveraging local opinion leaders showed minor absolute improvement in healthcare professionals' compliance with evidence-based practice.

Three ERIC strategies surrounding educational aspects were identified to address some of the CFIR constructs deemed as determinants of cRCT delivery in hospitals: Conduct educational meetings, Develop educational materials, and Distribute educational materials. A review by the EPOC Group investigating the effects of educational outreach visits (defined as "a personal visit by a trained person to healthcare professionals in their own settings[51]") on professional practice and healthcare outcomes concluded that this strategy has effects when used alone or in combination with other strategies on prescribing patterns, however, the effects on other healthcare practices were varied and it was not possible to explore or explain the variation in effect in the review[51]. Overall, the adjusted risk difference in compliance with desired practice showed a small improvement for the main comparison of the review (comparison of using educational outreach visits as a component in an intervention (with or without printed educational materials), compared with no intervention). Another review which explored the effect of printed educational materials on professional practice and healthcare outcomes probably improve the practice by healthcare professionals compared to no intervention[52].

While many ERIC strategies are aimed at addressing financial aspects of implementation (for example access new funding, alter patient/consumer fees, and contract for the clinical innovation, etc.), only one of these strategies was identified as relevant in this matching study: Access new funding. Several EPOC reviews have investigated various aspects of financial arrangements for their effect on implementation and healthcare behaviour change [53–57]. None of these reviews directly assessed the effect of accessing new funding, however, they can provide some evidence to other ERIC strategies identified in this mapping that were endorsed as Level 2 strategies for several of the CFIR constructs identified. An 'overview of reviews' by the EPOC group investigating the effect of financial incentives in changing healthcare professional behaviours and patient outcomes demonstrated mixed effects of the strategy[58]. This overview of reviews identified four reviews, reporting on 32 studies. The overview concluded that certain methods to improve the pre-specified outcomes (impact of financial incentives on healthcare professional behaviour and patient outcomes) were ineffective overall (for example payment for working for a specified time), some were generally effective (for example payment for each service, episode or visit; payment for providing care for a patient or specific population; payment for providing a pre-specified level or providing a change in activity or quality of care), and other mixed financial incentives demonstrated overall mixed effectiveness (for example financial incentives that comprised several of the incentives of investigations or incentives that were not classifiable).

Future research

This current study aimed to be a step in a research agenda aimed at facilitating cRCT delivery in hospitals. Researchers could use the list of strategies identified here as guidance to complete empirical evaluation of the effect of the strategies. While a list of potential strategies was identified, these strategies were generated through the use of the CFIR-ERIC matching tool, which is a tool created through expert-opinion, and the strategies were not empirically tested. Therefore, the strategies identified in this study were intended to provide a foundation for future research using the strategies, and their impact on the delivery of the cRCTs should be empirically evaluated in conjunction with relevant stakeholders (for example trialists, trial funders, hospitals).

Additionally, researchers intending to use this list to develop implementation plans for their cRCT should aim to tailor it to their specific context. This list is intended as a generalized list of strategies, and not as a step-by-step guide for researchers to select the top strategies by their cumulative percentage. Consideration should be given to what is feasible within their trial, and some strategies may be better suited to be used in combination to develop a multifaceted plan to facilitate the delivery and conduct of the cRCT.

Furthermore, it is recommended that researchers also perform their own needs assessment for their unique trial, to identify barriers to conducting their cRCT. The determinants identified for this matching study were partially derived from a single case study of one coordinating site. It is not clear whether the results of this case study can be generalizable to other trials. Further studies should attempt to validate the results in other coordinating sites to determine if similar CFIR constructs are identified.

Limitations

It must be noted that the CFIR-ERIC matching tool is a recently produced guide, and the use of the tool in producing truly effective strategies has yet to be thoroughly evaluated. Uncertainty remains as to the effectiveness of using these strategies for addressing the CFIR constructs to which they are matched, and further research is required. Furthermore, the CFIR-ERIC matching was performed by having experts in the field rank the ERIC compilation strategies to address the CFIR constructs. Therefore, the tool was created by expert opinion rather than empirical, evidence-based methods, further adding to the caution that must be taken in interpreting the results of studies using this tool.

Additionally, potential limitations must be noted from the methods used to identify the determinants, which involved using results from the scoping review and the qualitative study. A major conclusion of the scoping review was the identification of a reporting gap surrounding the conduct and delivery of cRCTs. These aspects were rarely the focus of the published trials and were only described briefly. Therefore, there is potential that some determinants may have been missed due to a lack of reporting. Furthermore, limitations associated with a single case sample with a small sample size must be recognized. The case of investigation in this study was of one coordinating site only, and the experiences and perceptions uncovered may not be generalizable to other coordinating sites. However, this may have been mitigated by there being a large overlap in the determinants identified from the case study also being identified in the scoping review, and therefore were unlikely to have just been specific to the one trial.

Conclusions

This study aimed to identify strategies to facilitate the delivery of cRCTs in hospitals using methods from implementation mapping. This study was informed by two studies previously conducted by our research group[14,15]. A scoping review investigating the conduct of cRCTs in hospitals and a qualitative case study exploring the coordinating site members' perceptions of what was influencing the delivery of the group's cRCT in Ontario hospitals served as a needs assessment to inform this study. Barriers and enablers to cRCT delivery were coded to CFIR constructs in those studies, and the constructs were listed as determinants of cRCT delivery in this study. These determinants were then mapped to strategies using the CFIR-ERIC matching tool.

This study was intended as a step in a needs assessment/gap analysis of the delivery of cRCTs in hospitals and can act as a resource for future researchers when planning their cRCT, with the expectation that the strategies identified here will be tailored to each context. This study, in combination with the scoping review which identified literature surrounding the conduct of cRCTs in hospitals, and the qualitative case study which identified the coordinating site staff's perceptions about the delivery of a cRCT, offers some merit in terms of the conceptual generalizability of the barriers and enablers to cRCT delivery. Various strategies may be better suited to individual situations and may be more feasible for certain trials. Future studies should attempt to further explore and evaluate the outcomes of the implementation plans derived from the strategies identified in this study.

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Chapter 5 - Systematic review of strategies for recruiting healthcare facilities to cluster randomized controlled trials

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Intended Journal – *Clinical Trials*

Abstract

Background: Engagement and recruitment of the clusters in cluster randomized control trials (cRCTs) can prove difficult, with poor response and participation from the intended sites. Various strategies can be used to encourage a site's participation in a trial. This systematic review aimed to identify reported strategies that were used to recruit healthcare facilities as clustered sites into cRCTs

Methods: The rigorous search strategy was designed to identify literature of reported recruitment strategies for the recruitment of healthcare facilities as clusters sites in cRCTs. A search was conducted using MEDLINE, EMBASE, PsycINFO, and Cochrane Central Register of Controlled Trials (CENTRAL) from the inception of the databases until the searches were run on December 6th, 2019. Literature was relevant if it reported engagement strategies for healthcare facility sites to participate in a cRCT. Data were extracted from included studies and were collated and summarized in an iterative process using the Expert Recommendations for Implementing Change (ERIC) compilation strategies as a coding book. Literature was assessed for methodological quality using the Revised Standards for Quality Improvement Reporting Excellence 2.0.

Results: Eleven studies met inclusion criteria and were included. 26 of 73 strategies of the ERIC compilation were identified. Most of the studies employed more than one strategy for site recruitment, with a maximum of 14 strategies used in one study. The top five most commonly identified strategies were: *involve executive boards, promote network weaving*, *conduct educational meetings, centralize technical assistance,* and *inform local opinion leaders* (n=4). It was not possible to decipher the success or failure rates of the recruitment strategies. The search could only identify potential literature that had strategies reported either in the title or abstract, which may have led to the identification of literature that was not representative of cRCTs.

Conclusions: In line with previous research by our group investigating the conduct and delivery of cRCTs, a large reporting gap was identified surrounding the methodology used by trialists while planning and conducting cRCTs. It would be beneficial for future studies to investigate the effect of various strategies on site recruitment, and for the development of reporting guidelines for cRCT delivery.

Keywords

cluster randomized control trial; Expert Recommendations for Implementing Change; healthcare facilities; recruitment; conduct

Introduction

Cluster randomized controlled trials (cRCTs) offer advantages over non-cluster randomized controlled trials (RCTs)[1], however, they also present some unique challenges to conduct and delivery of the trials[2]. cRCTs tend to be complex, and challenges in delivery of the trials can arise before patient recruitment and/or intervention launch[3,4]. Engagement and recruitment of the cluster sites themselves can prove difficult, with poor response and participation from the intended sites[5]. Various strategies can be used to encourage a site's participation in a trial.

Previous studies have emphasized the need to consider more empirical and generalizable research into the conduct and delivery of trials, to be able to provide lessons and guidance for future researchers[3]. Additionally, there has been a recent increase in focus on evaluating the delivery of trials, rather than solely investigating the clinical intervention itself[6]. A recent scoping review investigated literature surrounding the barriers and enablers to conducting cRCTs in hospitals[7]. This review identified a reporting gap for the delivery of cRCTs in hospitals and of strategies to recruit the hospitals into the trials. A recent qualitative study consisted of semi-structured interviews of a coordinating site staffs' perceptions of potential barriers and enablers to the launch and delivery of a cRCT the research group was (at the time of the interviews) preparing to launch in Ontario hospitals[8]. A theme that frequently emerged was the difficulty in recruiting and engaging the hospital sites to participate in the trial.

Identification of successful or non-successful techniques to facilitate cRCT delivery can be beneficial in guiding future researchers in conducting their cRCT. Strategies to circumvent barriers to cRCT delivery may be conceptually generalizable, however, there is currently limited information or guidelines to assist research teams in identifying and planning to overcome the challenges that are identified. These strategies are important to identify what methods are currently being used, what justification for why the selected methods were used, and if there was any evaluation of effectiveness.

Frameworks can be useful in describing barriers and link these to targeted change strategies [9]. Previous quantitative and qualitative studies have concluded that barriers and enablers of frameworks for assessment are consistent with previous literature in which non-theory based assessments were conducted[10,11]. These frameworks can allow for increased rigor in the design of interventions, comparisons of results between studies, and identification of successful factors in an intervention by enabling the comparison between studies[12–14]. The use of these frameworks in reviews could allow for the implementation of identified strategies, regardless of whether the study was theory-driven or not, to be classified and better understood, consistent with the advocacy for the frameworks as previously described framework[9].

There is an apparent knowledge gap in systematically identifying and evaluating strategies to recruit sites to cRCTs in hospitals. The objective of this systematic review was to answer the following research questions: *What strategies are reported for recruitment of healthcare facilities as clustered sites into cRCTs?*

Methods

Search strategy

The systematic review was performed according to a pre-specified protocol [Appendix K]. A search was conducted using MEDLINE, EMBASE, PsycINFO, and Cochrane Central Register of Controlled Trials (CENTRAL) from the inception of the databases until the searches were run on December 6th, 2019. Due to the limited literature identified in the narrow scope of hospitals, as well as the assumed similarity in strategies that would be used in different healthcare facility types, this review included any type of healthcare facility as sites randomized in a cRCT. The search strategy [Appendix L] was developed with the guidance of the University of Ottawa Health Science library services and was also reviewed with the Peer Review of Electronic Search Strategies (PRESS)[15] [Appendix M]. The keywords and syntax were developed in MEDLINE and adapted to the EMBASE and PsycINFO. Medical subject headings (MeSH) terms were specified and supplemented as needed. Hand searching of the literature was conducted from the references of included articles. The journals *Clinical Trials* and *Contemporary Clinical Trials* were searched manually using keywords. Grey literature was also searched on Clinical Trial Ontario[16]. The PRISMA reporting guidelines for systematic reviews and meta-analyses were used throughout the paper (Appendix N)[17].

Article selection

References were screened against the following inclusion criteria:

Population: The population for inclusion was healthcare participating in a cRCT. These sites could be assigned to different engagement strategies, as well as possibly randomized to different clinical interventions.

Intervention: The intervention of interest was engagement strategies for sites to participate in a cRCT. These interventions could have been targeted at various levels within the site (directors, physicians, nurses, etc.). Strategies targeted specifically at the patients were excluded (although the clinical intervention can still be targeted at patients).

Comparator: No explicit strategies (for example, standard, unplanned implementation) or other implementation strategies.

Outcomes: The outcomes were success or failure rates of the strategy. This could have been participant recruitment rates by cluster, sites maintained in the cRCT, site perceptions and acceptance of the cRCT, etc. This was mapped to the ERIC compilations.

Study design: Study design for inclusion was cRCTs. Grey literature will also be searched. Stepped-wedge cRCTs and pragmatic cRCTs were also eligible, if the sites were randomized, and implementation was randomized between sites. To note, the engagement strategy (intervention in this review), did not need to be randomized between clusters, however the clinical intervention did need to be as a cRCT design.

Settings: Studies must have involved cRCTs of health interventions.

Year: There were no restrictions based on year of study publication.

Publication Status: Published articles were included. Abstracts, editorials and protocols were not considered for inclusion; however, efforts were made to determine whether the study had been published. Grey literature was also searched on appropriate sites (for example, Clinical Trials Ontario[18], and other sites identified using CADTH's Grey Matters tool[19]).

Studies that reported on strategies to recruit healthcare facility sites into a cRCT were included. The studies could include a comparison of strategies, or results of how the sites were recruited without a comparison of other strategies. References were excluded if they did not report on strategies or were not in English. Titles and abstracts were screened by two independent reviewers (AW and AA or KC). Full-text articles of potentially eligible references were then screened independently by the same reviewers (AW and AA or KC). Discrepancies at each level were resolved by discussion.

Data extraction

Data from all included studies were extracted into a pre-prepared form in Excel. Extracted data included: demographics of the study (i.e. years, country, type of clinical intervention), any mention of the use of an implementation framework or theory, information about the coordinating centre (i.e. the experience of the staff, relationship to the sites), and information about the strategies used to recruit the sites into the cRCT (i.e. description of the strategy, outcome definition as described by the authors of the papers, success descriptions of the strategy) [see Appendix O for detailed data extraction form]. One reviewer (AW) extracted all data, and a second independent reviewer (AA or KC) verified the data extraction from a random 30% sample of the included studies.

Quality Assessment

All included studies were assessed for methodological quality using the Revised Standards for Quality Improvement Reporting Excellence (SQUIRE) 2.0[20] (Appendix P). This tool was selected as the articles were published describing the challenges in the respective cRCTs, with the assumed intention for other researchers to learn from the studies and improve quality for future cRCTs.

Data analysis

Descriptive data (article type, location, site settings, study period and sample size, use of any implementation framework) were summarized in a table. Data regarding the strategies and methods used in the cRCT to recruit the hospitals were collated and summarized in an iterative process using the Expert Recommendations for Implementing Change (ERIC) compilation strategies as a coding book. The ERIC compilation is a list of 73 discrete implementation strategies that can be used as building blocks to plan the implementation, and potentially address anticipated barriers[21,22] (see Appendix B for strategies and their definitions). The ERIC compilation has been used in retrospective analyses of strategies for implementation[23,24], supporting its use in data analysis for this systematic review. One reviewer (AW) coded strategies identified in the articles to strategies from the ERIC compilation. Upon the first completion of coding, the coding was again checked by the first reviewer. This was done to ensure consistency and ensure that there was uniformity across the coding process, as understandings of the codes could have shifted. A second reviewer (KC) verified all the coding, and any discrepancies between the two reviewers' coding were resolved by discussion. Strategies identified in the literature that fit multiple definitions from the ERIC compilation could be cross-coded. If there was uncertainty regarding coding, a third reviewer (JP) with familiarity with the ERIC compilation strategy was available for consultation, however, this was not required. Quantitative data (for example number of sites approached for inclusion versus the number of

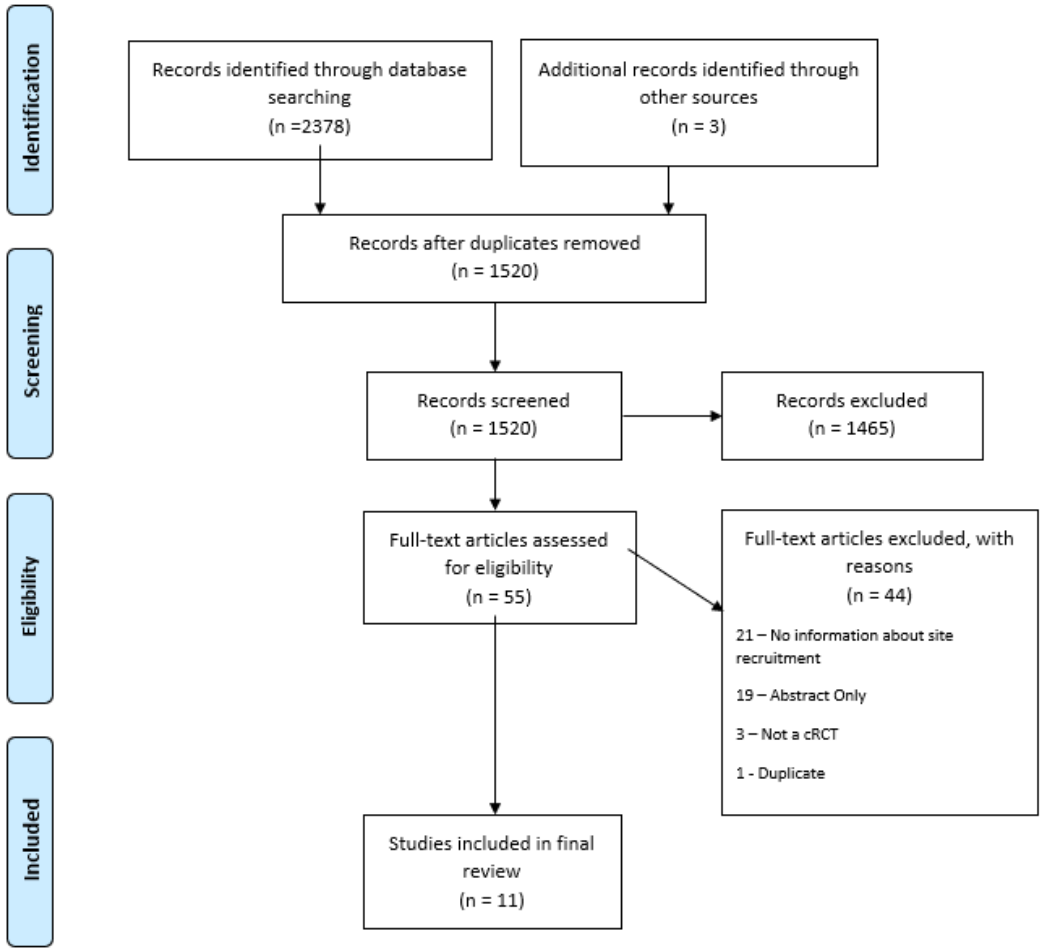
sites included in the trial) was represented as described and detailed by the articles. Outcome data (as described in the methods) was summarized and displayed in tables. There was no planned meta-analysis as it was predicted that there would be too much heterogeneity in identified data, and this was the case.

Results

Search results

The database search identified 2378 potentially relevant articles (Figure 1). Three additional articles were identified from the hand search of included articles. No additional content was identified in the grey literature search. Following de-duplication, 1517 abstracts were screened. Of these, 55 articles were selected for full-text review, from which 11 articles were selected as meeting inclusion criteria. Reasons for exclusion of the full texts are the following: 21 did not provide details about the recruitment of the sites, 19 were abstracts only, 3 were not cRCTs and 1 was a duplicate.

Figure 5.1 - PRISMA flow diagram[17] of study selection for the systematic review



Characteristics of included publications

General study characteristics of the literature are displayed in Table 5.1. Of the included studies, nine were reports of the lessons learned and reports about a cRCT[5,25–32] (two were described by the authors as a pragmatic cRCT[5,30]), and two were cRCTs embedded within a larger cRCT[33,34]. The studies were conducted in the United Kingdom (n=4)[25,33,34] and the United States (n=7)[5,26–28,30–32]. Dates of publication ranged from 2000-2018. Three studies were conducted in nursing homes[26,28,30], one in the secondary care hospital settings[25], one in the maternity wards of hospitals[29], one in the emergency department of hospitals[5], one in the outpatient clinics of Veterans Health Administrations hospitals[27], one in addiction treatment clinics[31], one in primary care practices[32], and two in hospitals with no specifications of hospital units or clinics[33,34].

A framework or theory was stated or described in three studies. Two studies[26,31] used Rogers Diffusion of Innovation in the design of the clinical intervention, one study[31] used the CFIR for the design of the clinical intervention, and one study[5] used the Pragmatic Explanatory Continuum Indicator Summary (PRECIS) -2 tool for trial organizers to assess whether pragmatisms was successfully incorporated into the trial design.

Table 5.1 - Characteristics of the articles included in the systematic review

Author	Year	Article Type	Location	Settings	Study Period of cRCT	Sample Size of cRCT	Implementation Framework used?
Ellis[32]	2007	secondary report of cRCT	USA	Primary care practices	Jul 2002 to Aug 2008	68 practices	None reported
Ersek[26]	2012	secondary report of cRCT	USA	Nursing home hospital	Sept 2006 to Nov 2009	22 originally selected (6 declined); with leveraged community connections, 28 recruited total (1 as the pilot site so leaving 27 for randomization)	Rogers Diffusion of Innovation
Fairhurst[33]	2017	embedded cRCT within a pragmatic cRCT	United Kingdom	Hospitals (general)	May 2013 to Mar 2017	37 units (2 excluded from 39 initially randomized as could not receive an agreement to formally take part in over cRCT)	None reported
Funkhouser[27]	2011	secondary report of cRCT	USA	community-based outpatient clinics within Veterans Health Administration medical centre	Dec 2003 to Dec 2005	48/66 (73%) recruited	None reported
Gravenstein[30]	2018	secondary report of pragmatic cRCT	USA	Nursing home hospital	Nov 2012 to Mar 2013	39 NH/253 (215 excluded: 195 already vaccinated residents, 8 no facility follow-up, 3 not correct location, 2 hospital-based, 4 did not want to participate)	None reported
Grazier[31]	2015	secondary report of cRCT	USA	Addiction treatment clinics	Jan 2007 to May 2010	201 addiction clinics of 648 eligible clinics	Rogers Diffusion of Innovation CFIR
Hanson[28]	2010	secondary report of cRCT	USA	Nursing home hospital	May 2007 to Jun 2010	24 (originally wanted 12 but expanded due to small participant recruitment problems at the sites)	None reported

Hundley[29]	2010	secondary report of cRCT	United Kingdom (Scotland)	maternity hospitals	Apr 2005 to Jun 2007	14/15 accepted, 1 declined	None reported
Johnson[5]	2018	secondary report of pragmatic cRCT	USA	Hospitals - ED	Sept 2015 to Mar 2020 (expected)	41/95 decided to participate (43%)	PRECIS -2
Maxwell[34]	2017	embedded SW-cRCT trial in cRCT	United Kingdom (Scotland, England, Wales)	Hospitals (general)	Mar 2015 to Feb 2017	72 sites (13/85 declined)	None reported
Walker[25]	2000	secondary report of cRCT	United Kingdom (Scotland and England)	Secondary care hospitals	Jan 2002 to May 2003	19 acute trusts (covering 32 directorates) approached and all recruited	None reported

Quality Assessments:

The SQUIRE guidelines for quality improvement studies were used to assess the quality of the articles. Overall, the reporting of the studies appraised with the SQUIRE guidelines were determined to be of high quality. Most studies reported enough detail in the titles and abstracts to allow them to be located by the systematic review search strategy. All studies provided the context of the trial and a summary of current knowledge. The studies also provided the steps for site recruitment for the cRCT in the form of flow charts or tables. Only three of the studies provided a framework or theory to explain the problem of investigation in the paper (for example challenges to site recruitment for the cRCT). None of the studies provided any details in the results of the association between the recruitment strategies and the outcomes. Some of the studies provided limitations and generalizability of the reports.

Recruitment strategies mapping to the ERIC compilation

Of the 73 strategies from the ERIC compilation, 26 were identified as being used to recruit the sites to participate in a cRCT (Table 5.2). The number of strategies used in the included studies ranged from 1 to 14. Multiple strategies were used in 10 of the 11 identified articles. The top five most commonly identified strategies (as retrospectively coded to the ERIC compilation strategies) were: *involve executive boards* (n=8), *promote network weaving* (n=7), *conduct educational meetings* (n=6), *centralize technical assistance* (n=4), and *inform local opinion leaders* (n=4).

Table 5.2 - Data mapping to the ERIC compilation strategies

ERIC Strategy	Number of studies with strategy coded (n)	Ellis[32]	Ersek[26]	Fairhurst[33]	Funkhouser[27]	Gravenstein[30]	Grazier[31]	Hanson[28]	Hundley[29]	Johnson[5]	Maxwell[34]	Walker[25]
Access new funding	**0**											
Alter incentive/allowance structures	**0**											
Alter patient/consumer fees	**0**											
Assess for readiness and identify barriers and facilitators	**2**			**x**						**x**		
Audit and provide feedback	**0**											
Build a coalition	**0**											

Capture and share local knowledge	**1**									**x**		
Centralize technical assistance	**4**			**x**	**x**					**x**		**x**
Change accreditation or membership requirements	**0**											
Change liability laws	**0**											
Change physical structure and equipment	**0**											
Change record system	**0**											
Change service sites	**0**											
Conduct cyclical small tests of change	**0**											
Conduct educational meetings	**6**	**x**		**x**		**x**	**x**			**x**	**x**	
Conduct educational outreach visits	**2**			**x**				**x**		**x**		
Conduct local consensus discussions	**3**								**x**			**x**
Conduct local needs assessment	**1**								**x**			
Conduct ongoing training	**1**							**x**				
Create a learning collaborative	**0**											
Create new clinical teams	**0**											
Create or change credentialing and/or licensure standards	**0**											
Develop a formal implementation blueprint	**1**				**x**							
Develop academic partnerships	**0**											
Develop an implementation glossary	**0**											
Develop and implement tools for quality monitoring	**0**											
Develop and organize quality monitoring systems	**0**											
Develop disincentives	**0**											
Develop educational materials	**3**	**x**				**x**						**x**
Develop resource sharing agreements	**0**											
Distribute educational materials	**3**	**x**			**x**							**x**
Facilitate relay of clinical data to providers	**0**											
Facilitation	**0**											
Fund and contract for clinical innovation	**0**											
Identify and prepare champions	**3**		**x**		**x**					**x**		
Identify early adopters	**0**											
Increase demand	**0**											
Inform local opinion leaders	**4**	**x**	**x**		**x**							**x**
Intervene with patients/consumers to enhance uptake & adherence	**0**											
Involve executive boards	**8**	**x**	**x**	**x**	**x**			**x**	**x**	**x**		**x**
Involve patients/consumers and family members	**1**									**x**		
Make billing easier	**0**											
Make training dynamic	**0**											
Mandate change	**0**											
Model and simulate change	**0**											
Obtain and use patients/consumers and family feedback	**1**									**x**		
Obtain formal commitments	**1**											**x**
Organize clinician implementation team meetings	**0**											
Place innovation on fee for service lists/formularies	**0**											
Prepare patients/consumers to be active participants	**0**											
Promote adaptability	**1**		**x**							**x**		
Promote network weaving	**7**	**x**	**x**		**x**	**x**	**x**	**x**		**x**		
Provide clinical supervision	**0**											
Provide local technical assistance	**2**			**x**				**x**				
Provide ongoing consultation	**1**							**x**				

Purposely re-examine the implementation	**0**											
Recruit, designate and train for leadership	**1**									**x**		**x**
Remind clinicians	**0**											
Revise professional roles	**0**											
Shadow other experts	**0**											
Stage implementation scale up	**0**											
Start a dissemination organization	**0**											
Tailor strategies	**1**									**x**		
Use advisory boards and workgroups	**1**											**x**
Use an implementation adviser	**0**											
Use capitated payments	**1**									**x**		
Use data experts	**0**											
Use data warehousing techniques	**0**											
Use mass media	**0**											
Use other payment schemes	**3**				**x**	**x**		**x**				
Use train the trainer strategies	**0**											
Visit other sites	**0**											
Work with educational institutions	**1**	**x**										
Total number of strategies coded in the study (n)	**-**	**7**	**5**	**6**	**8**	**4**	**2**	**7**	**3**	**14**	**1**	**9**

Involve executive boards

The most frequently coded strategy was the involvement of the executive boards of the facilities[5,25–29,32,33]. The constitution of the executive boards was not stated in all the studies, however, there was the inclusion of chief executives, site presidents and vice presidents, medical and research directors, ethics committee chairs, and administrators. None of the studies explicitly stated how the members were identified and whether they had ensured all relevant and/or influential members were involved in the site recruitment. The executive board members were stated as being involved in the initial discussions about the trials to obtain advice for identifying gatekeepers[25], to recommend the study to their colleagues[26,27], approval, and commitment to undertake the study[28,29,32,33], and the point of contact throughout the trial[5].

One study stated that cRCTs run the risk of being blocked when the gatekeepers and leaders are not identified early in the study, as these people can be decision-makers to decide whether the trial will be conducted at the site[25]. Furthermore, one study stated their experience when there was a change in leadership at a site, that although the leaders may have agreed to participate initially, they found that new incoming leaders did not always feel obliged to honour the commitment[26]. This is consistent with previous literature, whereby a change in leadership personnel has been found to be a barrier to implementing change in healthcare[35].

Another study stated that, after learning several sites were leaning towards refusal to participate (partially due to competing interests and "complex relationships with the main study site"), the sites agreed to participate in the study after high-level conversations with site administrators[5]. The article further went on to state that these conversations to recruit the sites would not have been possible if it were not for the involvement of a diverse team with a mix of skills and experiences (including the hospital administrative leadership). The article did not however justify this conclusion, and they further went on to state that a third of hospitals who declined to participate cited the reason as due to a decision at the hospital system level, and a fifth due to an inability to obtain support from the hospital decision-makers. This may leave questions as to

whether the conversations with the hospitals who were leaning towards refusal were effective or not at convincing the sites to participate in the trial.

While the direct effect of executive board involvement on site recruitment was rarely explained in the articles identified in this review, previous literature has emphasized the importance of early engagement of individuals within hospital sites for the process of a cRCT. The early engagement of the sites has been seen as a strength in studies for successful implementation[36–38], partially due to the ability to identify challenges within the organizations early in the process to be able to determine strategies to overcome them in advance[39,40].

Promote network weaving

Another strategy that was frequently mentioned in the included articles was the promotion of network weaving (i.e. "*identify and build on existing high-quality working relationships and networks within and outside the organization, organizational units, teams, etc. to promote information sharing, collaborative problem-solving, and a shared vision/goal related to implementing the innovation*" [21,22])[5,26–28,30,32]. Articles stated that they leveraged previous partnerships from prior collaborations to enroll sites[5,26,28,32], reached out to personal contacts to the study investigator to initiated facility recruitment[27,28,32], or recruited facilities with the assistance of stakeholder organizations with networks to the sites[30]. The study evaluating the value of recruitment strategies for a primary care cRCT determined they had a one third success rate from leveraging previous relationships to recruit sites, and that the cost per recruited sites averaged at 383$ USD[32]. They concluded that, contrary to previously published articles, the use of personal relationships to recruit sites and practitioners into the trial was not necessary for recruitment success, however, it was an effective and cost-efficient strategy when compared to other techniques the investigator used for site recruitment.

Conduct educational meetings

To inform and recruit sites into the cRCT, six articles described conducting educational meetings with the sites[5,30–34]. The articles described conducting meetings with hospital staff to discuss the cRCT, as well as to invite the sites to participate in the trial. These meetings were described as being conducted in person at site visits[31], remote via webinars and teleconferences[30,34], or a mix of both[5,33].

One study[33] performed an embedded cRCT to evaluate the effectiveness of on-site versus remote initiation visits for recruitment into the clinical trial. These meetings were conducted between the trial coordinator and the hospital staff to discuss the trial rationale and design. Sites were randomized to receive these meetings in person or over the phone. There was no significant difference in the total time from the first contact of the sites to first patient recruitment, or to the number of hospitals in each group who participated in the trial. The site receiving in-person visits accomplished most trial milestones (eg. contracts and ethical approvals obtained, site opening to patient recruitment for the clinical trial to participate (which is different than first patient recruitment)) than those receiving remote visits. The cost attributed to on-site visits was greater than the cost of remote visits. Most sites who received a remote visit would have preferred the meeting to be on-site, however, the on-site visit clusters were split on whether they would have preferred on-site or remote initiation visits. The authors concluded that while on-site visits may foster better relationships with the sites, both methods were feasible options for site initiation visits.

Inform local opinion leaders

Informing the local opinion leaders was also frequently coded as a strategy for site recruitment in four articles[25–27,32]. These opinion leaders were asked to recommend the trial to their colleagues and to other sites[25,26,32] and to facilitate communications between their peers[27]. One study investigating several site recruitment strategies for their cRCT concluded that contacting the opinion leaders was one of the least effective strategies for successfully recruiting the sites[32].

Centralize technical assistance

Four articles described centralizing aspects of technical assistance to facilitate site recruitment to the cRCT[5,25,33,34]. This included offering official multi-centre REB application processes[5,25], offering guidance from the coordinating site to prepare the trial site on how to obtain institutional approval to conduct the trial (for example from research and development departments)[5,27,33]. One study concluded that offering REB specialist was invaluable in facilitating the ethics approval at the sites[27].

Other

Several other strategies were described in the articles; however, these were not reported as frequently as those mentioned above (Table 5.2 for the number of studies with each of the ERIC compilation strategies coded), however previous research[7,8] has emphasized the potential importance of the following strategies for the conduct of cRCTs.

Two strategies aimed at incentives were reported, including *use capitated payments*[5], and *use other payment schemes*[27,28,30]. The capitated payments involved enticing the hospitals by offering per-case direct reimbursements for enrolling study participants to the clinical intervention and completing the trial visits[5]. Other payment schemes involved giving the sites a one-time lump sum to cover the costs of participating[27], providing funded time for the providers to participate in the cRCT[28], and providing free vaccines to staff and residents in the trial sites[30].

Two studies described *promote adaptability*[5,26]. One article allowed the sites to delay enrolment into the cRCT for when would be more convenient timing for the site[26]. The other article described overcoming resource challenges felt by the site by providing flexibility for the various trial sites' staffing levels, financial resources, organizational structures, cultures, and inter-institutional relationships[5].

Discussion

To our knowledge, this is the first systematic review that has examined reported strategies for the recruitment of healthcare facilities into a cRCT. Eleven studies were identified as having met the inclusion criteria for the review. The studies described multiple strategies that had been used to recruit sites into the cRCT. Most of the studies employed more than one strategy, with a maximum of 14 strategies used in one study. The top five most commonly used strategies were: *involve executive boards*, *promote network weaving*, *conduct educational meetings*, *centralize technical assistance,* and *inform local opinion leaders*.

It was not possible to discern the success or failure rates of the recruitment strategies. The primary objective of the studies included in this review was to test the effect of the trials' clinical intervention, and not to test the site recruitment strategies. While one of the studies did explicitly test the two site recruitment strategies, the trial was embedded within the overall cRCT[33] and was

not powered or designed to formally test the different strategies. Furthermore, as most of the studies in this review described multiple strategies for recruiting the sites into the trial, it is difficult to determine the effects of the individual strategies. Several studies that included the same strategies (either in combination with other strategies or not) had varying levels of site recruitment success. There was also a large amount of heterogeneity in how the different studies reported the site recruitment rates, and it was unclear whether the rates were truly representative of the number of eligible sites compared to the number of successfully recruited sites. For example, some studies reported solely the number of sites recruited, with no other information about how many sites were eligible, and some reported the number of studies approached, which may again not equate to the number of eligible sites.

Most studies described multiple site recruitment strategies that were employed in combination; however, it was unclear whether the use of multiple strategies had any beneficial effect on site recruitment. While multifaced implementation strategies have been thought to be more successful than when a single strategy is used[41], mixed results have been shown. Some studies have shown no benefit of multifaceted strategies over passive or single strategies[42–44], while some studies have shown a limited effect in improving implementation[45,46]. It was not possible to determine the effect of the strategies identified in this review on site recruitment, and therefore the effect of using multiple strategies on recruiting sites into the cRCT remains unclear. For example, the study that included the largest number of strategies described reported one of the lowest site recruitment rates compared to the other studies[5].

Although the effects of the specific strategies on site recruitment could not be inferred from the studies in this systematic review, previous systematic reviews from the Effective Practice and Organisation of Care (EPOC) Group[47] of the Cochrane Review Group have investigated the effects of various strategies for implementation of clinical trials and behaviour change in healthcare. EPOC published an overview of reviews investigating the effect of financial incentives in changing health care that demonstrated mixed effects[48]. One of the reviews included in this overview concluded that capitated financial incentives may be effective in changing primary care physicians' behaviour [49], however, two other reviews included in the overview also showed insufficient evidence to support the use of financial incentives on improving the quality of primary healthcare services[50,51]. Two further reviews by EPOC of performance-based financial incentives showed uncertain and unclear results of this payment method's effectiveness on increasing the efficacy of care by health care providers[52,53]. Another review by EPOC investigating the effects of educational outreach visits on professional practice and healthcare outcomes concluded this strategy has effects when used alone or in combination with other strategies on prescribing patterns, however, the effects on other healthcare practices were varied and it was not possible to explore or explain the variation in effect in the review[54]. For the strategy of using local opinion leaders to disseminate and implement evidence, another EPOC review demonstrated that the strategy alone or in combination with other interventions can be effective to promote practice change[55]. While none of these reviews directly explored the effect of the strategies on cRCT site recruitment, they may offer some insight into whether these strategies were effective or not in the context of site recruitment.

Future research

In line with previous research by our group investigating the conduct and delivery of cRCTs[7,8], a large reporting gap was identified surrounding the methodology used by trialists while planning

and conducting cRCTs. While our search strategy was detailed, few studies were identified. There are many cRCTs (whether currently or previously conducted), however, a limited number of articles were identified, bringing into question why there is such a gap in reporting of the methods used during the trial, including the methods for recruiting sites.

It would be beneficial for future studies to investigate the effect of various strategies on site recruitment to further understanding, however, these studies are unlikely to occur as researchers would likely prefer to maximize recruitment into a clinical trial rather than test various strategies to recruit a site. Furthermore, researchers tend to be focused on the effectiveness of a clinical trial, and there are fewer researchers (and research funds) targeting strategies to improve recruitment. A primary step to increase knowledge about conducting cRCTs would be to improve and standardize the reporting of cRCT conduct, including the strategies used to recruit sites. While reporting guidelines exist for publications such as systematic reviews, there are currently no widely used guidelines for reporting cRCT implementation issues. The creation of a guideline or checklist could assist future trialists by having access to the experiences and methods used in previous cRCTs.

Limitations

Limitations in the search strategy must be noted. The review limited included studies to English language only. While we had originally planned to include only cRCTs with hospitals as the randomized clusters, there were limited studies identified, and the review was expanded to include any type of healthcare facility. The search could only identify potential literature that had strategies reported either in the title or abstract, which may have led to the identification of literature that was not representative of cRCTs. There may have also been some reporting bias, whereby studies were more likely to report about their recruitment strategies if the authors deemed there was a large degree of success or failure associated with the strategies.

Furthermore, there are limitations to the conclusions that can be drawn from this systematic review. Only a small number of studies were identified, with heterogeneity in their design (i.e. lessons learned vs. embedded trial within a cRCT). Therefore, no analyses or conclusions about the effectiveness of the recruitment strategies were possible.

Additionally, while frameworks and standardized descriptions can allow for comparisons between studies[12–14], there does remain some uncertainty when used retrospectively to identify aspects (strategies in the case of this review) as to whether the coding is accurate. To increase the reliability of the coding, two reviewers coded the data, however, there remains the limitation that the original studies did not use the coding framework used in this systematic review (the ERIC compilation), and therefore there remains uncertainty as to whether the codes truly represent the strategies.

Conclusions

This systematic review aimed to identify reported strategies for the recruitment of healthcare facility sites into cRCTs and to map the literature to the ERIC implementation strategy compilation. To the best of our knowledge, this is the first systematic review to identify strategies used to recruit sites into cRCTs. This review identified numerous strategies used to recruit healthcare facility sites into cRCTs. Strategies that were commonly cited were: *involve executive boards, promote network weaving, conduct educational meetings, inform local opinion*

leaders, and centralize technical assistance. While the articles described the strategies used, they rarely evaluated whether the strategies had any effect on site recruitment. A reporting gap was identified surrounding the methodology for recruiting sites into cRCTs. Future research should focus on evaluating recruitment strategies and on developing reporting guidelines

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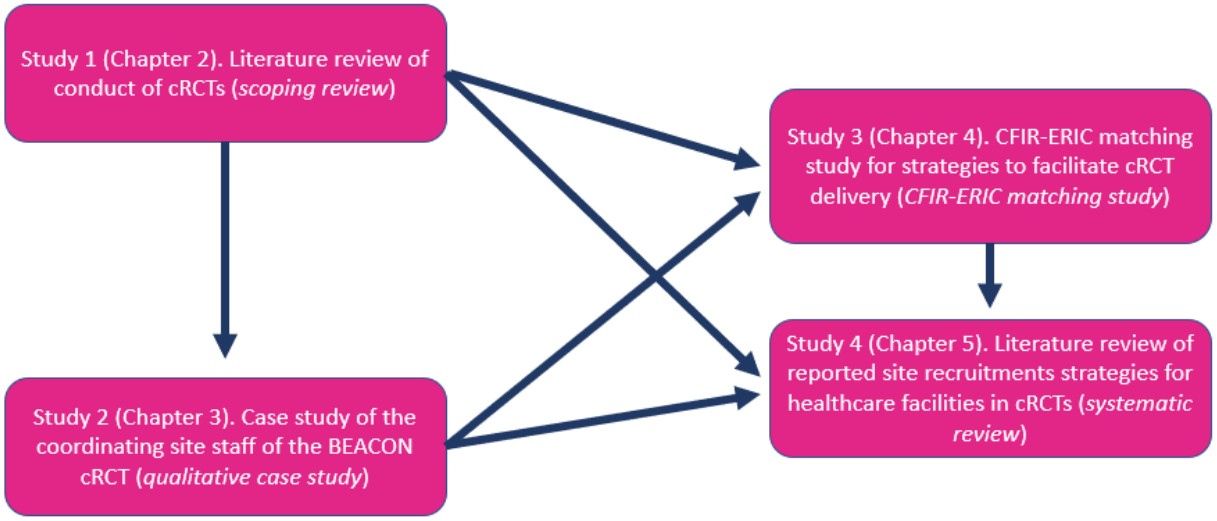
Chapter 6: Integrated Discussion

Overview

This dissertation aimed to explore barriers and enablers to conducting cRCTs in hospitals and to identify potential strategies that facilitate their delivery. The specific aims of this thesis were: 1) To explore the current knowledge and evidence surrounding the implementation of cRCTs in hospitals; 2) To explore from the perspective of the coordinating site, what is influencing the delivery and hospital engagement of an ongoing cRCT, and what challenges are being encountered; 3) To identify strategies to facilitate the delivery of cRCTs in hospitals, and; 4) To systematically identify reported recruitment strategies for healthcare facilities in cRCTs.

The studies in this dissertation were conceived in an iterative manner, where the results of the first study (*Chapter 2: Scoping review of the conduct of cRCTs in hospitals*[1]) informed the direction and design of the subsequent study (*Chapter 3: Qualitative case study of the coordinating site staff of the BEACON cRCT*[2]*).* Findings from these first two studies (the scoping review and qualitative case study) identified an evidence gap in reported conduct and delivery strategies for cRCTs, and this identified a gap that drove the final two studies (*Chapter 4: CFIR-ERIC matching study for strategies to facilitate cRCT delivery* and *Chapter 5: Systematic review of reported site recruitments strategies for healthcare facilities in cRCTs)*. Additionally, *Chapter 4: CFIR-ERIC matching study for strategies to facilitate cRCT delivery* informed the direction of *Chapter 5: Systematic review of site recruitments strategies for healthcare facilities in cRCTs*, as it partially contributed to identifying the potential for exploring strategies for a specific step of trial conduct, namely the site recruitment step. The sequential nature of the studies in this dissertation and the mixed methodology helped to complement, strengthen, and confirm the findings by allowing triangulation of the findings and a deeper investigation into perceived gaps. The sequence of study flow can be seen in Figure 6.1. Key findings from the studies are summarized in Table 6.1 and are described in more detail in the next section of the discussion.

Figure 6.1 - Sequence of the studies in this dissertation



Throughout the discussion, ***domains from CFIR are written in bold underlined italics***, *constructs from CFIR are written in underlined italics*, and strategies from ERIC compilation are underlined.

Table 6.1 - Summary of key findings of the dissertation by chapter

Chapter 2: Scoping review of the conduct of cRCTs in hospitals[1]	Objective: To explore the current literature surrounding the conduct of cRCTs in hospitals to investigate the knowledge on this topic Findings: • All data extracted for factors related to cRCT conduct were able to be mapped to CFIR • Four CFIR domains coded: ***intervention characteristic***, ***outer settings***, ***inner settings,*** and ***process*** • Enablers to cRCT conduct: *adaptability* to tailor the trial to each site; early *engagement of opinion leaders*, *champions,* and *formally appointed implementation leaders* in the cRCT process • Barriers to cRCT conduct: A site not perceiving a *relative priority* for the trial or *tension for change* for the clinical field; limited *available resources* • Identification of a reporting gap for conduct and delivery strategies for cRCTs in hospitals
Chapter 3: Qualitative case study of the coordinating site staff of the BEACON cRCT[2]	Objective: To explore from the perspective of the coordinating site, what is influencing the delivery and hospital engagement of an ongoing cRCT, and what challenges are being encountered for trial delivery Findings: • All data extracted to address the research question were able to be coded using CFIR • CFIR domains and constructs identified were similar to those identified in the scoping review as potentially influential for cRCT conduct • Importance of the *adaptability* of trial, a *tension for change* for the intervention area, the *availability of resources*, and the early *engagement* of leaders to facilitate a site accepting inclusion in the trial • Lack of perceived importance from the potential sites of pilot studies *evidence strength and quality* on facilitating cRCT conduct and engaging sites
Chapter 4: CFIR-ERIC matching study for strategies to facilitate cRCT delivery	Objective: To identify potential strategies to facilitate the delivery of cRCTs in hospitals Findings: • The CFIR-ERIC matching tool was used to identify potential strategies

	• Identified strategies were general strategies to facilitate cRCT conduct and delivery, and not aimed at facilitating any specific aspect of the cRCT delivery • Strategies identified as Level 1 strategies (endorsed by ≥ 50% of the experts) for the CFIR domains deemed as determinants of cRCT delivery were: 1) Identify and prepare champions, 2) Conduct local needs assessment, 3) Conduct educational meetings, 4) Inform local opinion leaders, 5) Build a coalition, 6) Promote adaptability, 7) Develop a formal implementation blueprint, 8) Involve patients/consumers and family members, 9) Obtain and use patients/consumers and family feedback, 10) Develop educational materials, 11) Promote network weaving, 12) Distribute educational materials, 13) Access new funding, and 14) Develop academic partnerships
Chapter 5: Systematic review of reported site recruitments strategies for healthcare facilities in cRCTs	Objective: To systematically review reported recruitment strategies for healthcare facilities in cRCTs Findings: • Due to limited literature focusing on cRCTs in hospitals, the scope of the review was expanded to include all types of healthcare facilities • All data extracted for strategies for recruiting sites into cRCTs were able to be mapped to the ERIC compilation • Strategies that were commonly described: involve executive boards, promote network weaving, conduct educational meetings, inform local opinion leaders, and centralize technical assistance. While the articles described the strategies used, they rarely evaluated whether the strategies had any effect on site recruitment • The strategies identified in the literature were rarely explored or evaluated for their effect on site recruitment

Summary of Findings

Chapter 2: Scoping review[1]

The purpose of the first section of the dissertation (Chapter 2) was to explore the current literature surrounding the conduct of cRCTs in hospitals by performing a scoping review. This method was chosen as it was determined from a preliminary search that the literature addressing this question was limited, heterogeneous, and there were no guidelines to assist research teams in identifying and circumventing these challenges.

The literature search identified 22 articles that met the eligibility criteria. All factors identified in the literature were able to be mapped to the CFIR framework. Four of the five CFIR domains were identified in the literature: ***intervention characteristics***, ***outer settings***, ***inner settings,*** and ***process***. Several key domains were identified as being influential for conducting the cRCTs in hospitals, described further next. The *adaptability* to tailor the trial to each site and the early *engagement of opinion leaders*, *champions,* and *formally appointed implementation leaders* in the cRCT process were deemed as enablers to conducting the trial. A site not perceiving a

relative priority for the trial or *tension for change* for the clinical field, as well as limited *available resources* were determined to present barriers to conducting the cRCT.

Additionally, the scoping review identified a gap in the reporting of conduct and delivery strategies for cRCTs in hospitals. While these aspects of the trial were briefly described in study publications, they were rarely the focus of published articles, contributing to a lack of guidance for researchers aiming to conduct these types of studies. The literature identified in this scoping review described primarily the authors' personal experiences and lessons learned from the delivery of their studies. This highlighted the need for further research investigating the gap, as well as a need for research to identify strategies for conducting cRCTs in hospitals. The results of this scoping review were used to guide the second study in the dissertation, the qualitative case study of the BEACON cRCT, which is further discussed below.

A further search was also conducted to determine whether the search strategy used in the scoping review was biased in identifying literature with a focus on knowledge translation terms. The original scoping review search included search terminology aimed to specifically identify literature which included several potential terms that were used in implementation science (for example, knowledge translation, dissemination, implementation; for further details see Appendix E lines 17 to 29). There was concern that these search terms would introduce bias to the identified references for literature that would be specifically focused on the implementation of the trials and would not be representative of the wider literature of cRCTs in hospitals. Therefore, a broader search was performed which excluded the implementation science specific terms.

The search was performed in MEDLINE using the OVID platform. A total of 4055 potential references were identified and uploaded to Covidence. The references were de-duplicated from the original search, leaving 3029 potential new references from the revised search strategy. The first 200 references were screened by one reviewer (AW) at the title and abstract level.

No additional literature (literature that was not identified in the primary search) was identified from the sample of abstracts screened. While acknowledging that this screen was performed on only a small sample of the literature identified in the search, this result reinforces that the primary search was adequately designed to identify literature that would address the research question of the scoping review.

Chapter 3: Qualitative case study[2]

The second section of the thesis (Chapter 3) involved a qualitative case study using semi-structured interviews to explore from the perspective of the coordinating site, what is influencing the delivery and hospital engagement of an ongoing cRCT, and what challenges are being encountered for trial delivery.

The barriers and enablers to conducting a cRCT that were identified from the literature in the scoping review informed the content of the interview guide. CFIR constructs identified in the scoping review as potential barriers or enablers to conducting the cRCTs were further explored with the interview questions. Furthermore, CFIR constructs that were not identified in the scoping review but were thought to be possibly relevant to cRCT conduct were explored in the interview questions. This was done to further investigate whether they were not perceived as

relevant to cRCT conduct, or whether they were just not reported in the literature identified in the scoping review.

The qualitative case study identified CFIR domains and constructs similar to those identified in the scoping review as potentially influential for cRCT conduct, including the emphasis on the *adaptability* of trial, the importance of *tension for change,* the *availability of resources*, and the early *engagement* of leaders to facilitate a site accepting inclusion in the trial. The interviews also explored the domains and constructs that were not identified in the literature of the scoping review, such as ***characteristics of the individuals*** and *evidence strength and quality*, which were not perceived as overly influential on facilitating cRCT conduct.

The coordinating site staffs' perceptions about what was influencing the delivery and conduct of the cRCT built upon the scoping review, which identified several key CFIR domains as being influential for conducting the cRCTs in hospitals (for example, *adaptability*, *engagement of opinion leaders*, *champions*, and *formally appointed implementation leaders*, the importance of a *relative priority* for the trial and *tension for change* for the clinical field, and the importance of the *available resources*). However, this qualitative case study investigated the staffs' perceptions only, without empirically testing whether the identified domains were influential on trial conduct. The findings from the scoping review and the qualitative case study exposed an evidence gap in reported conduct and delivery strategies for cRCTs, which informed the direction of the final two studies in this dissertation (the CFIR-ERIC matching study which aimed to identify strategies to facilitate cRCT delivery in hospitals, and the systematic review which aimed to identify strategies to facilitate recruitment of healthcare facilities into cRCTs).

Chapter 4: CFIR-ERIC matching study

The third section of the thesis (Chapter 4) used the CFIR-ERIC matching tool to identify potential strategies to facilitate the delivery of cRCTs in hospitals. The previous studies in the dissertation demonstrated a reporting and knowledge gap in methodology for the delivery of cRCTs in hospitals. Strategies to circumvent barriers to cRCT conduct and delivery may be generalizable, and identification of successful or unsuccessful techniques can be beneficial in guiding future researchers in conducting their cRCT. Barriers to the conduct of cRCTs can have commonalities between studies, however, there is currently limited widespread information or guidelines to assist research teams in identifying and circumventing these challenges.

The CFIR-ERIC matching tool was selected for use in this study due to the previous studies in the dissertation using CFIR to guide the studies and analyze the data. The CFIR-ERIC matching tool was developed to allow for the capacity of building an implementation plan using the ERIC compilation strategies matched to specific determinants from CFIR [3,4]. This tool was developed by having expert consensus on ERIC strategies that would address CFIR constructs[3]. Strategies that were endorsed by ≥ 50% of the experts were deemed as "Level 1" strategies, and strategies that were endorsed by 20-49.9% of the experts were deemed as "Level 2" strategies. The previous studies in this dissertation (the scoping review and qualitative case study) informed the determinants of cRCT delivery in hospitals by allowing the identification of barriers and enablers to delivering the cRCTs.

A list of strategies was generated using the CFIR-ERIC matching tool. The strategies that were endorsed as a Level 1 strategy for any or multiple CFIR domains were: 1) Identify and prepare

champions, 2) Conduct local needs assessment, 3) Conduct educational meetings, 4) Inform local opinion leaders, 5) Build a coalition, 6) Promote adaptability, 7) Develop a formal implementation blueprint, 8) Involve patients/consumers and family members, 9) Obtain and use patients/consumers and family feedback, 10) Develop educational materials, 11) Promote network weaving, 12) Distribute educational materials, 13) Access new funding, and 14) Develop academic partnerships

This CFIR-ERIC matching study aimed to be a step in the identification of strategies to facilitate cRCT delivery, with the expectation that the strategies identified with the tool would need to be tailored for individual cRCT, and that various strategies and/or combination of strategies may be more feasible for different trials. As the strategies identified in this study were general to cRCT conduct and delivery, and not aimed at facilitating any specific aspect of the cRCT delivery, the results directed the next chapter of the thesis, in which strategies specific to one part of trial delivery (site recruitment) were explored.

Chapter 5: Systematic review

The final study of the thesis (Chapter 5) involved a systematic review aimed at identifying reported strategies for recruiting healthcare facility sites into cRCTs. As previously stated, the scoping review and qualitative case study identified a knowledge gap in methodology for the delivery and conduct of cRCTs in hospitals. Next, the CFIR-ERIC matching study was performed to identify a list of strategies to facilitate cRCT delivery, however, these strategies were not targeted at any specific aspect of trial conduct. Therefore, this systematic review was conducted to identify strategies that can be used for the specific task of recruiting sites into a cRCT. Due to the limited literature identified in the initial narrow search scope of hospitals, as well as the assumed similarity in strategies that would be used in different healthcare facility types, this review included any type of healthcare facility as sites randomized in a cRCT.

The methodology of systematic reviews was selected as systematic reviews aim to provide critically appraised evidence to address a research question[5]. As the aim of this study was to produce a list of implementation strategies used in previous cRCTs and to critically appraise the reporting of the evidence, a systematic review was deemed as ideal to address the research question. Data regarding the strategies and methods used in the cRCTs to recruit the hospitals were collated and summarized in an iterative process using the ERIC compilation strategies as a coding book. The ERIC compilation has been used in retrospective analyses of strategies for implementation[6,7], supporting its use in data analysis for this systematic review.

The rigorous literature search identified eleven articles that were deemed as meeting the eligibility criteria. Most of the studies employed more than one strategy, with a maximum of 14 strategies used in one study. Due to the nature of reporting, it was not possible to decipher the success or failure rates of the recruitment strategies. All the strategies identified from the included literature were able to be mapped to the ERIC compilation. The review identified numerous strategies used to recruit healthcare facility sites into cRCTs. Strategies that were commonly cited were: involve executive boards, promote network weaving, conduct educational meetings, inform local opinion leaders, and centralize technical assistance. While the articles described the strategies used, they rarely evaluated whether the strategies had any effect on site recruitment.

Integration and Discussion

This dissertation aimed to explore and identify strategies to facilitate the delivery and conduct of cRCTs in hospitals. Four studies were completed to address the research agenda: 1) a scoping review of the conduct of cRCTs in hospitals, 2) a qualitative case study of the coordinating site staff of the BEACON cRCT, 3) a CFIR-ERIC matching study for strategies to facilitate cRCT delivery, and 4) a systematic review of reported site recruitments strategies for healthcare facilities in cRCTs. The use of multiple methods of data sources facilitated developing a more comprehensive understanding of the research question and results[8]. Using implementation science concepts facilitated comparisons between the four studies of the dissertation and enabled building upon the results of the studies with each subsequent chapter of the dissertation (further discussed below).

This dissertation provided a foundation exploration of barriers and enablers to cRCT conduct in hospitals and identification of strategies to facilitate the delivery of the trials, however, the interpretation and discussion of the results must be considered in light of numerous limitations. The scoping review and the systematic review concluded that there was a large reporting gap for the conduct of cRCTs in hospitals and strategies for the recruitment of sites into cRCTs in healthcare facilities. While this was an important finding that drove the direction of the research agenda for the dissertation, it is pertinent to recognize the limitations from this gap, given that the scoping review was used to inform the subsequent studies. CFIR constructs identified in the scoping review as relevant to cRCT conduct were used to inform the interview guide for the qualitative case study. This allowed the possibility that some potentially relevant constructs for cRCT delivery may have been missed. Additionally, limitations associated with using a single case sample must be recognized. The case of investigation was of one coordinating site of a potentially challenging trial to conduct, with a small sample size of interviewees. The results from this case study, and the dissertation as a whole may not be generalizable to other coordinating sites.

Triangulation of the barriers and facilitators to cRCT conduct coded with CFIR

CFIR was used to guide the design and data analysis of the first two studies in this dissertation (the scoping review and the qualitative case study). The scoping review identified literature surrounding the conduct of cRCTs in hospitals. The data extracted from the included literature were coded to the constructs from CFIR. The qualitative case study built on the scoping review, by using the results of the main CFIR domains identified in the literature of the scoping review to inform the design of the semi-structured interviews. Overall, the results between these two studies (Chapters 2 and 3) were similar. Key CFIR domains that were identified as influential (whether as a barrier or as a facilitator) on cRCT conduct are further discussed below.

Both studies emphasized the importance of the *adaptability* of the trial in conducting cRCTs. A trial's adaptability was coded multiple times in the literature identified in the scoping review[1] as being a facilitator for the hospitals for participation in the cRCT[9–16]. This was also echoed in the responses from the participants in the qualitative case study[2], whereby the adaptability of the study for each site was emphasized by all participants, and this was thought to be a strength of the study.

The *tension for change* in the clinical gap was also noted by the participants in the qualitative case study[2] as important to facilitate cRCT delivery. The participants stated that there were no

programs at that time that were similar to the intervention of the cRCT they were conducting (the BEACON trial of smart-phone app assisted therapy for men who present to the emergency department with self-harm). The participants thought it was therefore possible the hospitals may have been more likely to accept inclusion into the trial as they perceived this as an area that needs improvement, and they prioritized an agenda addressing this gap. The literature identified in the scoping review also supported this perception[1]. One of the included studies stated that successful trial delivery was facilitated when they were able to align their priorities with those of the hospitals[17]. Therefore, the current tension for change and alignment with the hospitals' priorities may be facilitating factors for a site's agreement to participate and actively engage in a cRCT. If there are pre-established needs and desires to bring about change, in an area that is under investigation by the study, this could help facilitate the cRCT delivery in this hospital, as the hospital may be more engaged.

Furthermore, the importance of *engagement* (*internal implementation leaders*, *opinion leaders*, *champions*, and *external change agents*) early in planning and delivery of the cRCT were important factors identified in both the scoping review[1] and the qualitative case study[2] as potential facilitators for delivery of the cRCT. The literature identified in the scoping review described the importance of early engagement with relevant personnel. This was often cited in terms of meeting with the key stakeholders (for example directors, physicians, administrators, patients) to seek their prior engagement to participate in the trial [10,14,16,18–22]. Engaging the opinion leaders, champions, and implementation leaders from the start were noted as a facilitator to developing and then conducting the trial[17,20], and it was also proposed in one of the included articles as a solution to overcoming some of the barriers that were encountered[23]. A review[12] identified and included in the scoping review concluded that engaged and solid leadership was often seen in successful implementation efforts. The participants in the qualitative case study also stated that the engagement of the relevant individuals of the hospitals included in their cRCT was crucial to facilitate the delivery of the trial. These influencers may be able to facilitate conducting the trial by offering insight into the hospitals in which the trial is intended to tailor the trial to the sites for more success in implementation

In terms of key barriers to trial conduct, both the scoping review[1] and the qualitative case study[2] identified that a concern for the limited *availability of resources* from the sites presented challenges to enrolling sites and conducting the cRCT. The literature included in the scoping review often cited the limited availability of resources, including time, personnel, finances, and information were seen as a barrier for implementation[17,24–26]. The participants in the qualitative case study also viewed the availability of resources as having a major impact on the trial, primarily at the level of the local sites. It was noted that these resources were not solely financial resources, but time and personnel as well. The availability of resources was perceived as a potential barrier to the initial agreement for participation of the sites if the leaders deemed that it would burden their hospitals. The perceived lack of resources by the sites was thought to be the reason they declined to participate.

The CFIR domain of ***characteristics of individuals*** was not coded at all in the scoping review[1], and this domain was explored in the qualitative case study[2]. The coordinating site staff participants spoke about their personal *knowledge and beliefs about the intervention* (one of the constructs in the domain of ***characteristics of individuals***), as well as about the impressions they were getting from the sites about the study. They described an overall positivity for the

intervention of the trial experienced by themselves, and that the sites appeared to be having the same optimism. There is however limited evidence exploring the influence of a coordinating site's beliefs about a trial, and it was not possible to determine how and to what extend their positivity had influenced site engagement and implementation progress.

The scoping review[1] also did not identify literature in which *patient needs and resources* were mentioned. This CFIR construct was explicitly investigated in the qualitative case study[2]. The participants in the qualitative case study (the coordinating staff of the BEACON cRCT) emphasized their perception of the importance of the focus on *patient needs and resources* in the development of the cRCT. While the perceived importance of this construct differed from the scoping review, in which the construct was not coded from the included literature, the contrast between the two studies may have been due to the BEACON study receiving funding from an organization focusing on patient-oriented research, potentially influencing the emphasis and discussions of the construct in the qualitative case study[27].

Additionally, the scoping review[1] identified limited literature in which the CFIR construct *evidence strength and quality* were coded. This left uncertainty as to whether having evidence of testing the intervention presented to the potential sites was an enabler for cRCT conduct. Results of the qualitative case study[2] supported that this construct does not appear to be influential in the success of conducting the trial, as most of the interviewees agreed that they did not feel that previous evidence from a pilot trial had much influence on engaging the sites.

To note, the qualitative case study explored the perceptions of a single site only (coordinating site of the BEACON trial). As previously stated, the BEACON trial has encountered numerous challenges during the launch of the trial, leading to lengthy time delays. These challenges have included delays in obtaining ethical approval at both the coordinating site and the hospital sites, challenges in engaging key members at the sites, and technical issues involving the intervention app. Additionally, as the coordinating site was composed of a small number of people who work in close relation to each other, there may have been an overlap in perceptions. While it was intended to perform a further study to interview members from the hospital sites, the site staff provided limited replies for participation. Therefore, it's not clear whether the perceptions of the coordinating staff also could be representative of the trial sites or whether their perceptions are generalizable to other cRCTs in hospitals.

Triangulation of the strategies to facilitate cRCT delivery and site recruitment coded to the ERIC compilation

The next two studies in the dissertation (CFIR-ERIC matching study and the systematic review of recruitment strategies) aimed to identify generalizable strategies to facilitate cRCT delivery in hospitals. Both of these final two studies in the dissertation used the ERIC compilation to guide the data analysis. The CFIR-ERIC matching study also used CFIR to guide the study and analyze the data. The CFIR-ERIC matching study aimed to identify general strategies to facilitate cRCT delivery in hospitals, while the systematic review was more specific in aiming to identify strategies that have been reported in previous cRCTs to facilitate the recruitment of healthcare facility sites into a cRCT (a part of cRCT delivery). The scope of the systematic review was broader than the other studies, as it included literature with all types of healthcare facilities and not just hospitals. This was due to the limited literature identified in a preliminary search using the narrower scope of cRCTs in hospitals only.

The CFIR-ERIC matching study (Chapter 4) and the systematic review (Chapters 5) both identified some similar ERIC strategies, with some discrepancies in the strategy list between the two studies. As the CFIR-ERIC matching study was designed to be a general list of strategies for facilitating cRCT delivery, it may be reasonable to assume that the identified strategies would also be included in those that have been used for recruiting sites, as this is one part of the trial delivery. However, some differences were noted. The CFIR-ERIC matching study identified the following strategies that were endorsed as a Level 1 strategy for one or more CFIR domains: 1) Identify and prepare champions, 2) Conduct local needs assessment, 3) Conduct educational meetings, 4) Inform local opinion leaders, 5) Build a coalition, 6) Promote adaptability, 7) Develop a formal implementation blueprint, 8) Involve patients/consumers and family members, 9) Obtain and use patients/consumers and family feedback, 10) Develop educational materials, 11) Promote network weaving, 12) Distribute educational materials, 13) Access new funding, and 14) Develop academic partnerships. The systematic review identified the following strategies that were commonly cited as being used for site recruitment: involve executive boards[24,28–34], promote network weaving[24,29–32,35], conduct educational meetings[24,32,33,35–37], inform local opinion leaders[28–30,32], and centralize technical assistance[24,28,33,36]. When comparing the results between the two studies, only promote network weaving, conduct educational meetings, and inform local opinion leaders were found in both strategies list.

The differences between strategies identified in each of these two studies can be for several reasons. First, the scope of the strategies for the CFIR-ERIC matching study was broader than that of the systematic review. As previously stated, the CFIR-ERIC matching study aimed to identify strategies to facilitate cRCT delivery in general, while the systematic review identified reported strategies specific to site recruitment. The strategies identified in the CFIR-ERIC matching were 'ranked' according to how many CFIR constructs for which the strategy was endorsed as a Level 1 strategy while ignoring the ERIC strategies that were endorsed as a Level 2 strategy. It is possible that strategies that were endorsed as Level 2 strategies for a large number of CFIR domains identified as determinants may be more impactful for facilitating cRCT delivery than a strategy that is endorsed as a Level 1 strategy for a fewer number of CFIR domains. Furthermore, strategies with a large number of CFIR domains for which they are listed as a Level 2 strategy may have better suited to address the specific aspect of site recruitment than some of the strategies identified in the CFIR-ERIC matching as 'top' strategies (by the number of CFIR domains for which the strategy was a Level 1 strategy). Unlike in the CFIR-ERIC matching study which focused on the delivery of cRCTs in general, the strategies identified in the systematic review were aimed at facilitating site recruitment (or explaining barriers to site recruitment), and therefore the strategies from the systematic review may have been more specific to addressing that research question (strategies to recruit sites).

The differences between the two studies could also be due to the different methods used. The CFIR-ERIC matching study was designed to prospectively identify strategies to facilitate cRCT delivery. These strategies were identified based on the theory behind CFIR, the ERIC compilation, and the CFIR-ERIC matching tool. The strategies were not empirically tested, and therefore it was unknown their true impact on cRCT delivery. Contrarily, strategies for site recruitment reported in the included literature were retrospectively identified in the systematic review. These were strategies that had been used by researchers for cRCT site recruitment, however, in line with the findings from the scoping review, there was a large reporting gap identified for site recruitment. The search could only identify potential literature that had

strategies reported either in the title or abstract, which may have led to the identification of literature that was not representative of cRCTs. There may have also been some reporting bias, whereby studies were more likely to report about their recruitment strategies if the authors deemed there was a large degree of success or failure associated with the strategies. Again, these strategies were not empirically tested, and their influence on site recruitment was not fully elucidated.

Utility of using theoretical frameworks throughout the dissertation

While the use of frameworks and theory in research is beneficial to facilitate the research for many reasons, including allowing for the systematic comparison of the strategies between studies[38–40], there is widespread underuse, superficial use, and misuse of theories[38,41,42]. This is thought to potentially be due to challenges in selecting from the many theories that exist within the field of implementation science[43,44].

A review by Nilsen et al. (2015) identified several classifications and intended major aims for theories, models, and frameworks in implementation science: describing the process of implementation, understanding the factors of implementation, and evaluating the process[45]. Several of the implementation theories, models, and frameworks in use have overlap between the categories, allowing for sections of each to be used to accomplish the different goals. With the vast number of potential theoretical concepts that can potentially be used, researchers may have difficulty in understanding the differences and selecting the appropriate theoretical concepts for their research[38].

Birken et al. (2017) conducted a survey of self-identified implementation scientists to explore how these researchers selected the theories in their studies[46]. The study found that there are a wide variety of theories used, with little consensus on how they are selected. Reviews by Strifler et al.[47] and Esmail et al.[48] have also concluded that while many implementation science theories, models, and frameworks have been used in studies, there is little evidence to guide researchers or to justify the use of each theory. Overall, Birken et al. concluded that researchers intending to use theory in their studies need guidance on which theories to select[46].

To guide the design of the studies in this dissertation and to analyze the data, two concepts from implementation science were used: 1) CFIR[49] – a determinant framework that can be used to systematically assess potential barriers and enablers to implementation of a trial[3], and 2) the ERIC compilation[50] – a list of discrete implementation strategies that can be used to systematically report strategies used by researchers (both retrospectively and prospectively). Using CFIR and the ERIC compilation, both with operationalized definitions for each concept, allowed for comparisons to be made between the studies identified for the literature review studies (the scoping review and the systematic review), as well as between the four studies of the dissertation.

The use of frameworks and theory in research can allow for a comparison of the implementation strategies between studies[38–40]. This was demonstrated in the literature reviews, in which all the data to answer the research questions that were extracted from the identified studies were able to be mapped to the implementation science concepts (for example scoping review, which used CFIR, and systematic review which used the ERIC compilation). Coding the data to the implementation science concepts allowed for the organization of the data in a systematic fashion,

regardless of whether the original studies had used any framework or theory for designing their intervention or implementation process.

The use of the implementation science concepts also facilitated comparisons between the four studies of the dissertation and enabled building upon the results of the studies with each subsequent chapter of the dissertation. As the sections of this dissertation arose iteratively (whereby the results of each study drove the direction of the next study in the research agenda), having implementation science concepts that allowed for the sections to be linked was beneficial to interpret the overall results of the dissertation (discussed below). Two of the studies in this dissertation used CFIR alone (scoping review, qualitative case study), one study used the ERIC compilation alone (systematic review), and one study used a combination of both CFIR and the ERIC compilation, via the CFIR-ERIC matching tool (CFIR-ERIC matching study).

The use of these frameworks facilitated the integration of the results. The results from the sections could be linked together in a comprehensible way as there were overlapping elements (for example, the CFIR coding from the scoping review and the qualitative case study). The use of the same framework (CFIR) in these two studies enabled the exploration of CFIR constructs that were not identified in the scoping review but were thought to be potentially relevant for cRCT conduct. In the scoping review, a knowledge and/or reporting gap surrounding the implementation of the cRCTs was highlighted, indicating a need to explore whether the gap was primarily due to a lack of reporting of certain concepts in the identified studies, or whether the gap was a true representation of limited importance of the domains for cRCT conduct.

While CFIR and the ERIC compilation were used in this dissertation, it is important to recognize the potential value of approaches using different implementation science concepts. CFIR can also be used in connection with another framework, the Theoretical Domains Framework[51]. Similar to the CFIR-ERIC matching tool that facilitated the identification of strategies aimed at targeting specific barriers and enablers to implementation, the TDF has also been matched to discrete implementation strategies[52]. However, as the primary use of TDF is the investigation of barriers and facilitators at the individual level, it was not used as a framework in this dissertation. The dissertation aimed to explore the barriers and enablers to conducting cRCTs at the more macro level of the hospitals, and therefore CFIR, which is often used at the organizational level level[53,54], was selected for use in combination with the ERIC compilation.

Lack of literature in this area

A lack of literature on the conduct and delivery of cRCTs in hospitals was identified throughout the studies in this dissertation. In the scoping review[1], a limited number of studies were identified, highlighting the reporting gap surrounding the delivery of the cRCTs. Much of the literature and reports in the studies is opinion-based interpretations, without empirical data. Similar to the scoping review, limited literature was identified in the systematic review of recruitment strategies. While strategies were identified that were coded to the ERIC compilation, it was not possible to discern the success or failure rates of the recruitment strategies. The primary objective of the studies included in this review was to investigate the effect of the trials' clinical intervention, and not to test the site recruitment strategies. While one of the studies did explicitly test the two site recruitment strategies, the trial was embedded within the overall cRCT[50] and was not powered or designed to formally test the different strategies

Recommendations for the conduct and delivery of cRCTs

Researchers currently lack guidance on how to optimize the delivery of cRCTs in hospitals, and lessons can be learned from this dissertation. The key recommendations derived from this thesis for how to facilitate the delivery of cRCTs in hospitals are described next, with examples of how they may be used from the BEACON trial where appropriate. The recommendations were derived by summarizing the main themes from the CFIR constructs and domains identified as barriers and enablers to cRCT conduct and delivery and from the ERIC compilation strategies associated with addressing the corresponding CFIR domains.

Identify and engage the site executive boards, local opinion leaders, champions, and formally appointed implementation leaders early in trial development.
The intended sites for inclusion in the cRCT should be contacted early, to determine their buy-in and increase engagement from the site personnel (including internal implementation leaders, opinion leaders, champions, and external change agents (for example, local community organizations)). Early engagement of a variety of personnel was an important facilitator identified for cRCT delivery[1,2,22,24,28–34,10,14,16–21]. Patients/consumers of the planned intervention and their family members should also be included in the trial development early to be able to provide their feedback and experiences and act as champions by advocating for the intended research.

Results from this dissertation indicate that the evidence from prior studies does not appear to be highly influential in facilitating a site's agreement to participate[1,2], and therefore, if a balance of timing between approaching sites early or waiting for pilot trial evidence is perceived, the early engagement of the sites should be prioritized. However, it also must be recognized that the risk of early engagement, is that key staff can leave before the trial starts due to the high turnover of personnel in the health service.

Example: In the BEACON trial, sites were contacted after the study proposal had been funded. In retrospect, while there was a limited time between announcement of the grant competition and the grant submission deadline to engage all intended sites, there may have been a higher success rate of sites participating had they been contacted sooner and been engaged throughout the study proposal development. However, while the sites randomized to receive the BEACON trial were approached after the grant was successfully awarded, there were time delays before the trial could be launched. The timing of hiring and engaging new staff had to be balanced with the timelines as they progressed (for example, not hiring a local research therapist too long in advance of enrolling patients). In several sites staff in key leadership roles who had signed off on the study and were champions left for posts in different organizations.

Promote network weaving to enable the identification of relevant personnel, including the hospital executive boards, champions, and opinion leaders[24,29–32,35]. During the planning phase, in which the sites should be approached for engagement (as described above), the coordinating site will need to identify the relevant personnel (including the hospital executive boards, champions, and opinion leaders) early in the study planning[17,20]. This can be done by using existing networks (for example, if members from the sites are already connected as part of a professional association), and by leveraging these networks to further identify who will need to be approached. Network weaving can also allow for the development of academic partnerships. Researchers with similar interests can connect through these networks to facilitate collaboration.

Example: This was demonstrated in the BEACON trial whereby the principal investigator approached and engaged the head of psychiatry at one of the intended BEACON sites at a meeting from an association in which they were both members. This person then agreed to become a co-principal investigator on the study and was engaged throughout the trial conceptualization. This also demonstrated the utility of the early engagement of members from the sites to allow them to participate in designing the trial.

Conduct a local needs assessment for the clinical area and determine the tension for change. Early in the trial design, meetings should focus on conducting needs assessments for the sites to determine whether there is a tension for change within the clinical area. Determining the perceived tension for change at a site and the alignment with the hospitals' priorities may be facilitating factors for a site's agreement to participate and actively engage in a cRCT[1,2,17].
Example: In the BEACON trial, sites were not approached before randomization to determine whether they had a perceived clinical gap in the area of men who present to the emergency department with self-harm.

Ensure there are adequate resources (including time and finances) for the sites to participate in the trial. A key barrier that was identified for a site to participate in a cRCT was a perceived limit of available resources[1,2,17,24–26], including time, personnel, finances[17,24–26], and a desire to conserve the resources that were currently available[2]. If necessary, accessing new funding may be required to be able to promote the availability of resources.

Adapt the intervention for the local site. The ability to adapt the trial for the local context was an enabler frequently identified in this dissertation to facilitate cRCT delivery [2,9–16]. Early engagement of the sites (as mentioned above) may also enable the adaptability of the trial. With support and input from the sites, plans can be made in advance to allow for site-specific adaptations, while also aiming to ensure trial validity and maintain the ability to compare the intervention across sites
Example: In the BEACON trial, the intervention was able to be adapted to the local settings of a hospital with a high proportion of indigenous patients. The intervention was tailored to include indigenous images and audio. This site would not have agreed to participate had these adaptations not been possible.

Conduct educational meetings with the sites throughout the study planning and conduct[24,32,33,35–37]. Further meetings can be educational meetings, in which members from the sites learn more about the trial and how to conduct the intervention locally. This can allow for the site members to express concerns and questions.
Example: In the BEACON trial, when a site was nearing the launch of the trial, the principal investigator and the research coordinators visited the sites in person to present their Site Initiation Visit, with prepared educational materials to train the local site staff and to answer questions.

Develop a formal plan for the delivery of the cRCT as part of the grant application. This final recommendation should aim to formally include the previously described recommendations. Explicitly planning for the delivery and the conduct of the trial can assist in identifying challenges that may arise [16,55]. A barriers and enablers assessment may be beneficial to systematically plan on how to address the challenges[56,57]. As with all parts of the study

development, engagement of relevant stakeholders should be included to facilitate the delivery of the cRCT [1,2,22,24,28–34,10,14,16–21]. This formal plan can also assist in a systematic and rigorous reporting of the methods that were used to facilitate the cRCT delivery, thereby also contributing to addressing the lack of reporting for research in this area.

While the strategies described above may already be employed to a certain extent by researchers planning or conducting cRCTs in hospitals, the recommendations provided here can assist in systematically incorporating the techniques in the trials. Future researchers may be able to explicitly include the strategies during the trial conceptualization, to facilitate the delivery of the cRCT and to optimize site recruitment.

Limitations

Limitations occurred both within the individual studies of the dissertation, as well as in the design of the dissertation as a whole. These limitations must be considered when interpreting the results, generalizability, and conclusions of the dissertation.

As previously stated, the scoping review and the systematic review concluded that there was a large reporting gap for the conduct of cRCTs in hospitals and strategies for the recruitment of sites into cRCTs in healthcare facilities. It is pertinent to recognize the limitations of this gap, as the scoping review was used to inform the subsequent studies. Some potentially relevant constructs for cRCT delivery may have been missed.

The cRCT that the coordinating team was launching experienced several challenges. The intervention of the trial was a mental health intervention that used technology, so it was unknown if this was not clear how much this unique intervention had introduced additional barriers to the trial conduct compared to other types of cRCT interventions (for example, not for mental health or not using technology). It's possible that the interview replies of the participants may have reflected specific perceptions driven by the frustrations associated with this specific trial, and that the determinants of cRCT conduct and delivery uncovered in the qualitative case study may not be generalizable to other cRCTs, and especially to other cRCTs that had fewer challenges in the launch.

The scoping review and the qualitative case study were then used to inform the identification of determinants of cRCT delivery in the CFIR-ERIC matching study. Therefore, there is the potential that CFIR constructs influential for trial delivery may have been missed in these first two studies, leading to a gap in the identification of determinants. This omission could then lead to some uncertainty in the identified strategies, whereby the strategies may not have been suited to address any missing determinants. Furthermore, if a missed determinant was relatively influential on cRCT delivery compared to some of the determinants that were identified, this may have had a large effect on identifying top strategies, as they were based on the number of many determinants for which the strategy was listed as a Level 1 strategy, then by how many determinants for which the strategy was listed as a Level 2 strategy.

These limitations were potentially mitigated by the triangulation of determinant identification by using two different study designs to identify CFIR constructs relevant for cRCT delivery. While the scoping review did inform the interview guide of the qualitative case study, other potentially relevant constructs were explored in the interviews to determine if the constructs were underreported or were truly not perceived as influential for cRCT conduct. Overall, the two

studies identified similar constructs. Furthermore, as the interviews were semi-structured (as opposed to fully structured), participants in the interviews were invited to express any other concerns or thoughts about cRCT conduct, and they were allowed freedom in their replies to discuss other aspects of the cRCT delivery (which were coded to the CFIR domains retrospectively). As the participants in the qualitative case study had direct experience with conducting cRCTs in hospitals, the potential for missing determinants was potentially lessened. As previously stated, it, however, must be cautioned that the qualitative case study was of one specific cRCT, and the findings may not be fully generalizable to other cRCTs Additionally, there may be some limitations in the use of frameworks and concepts from implementation science in general to guide the dissertation (which were used both in designing the studies as well as analyzing the data). While CFIR is a well operationalized and widely used framework, with several measures developed to assess the constructs[3,43,58], the ERIC compilation is more a novel concept, with limited empirical testing of the strategies included in the list. It must be noted that the CFIR-ERIC matching tool is recently developed, and the use of the tool in producing identifying effective strategies has yet to be thoroughly evaluated. Uncertainty remains as to the effectiveness of using these strategies for addressing the CFIR constructs to which they are matched, and further research is required. The ERIC compilation and the corresponding CFIR-ERIC matching tool were created by expert opinion rather than empirical, evidence-based methods, further adding to the caution that must be taken in interpreting the identification of the strategies.

The two literature review studies in the dissertation (the scoping review and the systematic review) used the implementation science concepts (CFIR and the ERIC compilation respectively) to retrospectively code the data extracted from the included literature, to facilitate data analysis. While frameworks can allow for comparisons between studies[44,59,60], there does remain some uncertainty when used retrospectively to analyze data as to whether the coding is accurate. None of the literature included in each of the reviews used the implementation science concepts in designing or analyzing the data in the studies. Therefore, there remains uncertainty as to whether the codes truly represent the strategies.

Using the concepts to analyze the conduct and the delivery of cRCTs was unique, as previously these frameworks have been used almost exclusively to guide and analyze the implementation of a trial. However, there may have been limitations associated with using the concepts external to their designed usage. This dissertation focused on the conduct and delivery of cRCTs, which can be thought of a separate, yet interacting process than implementation of the intervention. The focus of the dissertation was related to the methodology of conducting cRCTs, which was not the original use of CFIR and the ERIC compilation. The use of these frameworks outside of the field of implementation science has not been rigorously evaluated, and therefore their suitability in this context was unknown. Their use was however supported by being able to chart all the data from the individual studies to the CFIR and ERIC compilation as appropriate, demonstrating and supporting their practicality outside of the original use.

Additionally, it was not clear how multiple ‘systems’ within an organization were to be accounted for when applying the CFIR for identifying barriers and enablers. Change in healthcare systems can be complex and can involve multiple processes, organizations, and stakeholders, which may present challenges when attempting to assess the hospital as one healthcare system. Multiple ‘sub-units’ (for example the research ethics boards, hospital management, and information services) may each have their unique barriers and enablers, which

presents challenges to applying the CFIR to the hospital as a single unit.[61] Evaluating the hospital sites as a whole may have led to a limited view of the enablers and facilitators to the conduct and delivery of the cRCTs. Future studies should aim to further understanding of how the sub-units of an organization may affect the cRCT conduct and delivery.

Future Steps

This dissertation focused on the identification of barriers and enablers to cRCT conduct in hospitals, and the identification of potential strategies to facilitate cRCT delivery. Further studies should aim to investigate whether the results obtained from this thesis can be generalized to other cRCTs in hospitals. Case studies of a variety of other cRCT coordinating sites would be beneficial. If similar perceptions were demonstrated from other coordinating sites, the results from this study would be reinforced that the findings were generalizable. However, if there was a large discrepancy in the perceptions from other coordinating sites, this could demonstrate a limit in the generalizability of the results and a potential variation in barriers and enablers to cRCT conduct depending on each unique trial. Additionally, it would be beneficial to conduct similar interviews with members from the sites to better understand their perceptions. While this was intended as a further study for this dissertation, the limited replies from the sites made the study not feasible to continue. Gaining an understanding of what the sites perceive as barriers and enablers to the trial would allow for unique insight which could benefit the design of targeted strategies for trial conduct. Additionally, future research should aim to investigate the 'sub-units' of the hospital sites to further explore whether there are differential enablers and facilitators to cRCT conduct and delivery from within the sites.

While a list of potential strategies to facilitate cRCT delivery in hospitals was identified, these strategies were not empirically tested. The strategies identified were intended to provide a foundation for future research using the strategies and investigating their impact on the delivery of the cRCTs. Research designs such as Study Within A Study[62] can be used to further investigate the impacts of the strategies. Researchers can incorporate studies to prospectively investigate the strategies as part of the research plan.

Conclusions

While acknowledging the limitations, this dissertation provided an exploration of barriers and enablers to cRCT conduct in hospitals, as well as a foundational identification of strategies to facilitate the delivery of the trials. The dissertation included four studies: a scoping review of the conduct of cRCTs in hospitals (Chapter 2); a qualitative case study of the coordinating site staff of the BEACON cRCT (Chapter 3); a CFIR-ERIC matching study for strategies to facilitate cRCT delivery (Chapter 4); and a systematic review of reported site recruitments strategies for healthcare facilities in cRCTs (Chapter 5). The study designs and data analyses were guided by two implementation science concepts: CFIR (Chapters 1-3) and the ERIC compilation (Chapters 3 and 4).

The results from the dissertation may potentially contribute to the knowledge for facilitating cRCT delivery in hospitals while recognizing the important limitations of the thesis. Overall, the key concepts and strategies to facilitate the conduct and delivery of cRCTs in hospitals that were uncovered and prevalent across all studies were: engage and inform all relevant stakeholders (including opinion leaders, champions, and formally appointed implementations leaders) early in planning the trial, promote network weaving, conduct local needs assessments to determine

whether there is a perceived tension for change for the clinical innovation and that there are sufficient resources for the trial, ensure that the trial is adaptable to each site, provide education in the clinical innovation to the intended cRCT sites, and formally develop a blueprint for the conduct and delivery of the cRCT in the grant application.

As barriers and enablers to the delivery of cRCTs were investigated, and strategies to facilitate the delivery were explored, the results may contribute to future studies in guiding trialists while planning for their cRCT, as well as for researchers intending to explore the methodology for trial delivery by empirically testing the strategies identified in the dissertation. Researchers should aim to address the reporting gap for cRCT conduct and delivery identified by this dissertation. I hope that the results of this dissertation can be used as "lessons learned" to facilitate the research process for cRCTs in hospitals.

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APPENDICES

Appendix A:

Consolidated Framework for Implementation Research Constructs

Construct		Short Description
I. INTERVENTION CHARACTERISTICS		
A	Intervention Source	Perception of key stakeholders about whether the intervention is externally or internally developed.
B	Evidence Strength & Quality	Stakeholders' perceptions of the quality and validity of evidence supporting the belief that the intervention will have desired outcomes.
C	Relative Advantage	Stakeholders' perception of the advantage of implementing the intervention versus an alternative solution.
D	Adaptability	The degree to which an intervention can be adapted, tailored, refined, or reinvented to meet local needs.
E	Trialability	The ability to test the intervention on a small scale in the organization, and to be able to reverse course (undo implementation) if warranted.
F	Complexity	Perceived difficulty of implementation, reflected by duration, scope, radicalness, disruptiveness, centrality, and intricacy and number of steps required to implement.
G	Design Quality & Packaging	Perceived excellence in how the intervention is bundled, presented, and assembled.
H	Cost	Costs of the intervention and costs associated with implementing the intervention including investment, supply, and opportunity costs.
II. OUTER SETTING		
A	Patient Needs & Resources	The extent to which patient needs, as well as barriers and facilitators to meet those needs, are accurately known and prioritized by the organization.
B	Cosmopolitanism	The degree to which an organization is networked with other external organizations.
C	Peer Pressure	Mimetic or competitive pressure to implement an intervention; typically because most or other key peer or competing organizations have already implemented or are in a bid for a competitive edge.
D	External Policy & Incentives	A broad construct that includes external strategies to spread interventions, including policy and regulations (governmental or other central entity), external mandates, recommendations and guidelines, pay-for-performance, collaboratives, and public or benchmark reporting.
III. INNER SETTING		
A	Structural Characteristics	The social architecture, age, maturity, and size of an organization.

B	Networks & Communications	The nature and quality of webs of social networks and the nature and quality of formal and informal communications within an organization.
C	Culture	Norms, values, and basic assumptions of a given organization.
D	Implementation Climate	The absorptive capacity for change, shared receptivity of involved individuals to an intervention, and the extent to which use of that intervention will be rewarded, supported, and expected within their organization.
1	Tension for Change	The degree to which stakeholders perceive the current situation as intolerable or needing change.
2	Compatibility	The degree of tangible fit between meaning and values attached to the intervention by involved individuals, how those align with individuals' own norms, values, and perceived risks and needs, and how the intervention fits with existing workflows and systems.
3	Relative Priority	Individuals' shared perception of the importance of the implementation within the organization.
4	Organizational Incentives & Rewards	Extrinsic incentives such as goal-sharing awards, performance reviews, promotions, and raises in salary, and less tangible incentives such as increased stature or respect.
5	Goals and Feedback	The degree to which goals are clearly communicated, acted upon, and fed back to staff, and alignment of that feedback with goals.
6	Learning Climate	A climate in which: a) leaders express their own fallibility and need for team members' assistance and input; b) team members feel that they are essential, valued, and knowledgeable partners in the change process; c) individuals feel psychologically safe to try new methods; and d) there is sufficient time and space for reflective thinking and evaluation.
E	Readiness for Implementation	Tangible and immediate indicators of organizational commitment to its decision to implement an intervention.
1	Leadership Engagement	Commitment, involvement, and accountability of leaders and managers with the implementation.
2	Available Resources	The level of resources dedicated for implementation and on-going operations, including money, training, education, physical space, and time.
3	Access to Knowledge & Information	Ease of access to digestible information and knowledge about the intervention and how to incorporate it into work tasks.
IV. CHARACTERISTICS OF INDIVIDUALS		
A	Knowledge & Beliefs about the Intervention	Individuals' attitudes toward and value placed on the intervention as well as familiarity with facts, truths, and principles related to the intervention.
B	Self-efficacy	Individual belief in their own capabilities to execute courses of action to achieve implementation goals.

C	Individual Stage of Change	Characterization of the phase an individual is in, as he or she progresses toward skilled, enthusiastic, and sustained use of the intervention.
D	Individual Identification with Organization	A broad construct related to how individuals perceive the organization, and their relationship and degree of commitment with that organization.
E	Other Personal Attributes	A broad construct to include other personal traits such as tolerance of ambiguity, intellectual ability, motivation, values, competence, capacity, and learning style.
V. PROCESS		
A	Planning	The degree to which a scheme or method of behavior and tasks for implementing an intervention are developed in advance, and the quality of those schemes or methods.
B	Engaging	Attracting and involving appropriate individuals in the implementation and use of the intervention through a combined strategy of social marketing, education, role modeling, training, and other similar activities.
1	Opinion Leaders	Individuals in an organization who have formal or informal influence on the attitudes and beliefs of their colleagues with respect to implementing the intervention.
2	Formally Appointed Internal Implementation Leaders	Individuals from within the organization who have been formally appointed with responsibility for implementing an intervention as coordinator, project manager, team leader, or other similar role.
3	Champions	"Individuals who dedicate themselves to supporting, marketing, and 'driving through' an [implementation]" [101] (p. 182), overcoming indifference or resistance that the intervention may provoke in an organization.
4	External Change Agents	Individuals who are affiliated with an outside entity who formally influence or facilitate intervention decisions in a desirable direction.
C	Executing	Carrying out or accomplishing the implementation according to plan.
D	Reflecting & Evaluating	Quantitative and qualitative feedback about the progress and quality of implementation accompanied with regular personal and team debriefing about progress and experience.

Appendix B:

The Expert Recommendations for Implementing Change compilation

Strategy	Definitions
Access new funding	Access new or existing money to facilitate the implementation
Alter incentive/allowance structures	Work to incentivize the adoption and implementation of the clinical innovation
Alter patient/consumer fees	Create fee structures where patients/consumers pay less for preferred treatments (the clinical innovation) and more for less-preferred treatments
Assess for readiness and identify barriers and facilitators	Assess various aspects of an organization to determine its degree of readiness to implement, barriers that may impede implementation, and strengths that can be used in the implementation effort
Audit and provide feedback	Collect and summarize clinical performance data over a specified time period and give it to clinicians and administrators to monitor, evaluate, and modify provider behavior
Build a coalition	Recruit and cultivate relationships with partners in the implementation effort
Capture and share local knowledge	Capture local knowledge from implementation sites on how implementers and clinicians made something work in their setting and then share it with other sites
Centralize technical assistance	Develop and use a centralized system to deliver technical assistance focused on implementation issues
Change accreditation or membership requirements	Strive to alter accreditation standards so that they require or encourage use of the clinical innovation. Work to alter membership organization requirements so that those who want to affiliate with the organization are encouraged or required to use the clinical innovation
Change liability laws	Participate in liability reform efforts that make clinicians more willing to deliver the clinical innovation
Change physical structure and equipment	Evaluate current configurations and adapt, as needed, the physical structure and/or equipment (*e.g.*, changing the layout of a room, adding equipment) to best accommodate the targeted innovation
Change record systems	Change records systems to allow better assessment of implementation or clinical outcomes
Change service sites	Change the location of clinical service sites to increase access
Conduct cyclical small tests of change	Implement changes in a cyclical fashion using small tests of change before taking changes system-wide. Tests of change benefit from systematic measurement, and results of the tests of change are studied for insights on how to do better. This process continues serially over time, and refinement is added with each cycle
Conduct educational meetings	Hold meetings targeted toward different stakeholder groups (*e.g.*, providers, administrators, other organizational stakeholders, and community, patient/consumer, and family stakeholders) to teach them about the clinical innovation

Conduct educational outreach visits	Have a trained person meet with providers in their practice settings to educate providers about the clinical innovation with the intent of changing the provider's practice
Conduct local consensus discussions	Include local providers and other stakeholders in discussions that address whether the chosen problem is important and whether the clinical innovation to address it is appropriate
Conduct local needs assessment	Collect and analyze data related to the need for the innovation
Conduct ongoing training	Plan for and conduct training in the clinical innovation in an ongoing way
Create a learning collaborative	Facilitate the formation of groups of providers or provider organizations and foster a collaborative learning environment to improve implementation of the clinical innovation
Create new clinical teams	Change who serves on the clinical team, adding different disciplines and different skills to make it more likely that the clinical innovation is delivered (or is more successfully delivered)
Create or change credentialing and/or licensure standards	Create an organization that certifies clinicians in the innovation or encourage an existing organization to do so. Change governmental professional certification or licensure requirements to include delivering the innovation. Work to alter continuing education requirements to shape professional practice toward the innovation
Develop a formal implementation blueprint	Develop a formal implementation blueprint that includes all goals and strategies. The blueprint should include the following: 1) aim/purpose of the implementation; 2) scope of the change (*e.g.*, what organizational units are affected); 3) timeframe and milestones; and 4) appropriate performance/progress measures. Use and update this plan to guide the implementation effort over time
Develop academic partnerships	Partner with a university or academic unit for the purposes of shared training and bringing research skills to an implementation project
Develop an implementation glossary	Develop and distribute a list of terms describing the innovation, implementation, and stakeholders in the organizational change
Develop and implement tools for quality monitoring	Develop, test, and introduce into quality-monitoring systems the right input—the appropriate language, protocols, algorithms, standards, and measures (of processes, patient/consumer outcomes, and implementation outcomes) that are often specific to the innovation being implemented
Develop and organize quality monitoring systems	Develop and organize systems and procedures that monitor clinical processes and/or outcomes for the purpose of quality assurance and improvement
Develop disincentives	Provide financial disincentives for failure to implement or use the clinical innovations
Develop educational materials	Develop and format manuals, toolkits, and other supporting materials in ways that make it easier for stakeholders to learn about the innovation and for clinicians to learn how to deliver the clinical innovation
Develop resource sharing agreements	Develop partnerships with organizations that have resources needed to implement the innovation

Distribute educational materials	Distribute educational materials (including guidelines, manuals, and toolkits) in person, by mail, and/or electronically
Facilitate relay of clinical data to providers	Provide as close to real-time data as possible about key measures of process/outcomes using integrated modes/channels of communication in a way that promotes use of the targeted innovation
Facilitation	A process of interactive problem solving and support that occurs in a context of a recognized need for improvement and a supportive interpersonal relationship
Fund and contract for the clinical innovation	Governments and other payers of services issue requests for proposals to deliver the innovation, use contracting processes to motivate providers to deliver the clinical innovation, and develop new funding formulas that make it more likely that providers will deliver the innovation
Identify and prepare champions	Identify and prepare individuals who dedicate themselves to supporting, marketing, and driving through an implementation, overcoming indifference or resistance that the intervention may provoke in an organization
Identify early adopters	Identify early adopters at the local site to learn from their experiences with the practice innovation
Increase demand	Attempt to influence the market for the clinical innovation to increase competition intensity and to increase the maturity of the market for the clinical innovation
Inform local opinion leaders	Inform providers identified by colleagues as opinion leaders or "educationally influential" about the clinical innovation in the hopes that they will influence colleagues to adopt it
Develop academic partnerships	Partner with a university or academic unit for the purposes of shared training and bringing research skills to an implementation project
Develop an implementation glossary	Develop and distribute a list of terms describing the innovation, implementation, and stakeholders in the organizational change
Intervene with patients/consumers to enhance uptake and adherence	Develop strategies with patients to encourage and problem solve around adherence
Involve executive boards	Involve existing governing structures (*e.g.*, boards of directors, medical staff boards of governance) in the implementation effort, including the review of data on implementation processes
Involve patients/consumers and family members	Engage or include patients/consumers and families in the implementation effort
Make billing easier	Make it easier to bill for the clinical innovation
Make training dynamic	Vary the information delivery methods to cater to different learning styles and work contexts, and shape the training in the innovation to be interactive
Mandate change	Have leadership declare the priority of the innovation and their determination to have it implemented
Model and simulate change	Model or simulate the change that will be implemented prior to implementation

Obtain and use patients/consumers and family feedback	Develop strategies to increase patient/consumer and family feedback on the implementation effort
Obtain formal commitments	Obtain written commitments from key partners that state what they will do to implement the innovation
Organize clinician implementation team meetings	Develop and support teams of clinicians who are implementing the innovation and give them protected time to reflect on the implementation effort, share lessons learned, and support one another's learning
Place innovation on fee for service lists/formularies	Work to place the clinical innovation on lists of actions for which providers can be reimbursed (*e.g.*, a drug is placed on a formulary, a procedure is now reimbursable)
Prepare patients/consumers to be active participants	Prepare patients/consumers to be active in their care, to ask questions, and specifically to inquire about care guidelines, the evidence behind clinical decisions, or about available evidence-supported treatments
Promote adaptability	Identify the ways a clinical innovation can be tailored to meet local needs and clarify which elements of the innovation must be maintained to preserve fidelity
Promote network weaving	Identify and build on existing high-quality working relationships and networks within and outside the organization, organizational units, teams, etc. to promote information sharing, collaborative problem-solving, and a shared vision/goal related to implementing the innovation
Provide clinical supervision	Provide clinicians with ongoing supervision focusing on the innovation. Provide training for clinical supervisors who will supervise clinicians who provide the innovation
Provide local technical assistance	Develop and use a system to deliver technical assistance focused on implementation issues using local personnel
Provide ongoing consultation	Provide ongoing consultation with one or more experts in the strategies used to support implementing the innovation
Purposely re-examine the implementation	Monitor progress and adjust clinical practices and implementation strategies to continuously improve the quality of care
Recruit, designate, and train for leadership	Recruit, designate, and train leaders for the change effort
Remind clinicians	Develop reminder systems designed to help clinicians to recall information and/or prompt them to use the clinical innovation
Revise professional roles	Shift and revise roles among professionals who provide care, and redesign job characteristics
Shadow other experts	Provide ways for key individuals to directly observe experienced people engage with or use the targeted practice change/innovation
Stage implementation scale up	Phase implementation efforts by starting with small pilots or demonstration projects and gradually move to a system wide rollout
Start a dissemination organization	Identify or start a separate organization that is responsible for disseminating the clinical innovation. It could be a for-profit or non-profit organization
Tailor strategies	Tailor the implementation strategies to address barriers and leverage facilitators that were identified through earlier data collection

Use advisory boards and workgroups	Create and engage a formal group of multiple kinds of stakeholders to provide input and advice on implementation efforts and to elicit recommendations for improvements
Use an implementation advisor	Seek guidance from experts in implementation
Use capitated payments	Pay providers or care systems a set amount per patient/consumer for delivering clinical care
Use data experts	Involve, hire, and/or consult experts to inform management on the use of data generated by implementation efforts
Use data warehousing techniques	Integrate clinical records across facilities and organizations to facilitate implementation across systems
Use mass media	Use media to reach large numbers of people to spread the word about the clinical innovation
Use other payment schemes	Introduce payment approaches (in a catch-all category)
Use train-the-trainer strategies	Train designated clinicians or organizations to train others in the clinical innovation
Visit other sites	Visit sites where a similar implementation effort has been considered successful
Work with educational institutions	Encourage educational institutions to train clinicians in the innovation

Appendix C:

Scoping review, Chapter 2 – Protocol for Scoping Review

Implementation of Cluster Randomized Control Trials in Hospitals: *A Protocol for a Scoping Review of Current Literature*

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BACKGROUND

Cluster Randomized Control Trials: Randomized control trials (RCT) are often deemed the "gold" standard of research[1]. Large scale RCTs are increasingly being conducted as a research method[2]. These multi-centre trials have the potential for larger generalizability of results, as well as the possibility of larger recruitment than what may be possible from a single site. While multi-centre trials offer advantages, they also present some challenges to organization of the trials[2]. These tend to be more complex and involve more personnel than what would be required for a single-site trial.

Multiple committees are often required in order to facilitate the research[2,3]. This may include a steering committee to oversee design and conduct, a data safety monitoring board to monitor trial safety and effectiveness, and adjudication committees to review end data to ensure the objectives of the study are met. Large scale trials also require detailed administration and documentation to ensure that the trials are properly conducted[3]. Coordination of this is generally conducted through the main trial personnel, who oversee the overall study management, including randomization, monitoring of sites and centralized data management. This centre ensures the trial is initiated and the protocol is followed at the sites.

Research Waste: Global funding in biomedical research was estimated at $240 billion USD in 2010[4]. This funding has allowed for important scientific discoveries in health sciences[4,5]. Despite the large advancements, much of the investment and research does not lead to any important findings. This can be due to hypothesis not holding true or producing the anticipated results, a largely justifiable and expected outcome in the research process. Alternatively, this lack of results may be due improper planning, research design or lack of an effective research team, leading to what is known as research waste.

Research waste is a large concern in biomedical research[4]. In 2014, the Lancet produced a five-paper series outlining the sources and providing recommendations on how to reduce this ongoing problem[4,6–9]. This series outlined various stages of the research process in which waste can occur, including setting priorities, design and conduct, regulation and management, accessibility and reporting.

Inefficient management of research and bureaucracy is a key focus of concern for research waste[7]. While these bureaucratic rules and regulations are necessary to facilitate proper research, there are some disadvantages. Multiple layers of regulation for research studies are in place, potentially leading to long delays, increased costs and abandonment of the research[10]. At the level of the ethics reviewal, committees may miss the opportunity to question unnecessary research, or put additional demands on the investigators leading to abandonment of a study[10,11].The research team is crucial in organization of the study[2]. A team must be able to communicate with and navigate these levels to ensure the study is effectively conducted[12,13]

Implementation Research: Implementation science is the systematic study of how to better achieve uptake of research into healthcare[14]. The use of theory in implementation research is beneficial in allowing for cross-disciplinary research, comparison of implementation strategies in various studies, systematic evaluation of the strategy and understanding of the underlying concepts of the implementation[15,16].

The use of theoretical frameworks in can be of great benefit to the implementation of evidence based research[17]. They allow for the more rigorous design of interventions, comparisons of results between studies and identification of successful factors in an intervention by enabling the comparison between studies[18–20]. When no framework is used, there is difficulty in comparing studies, and uncertainty as to whether comprehensive methods were used to identify all relevant aspects. Unfortunately, in accordance with all stages of implementation work, theory has seldom been used in the design of interventions targeted at changing behaviour in healthcare[15,21].

The Consolidate Framework for Implementation Research: The Consolidated Framework for Implementation Research (CFIR) is a recently introduced framework for use in implementation science[22]. This is a meta-theoretical framework, developed using previously published research to provide a guide for implementation of interventions. It is touted as comprehensive framework that organizes commonalities and overlapping themes from various theories and concepts of implementation science. The framework organizes 39 constructs into five domains: 1) characteristics of the intervention, 2) outer settings (eg. economic, social and political context of an organization), 3) inner settings (eg. structural, political and cultural context of the implementation), 4) individuals involved with the process, and 5) the implementation process. Barriers and facilitators to implementation may be evaluated within each of the domains[23].

The CFIR may be used as a guiding framework for development of an implementation strategy, as well as for evaluation of the implementation[22]. It is beneficial in providing guidance for the larger process of an implementation study. While it does provide details on barriers and facilitators at multiple levels, the CFIR has been used and tested more systematically with an organization being the unit of study rather than the individual[23–25].

Goals:

The objective of this review will be to answer the following research question:

What is the current knowledge and evidence surrounding the implementation of cluster randomized control trials in hospitals?

There has yet to be a scoping review performed regarding the literature surrounding implementation of cluster RCTs in hospitals. A systematic review evaluating components of implementation in hospital cluster RCTs with multifaceted interventions with evidence of efficacy identified components cited as part of interventions in 46 included studies[26]. This study identified nine implementation components: leadership, barrier identification, tailoring to context, patient involvement, communication, education, supportive supervisor, provision of resources, and audit and feedback. Despite these initial studies, more work is necessary to get a better understanding of the literature and identify any potential knowledge gaps.

Purpose: This study will potentially help to supplement and understand the existing literature for implementation of cluster randomized trials. It will also help to map current literature onto a framework frequently cited in implementation research. The review will include literature identified through qualitative and quantitative studies, as well as any previously published reviews in the field. This may lead to improved implementation of cluster RCTs in hospitals. Additionally, the review will serve to inform the design of further study for evaluating

the implementation of a cluster RCT by highlighting some potential constructs to refine the interview guide.

Table 1: Description of PCC statement

Criteria	Description
Population	The population of study are administrators and decision makers within the hospitals.
Concept	The "intervention" of interest is elements related to implementation of cluster randomized control trials in hospitals. The hospitals are the units that are randomized.
Context	The context is cluster RCTs with hospitals as the unit of randomization. This may include studies from various healthcare fields.
Outcome	The outcomes will be descriptive.
Study Design	Study design for inclusion will be review articles, editorials, guidelines, randomized control trials (RCTs), cohort studies, cross sectional studies and qualitative research designs.

Methods:

Eligibility criteria

Population: The population of study are administrators and decision makers within the hospitals. It may include research groups and organizations who are implementing clinical control trials in the hospitals.

Concept: The "intervention" of interest is elements related to implementation of cluster randomized control trials in hospitals. The hospitals are the units that are randomized. Key to this review is that the interest is in the implementation of the clinical control trial, not the intervention of the clinical control trial itself.

Context: The context is cluster RCTs with hospitals as the unit of randomization. This may include studies from various healthcare fields.

Study design: Study design for inclusion will be review articles, editorials, guidelines, randomized control trials (RCTs), cohort studies, cross sectional studies and qualitative research designs. Protocols will not be included.

Settings: There will be no restrictions based on study settings:

Language: There will be no restrictions based on language.

Year: There will be no restrictions based on year of publication.

Publication Status: There will be no restrictions based on publication status.

Search Strategy

The scoping review search methodology Arksey & O'Malley (2002)[27] and modified by Levac et al. (2010)[28] will be used. A comprehensive literature search will be conducted of MEDLINE, EMBASE and PsychINFO. The search strategy has been developed with the guidance of the

University of Ottawa Health Science library services [Appendix F]. The vocabulary and syntax were developed in MEDLINE and adjusted and applied to the other databases. Medical subject headings (MeSH) terms were specified and supplemented as needed. Hand searching of the literature will be conducted from the references of relevant articles as well. Grey literature will be hand searched in appropriate organization sites (ie. Clinical Trials Ontario, Canadian Institute of Health Research, Canadian Foundation for Healthcare Improvement, etc.).

Data Management

Articles collected from the literature search will be exported to and managed in Mendeley[29]. Results will be de-duplicated prior to abstract and full text-screening. Articles will be exported to Covidence[30] for screening and data extraction.

Selection Process

Screening will be performed at both the title/abstract level and full text level. Two independent reviewers will screen a 20% random sample of studies at each level. If reviewer agreement is at 80% or greater, one reviewer will screen the remaining studies for selection. If agreement is lower than 80%, the screening will be calibrated between the reviewers, and both reviewers will screen the remainder of studies at each level. Conflicts will be resolved by consensus, or by consultation with a third person as required. Results of the screening will be displayed in a Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram[31] with explanations for full text exclusions.

Data Collection

The publications will be classified according to empirical papers, review papers and grey literature. A data extraction form will be made to simplify the data collection process and to ensure that all relevant data is collected [Appendix G]. This form will be converted into a Microsoft Excel spreadsheet. Extraction forms will be tested independently by the two reviewers on a random sample of 5 articles and adjusted iteratively as required. Two independent reviewers will extract from a 20% random sample of studies. If reviewer agreement is at 80% or greater, one reviewer will extract from the remaining studies. If agreement is lower than 80%, the extraction will be calibrated between the reviewers, and both reviewers will extract from the remainder of studies at. Conflicts will be resolved by consensus, or by consultation with a third person as required.

The following information below will be collected from all selected literature. As previously stated, and is common of scoping reviews due to its iterative nature, additional information will be collected as deemed appropriate:

- Publication classification
- Study information: Authors, year of publication, journal info, sources of funding and publication status
- Study characteristics: Study design, country, study period, implementation framework used (if any), sample size, inclusion and exclusion criteria, funding,
- Hospital characteristics: Location of hospital, department, health worker type (eg, physician, nurse, etc.)
- Intervention characteristics: Type of clinical trials to be implemented, field of study (eg. Mental health, emergency, orthopedics)

- Study Objectives
- Key conclusions from authors
- Miscellaneous comments from authors
- References to other relevant studies

Data Analysis

Data will be analysed using the CFIR. Implementation frameworks can be used to provide guidance in a review. Previous studies, in both the quantitative and qualitative methods, have concluded that the barriers and facilitators identified using frameworks for assessment are consistent with previous literature in which non-theory based assessments were performed[32,33]. The use of these frameworks in reviews could allow for the implementation strategies identified, regardless of whether the study was theory-driven or not, to be classified and better understood, consistent with the advocacy for the frameworks as previously described. It can also allow for a determination of whether previously published studies identified in the search thoroughly planned the implementation process, by determining whether the study methods were sufficient to encompass assessment of all the key domains of the framework[17].

The CFIR has most often been used to investigate interventions retrospectively, as is inherently the case of reviews, and has been shown to be adequate in classifying many of the implementation concepts identified[34,35]. The CFIR is not only intended as a framework for assessment of barriers and facilitators, but instead as an encompassing framework for interventions. It can be applied to any part of the intervention process[36], and therefore will be useful for investigating implementation of clinical trials. The trial will be treated as the "intervention' in this analysis.

Data will be analyzed using directed content analysis[37]. The information from the data extraction will be classified into domains. The CFIR domains will inform the coding, and two independent coders will be used. The CFIR website also provides additional guidance for coding and will be consulted. Domains can be deemed relevant if they are either frequently mentioned, have conflicting views, or may strongly influence the behaviour[38,39].

Quality assurance

The protocol has been developed using Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 checklist[40], which is recommended for use in scoping review protocols while the PRISMA-SR, a modified version for scoping reviews is in development[41]. Any modifications to the protocol will be reported and justified and included in the final report.

PRISMA-P 2015 checklist[40]

Y=Yes, N=No, N/A=Not Applicable

<u>Administrative Information</u>

1. Title:
    a. Identification: Identify the report as a protocol of a systematic review [Y]
    b. If the protocol is for an update of a previous systematic review, identify as such [N/A]

2. Registration: If registered, provide the name of the registry and registration number [N/A – will be registered in PROSPERO]

3. Authors:

    a. Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author [Y]
    b. Describe contributions of protocol authors and identify the guarantor of the review. [Y]

4. Amendments: If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments [Y]

5. Support: [to be addressed in subsequent version of the protocol]

    a. Indicate sources of financial support for the review
    b. Provide the name of the review funder and/or sponsor
    c. Describe the roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol

<u>Introduction</u>

6. Rationale: Describe the rationale for the review in the context of what is already known [Y]

7. Objectives: Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO) [Y – PCC as is scoping review]

<u>Methods</u>

8. Eligibility Criteria: Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review [Y]

9. Information Sources: Describe all intended information sources (such as electronic database, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage [Y]

10. Search Strategy: Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated [Y]

11. Study Records:

    a. Data Management: describe the mechanism(s) that will be used to manage records and data throughout the review [Y]
    b. Selection Process: State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis) [Y]
    c. Data Collection Process: Described planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators [Y]

12. Data Items: List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications [Y]

13. Outcomes and Prioritization: List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale [Y]
14. Risk of Bias in Individual Studies: Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis [N/A – scoping review]
15. Data Synthesis:
    a. Describe criteria under which study data will be quantitatively synthesized [N/A]
    b. If data are appropriately for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency [N/A]
    c. Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression) [N/A]
    d. If quantitative synthesis is not appropriate, describe the type of summary planned [Y]
16. Meta-bias(es): Specify any planned assessment of meta-bias(es) (such as publication bias, selective outcome reporting within studies) [N/A]
17. Confidence in Cumulative Evidence: Describe how the strength of the body of evidence will be assessed (such as GRADE) [N/A]

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Appendix D:

Scoping review, Chapter 2 – Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	5
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	5
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	6
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	7
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	7
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Additional File 2

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	8
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	8
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	n/a
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	9
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	Figure 1
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	10
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	n/a
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	10-13
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	Table 2
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review	15-17

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
		questions and objectives, and consider the relevance to key groups.	
Limitations	20	Discuss the limitations of the scoping review process.	17
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	17-18
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	19

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

Appendix E:

Scoping review, Chapter 2 – Search strategy

MEDLINE

1. exp randomized controlled trial/
2. exp Randomized Controlled Trials as Topic/
3. (randomized or randomised).ti,ab.
4. placebo.ti,ab.
5. randomly.ti,ab.
6. trial.ti,ab.
7. groups.ti,ab.
8. exp cluster analysis/
9. cluster*.ti,ab.
10. 8 or 9
11. 1 or 2 or 3 or 4 or 5 or 6 or 7
12. 10 and 11
13. exp Hospitals/
14. (hospital or hospitals).ti,ab.
15. ((healthcare or health care) adj3 facilit*).ti,ab.
16. 13 or 14 or 15
17. exp Health Knowledge, Attitudes, Practice/
18. exp Translational Medical Research/
19. exp Knowledge Management/
20. "diffusion of innovation"/
21. implement*.ti,ab.
22. disseminat*.ti,ab.
23. ((knowledge or research or evidence) adj2 translat*).ti,ab.
24. ((knowledge or research or evidence) adj2 exchang*).ti,ab.
25. ((knowledge or research or evidence) adj2 utili*).ti,ab.
26. ((knowledge or research or evidence) adj2 transf*).ti,ab.
27. ((knowledge or research or evidence) adj2 diffus*).ti,ab.
28. ((knowledge or research or evidence) adj2 uptake).ti,ab.
29. ((knowledge or research or evidence) adj2 dissemina*).ti,ab.
30. 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
31. 12 and 16 and 30

Appendix F:

Scoping review, Chapter 2 – PRESS Review of Search strategy

PRESS Guideline — Search Submission & Peer Review Assessment

SEARCH SUBMISSION: THIS SECTION TO BE FILLED IN BY THE SEARCHER

Searcher: Arielle Weir	Email:
Date submitted: July 31, 2018	Date requested by: A week if possible [Maximum = 5 working days]

Systematic Review Title:

Implementation of Cluster Randomized Control Trials in Hospitals: *A Scoping Review of Current Literature*

This search strategy is…

☒	My PRIMARY (core) database strategy — First time submitting a strategy for search question and database
☐	My PRIMARY (core) strategy — Follow-up review NOT the first time submitting a strategy for search question and database. If this is a response to peer review, itemize the changes made to the review suggestions
☐	SECONDARY search strategy— First time submitting a strategy for search question and database
☐	SECONDARY search strategy — NOT the first time submitting a strategy for search question and database. If this is a response to peer review, itemize the changes made to the review suggestions

Database
(i.e., MEDLINE, CINAHL…): [mandatory]

Medline

Interface
(i.e., Ovid, EBSCO…): [mandatory]

Ovid

Research Question
(Describe the purpose of the search) [mandatory]

What is the current knowledge and evidence surrounding the implementation of cluster randomized control trials in hospitals

PICO Format
(Outline the PICOs for your question — i.e., Patient, Intervention, Comparison, Outcome, and Study Design — as applicable)

P	
I	

C	
O	
S	

**PCC as it is a scoping review

Population	The population of study is open and broad.
Concept	The "intervention" of interest is implementation of cluster randomized control trials in hospitals. The hospitals are the units that are randomized.
Context	The context is open and broad

Inclusion Criteria
(List criteria such as age groups, study designs, etc., to be included) [optional]

Exclusion Criteria
(List criteria such as study designs, date limits, etc., to be excluded) [optional]

No exclusion criteria

Was a search filter applied?
Yes ☒ No ☐

If YES, which one(s) (e.g., Cochrane RCT filter, PubMed Clinical Queries filter)? Provide the source if this is a published filter. [mandatory if YES to previous question]

Abridged search filters for RCTs from Cochrane

Other notes or comments you feel would be useful for the peer reviewer? [optional]

Please copy and paste your search strategy here, exactly as run, including the number of hits per line. [mandatory]

1. exp randomized controlled trial/ 465589
2. exp Randomized Controlled Trials as Topic/ 119669
3. (randomized or randomised).ti,ab. 536775
4. placebo.ti,ab. 195778
5. randomly.ti,ab. 295377
6. trial.ti,ab. 510021
7. groups.ti,ab. 1843027
8. exp cluster analysis/ 59112

9. cluster*.ti,ab. 315652

10. 8 or 9 343781

11. 1 or 2 or 3 or 4 or 5 or 6 or 7 2703123

12. 10 and 11 57565

13. exp Hospitals/ 253424

14. (hospital or hospitals).ti,ab. 987583

15. ((healthcare or health care) adj3 facilit*).ti,ab. 11820

16. 13 or 14 or 15 1099284

17. "diffusion of innovation"/ 16516

18. implement*.ti,ab. 398673

19. disseminat*.ti,ab. 110447

20. ((knowledge or research or evidence) adj2 translat*).ti,ab. 15299

21. ((knowledge or research or evidence) adj2 exchang*).ti,ab. 1277

22. ((knowledge or research or evidence) adj2 utili*).ti,ab. 4966

23. ((knowledge or research or evidence) adj2 transf*).ti,ab. 4975

24. ((knowledge or research or evidence) adj2 uptake).ti,ab. 920

25. 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 536017

26. 12 and 16 and 25 678

PEER REVIEW ASSESSMENT: THIS SECTION TO BE FILLED IN BY THE REVIEWER

Reviewer: Lindsey Sikora	Email: [redacted]	Date completed: August 10, 2018

1. TRANSLATION

A --No revisions	☐
B -- Revision(s) suggested	☐
C -- Revision(s) required	☐

If "B" or "C," please provide an explanation or example:

2. BOOLEAN AND PROXIMITY OPERATORS

A --No revisions	☐

B -- Revision(s) s	☐
C -- Revision(s) required	☐

If "B" or "C," please provide an explanation or example:

3. SUBJECT HEADINGS

A --No revisions	☐
B -- Revision(s) suggested	☐
C -- Revision(s) required	☐

If "B" or "C," please provide an explanation or example:
I would suggest adding the MeSH **Health Knowledge, Attitudes, Practice/**, **Translational Medical Research/** and **Knowledge Management/**, as they all deal with aspects of implementation. You can search the MeSH database on PubMed to verify their definitions, if you like: https://www.ncbi.nlm.nih.gov/mesh

4. TEXT WORD SEARCHING

A --No revisions	☐
B -- Revision(s)suggested	☐
C -- Revision(s) required	☐

If "B" or "C," please provide an explanation or example:

I would suggest adding knowledge diffusion and knowledge dissemination as keywords to search as well.

((knowledge or research or evidence) adj2 diffus*).ti,ab.

((knowledge or research or evidence) adj2 dissemina*).ti,ab.

5. SPELLING, SYNTAX, AND LINE NUMBERS

A --No revisions	☐
B -- Revision(s)suggested	☐
C -- Revision(s) required	☐

If "B" or "C," please provide an explanation or example:

6. LIMITS AND FILTERS

A --No revisions	☐
B -- Revision(s) suggested	☐
C -- Revision(s) required	☐

If “B” or “C,” please provide an explanation or example:

OVERALL EVALUATION (Note: If one or more “revision required” is noted above, the response below must be “revisions required”.)

A --No revisions	□
B -- Revision(s) suggested	□
C -- Revision(s) required	□

Additional comments:

Appendix G:

Scoping review, Chapter 2 – Data Extraction Form

Reviewer Initials:

Study ID:

Study Title:

Publication classification:

Study information

Author(s):

Year:

Journal, Volume, Page Number:

Publication Status:

Study Characteristics

Characteristic	
Study design	
Country	
Settings	
Study period	
Study Objective	
Implementation Framework used?	
Sample size	
Inclusion/exclusion criteria	
Funding	
Ethics Approval	

Hospital Characteristics

Location of hospitals	
Department	

Health Worker Type Targeted	
Miscellaneous hospital information	

Intervention Characteristics

Type of clinical trial implemented	
Field of study	
Components of the intervention	

Miscellaneous

Key points about the implementation of the RCT	
Key Conclusions about the study	
Miscellaneous comments from authors	
References to other relevant studies	

Appendix H:

Qualitative case study, Chapter 3 – Ethics Approval from the Ottawa Hospital Research Institute

The Ottawa Hospital RESEARCH INSTITUTE | L'Hôpital d'Ottawa INSTITUT DE RECHERCHE

December 07, 2018

Dr. Simon Hatcher

The Ottawa Hospital - General Campus Liaison Psychiatry Mental Health Unit 501 Smyth Road, 4th Floor, Main Block Ottawa, Ontario K1Z 7K4

Re: OHRI Institutional Approval for Ottawa Health Science Network Research Ethics Board (OHSN-REB) Submission

20180835-01H;

Evaluation of Barriers and Facilitators to Implementation of the BEACON Multi-Centre Cluster Randomized Control Trial

Dear Dr. Simon Hatcher,

This letter serves as **Ottawa Hospital Research Institute (OHRI)** Institutional Approval for the above-referenced study. Please maintain this documentation in your investigator study file.

Based on the information you provided about this study through the Clinical Research Registration Form, you have satisfied the requirements for institutional (OHRI) approval. This includes initial research ethics approval by OHSN-REB, appropriate departmental/service area notifications and execution (fully signed versions) of all agreement(s) required to begin the study locally. Please note there may be additional agreement(s) pending execution that are required to send funds, samples, or data to external sites, but are not required for you to begin your study locally.

Changes and/or additions to your study that may require additional agreement(s) or revisions to existing agreement(s) must be communicated to the OHRI Contracts Office. This should be undertaken simultaneously with any related OHSN-REB amendment submission.

Changes and/or additions to your study that affect various hospital/institution departments (e.g., pharmacy, Department of Medical Imaging, EORLA, EEG, etc.) must be communicated to the relevant departments.

As mentioned in the 'Response' tab of the Ethics application, you have 3 months from the date of initial OHSN-REB approval to submit French documents including the translation certificate to OHSN-REB through the Translated Documents section of the ethics application (if applicable).

Should you have any questions, please contact REBadministration@ohri.ca or 613-798-5555 extension 16719.

Nancy Camack, BScN RN MBA CCRP
Director, Clinical Research Administration
Ottawa Hospital Research Institute | Institut de recherche de l'Hôpital d'Ottawa

Civic Campus, Box 675, 725 Parkdale Avenue, Ottawa, Ontario, K1Y 4E9
613-798-5555 extension 16719 Fax : 613-761-4311 http://www.ohri.ca/ohsn-reb

Appendix I:

Qualitative case study, Chapter 3 – Interview Guide

Identifying Questions

1. Can you describe your role as a XXX (e.g. research coordinator, research assistant, REB staff)?
2. What is your role in relation to the BEACON cluster RCT (specified to type of role)?
3. What activities do you undertake in bringing the BEACON study to life?
4. Who do you interact with in relation to research related activities?
5. What is your perception of other people's roles in relation to the study?
6. Can you describe a case that was a 'successful' communication between team members? Can you describe a case that was a 'unsuccessful" communication between team members?
7. Can you describe a case that was a 'successful' communication with the sites? Can you describe a case that was a 'unsuccessful" communication with the sites?

CFIR Driven Questions

Construct	Questions	Probe /Notes
Intervention Source	Why is BEACON being implemented in your setting? Who decided to accept inclusion in the BEACON study? How was the decision made to accept inclusion in the BEACON study? Who was included in the process of making the decision?	This question is also related to Process: Engaging. Code responses related to source of the intervention here. Code responses related to who participated in the decision process under Engaging, as an indication of early (or not) engagement. Participation in decision-making is an effective engagement strategy to help people feel ownership of the intervention.
Evidence Strength & Quality	What kind of supporting evidence or proof was/is needed about the effectiveness of the BEACON study to get staff (co-workers, admins, physicians) on board?	Information from your own experience, published literature, or other sources? From co-workers? From supervisors? To what degree did this evidence influence your opinion of BEACON before it was implemented?
Knowledge & Beliefs about the Intervention	How do you feel about BEACON being used in the intended settings?	Do you have any feelings of anticipation? Stress? Enthusiasm? Why?
Relative Advantage	How does BEACON compare to other similar existing programs in your setting?	If worked on previous studies*

Compatibility	How well does BEACON fit with existing work processes and practices in the settings you've collaborated with?	What are likely issues or complications that may arise?
Adaptability	What kinds of changes or alterations do you think you will need to make to BEACON so it will work effectively in various hospital setting? Who will decide (or what is the process for deciding) whether changes are needed to the intervention so that it works well in the hospital setting? How will you know if it is appropriate to make any changes?	Do you feel there is enough flexibility in the BEACON study to be able to make the required changes?
Planning	Can you describe the plan for implementing BEACON?	How detailed is the plan? Who knows about it? Is the plan overly complex? Understandable? Realistic and feasible? What is your role in the planning process? Who is involved in the planning process? What are their roles? Are the appropriate people involved in the planning process? How engaged are they? Do you plan to track the progress of implementation based on your plan? What if you have to modify or revise your plan due to barrier, errors, or mistakes?
Patient Needs & Resources	To what extent were the needs and preferences of the patients seen in emergency for self-harm by your	Can you describe specific examples? Will the intervention be altered to meet their needs and preferences?

	hospital considered when deciding to implement the intervention? How well do you think the intervention will meet the needs of these people?	In what ways will the intervention meet their needs? For example, improved access to services? Reduced wait times? Help with self-management? Reduced travel time and expense?
External Policies & Incentives	What kind of financial or other incentives influenced the decision to implement BEACON in the hospitals?	How will the BEACON affect payment or revenue for your organization?
Structural Characteristics	How will the infrastructure of the individual hospitals (social architecture, age, maturity, size, or physical layout) affect the implementation of BEACON?	How will the infrastructure facilitate/hinder implementation of BEACON? How will you work around structural challenges?
Tension for Change	How do people feel about current programs/practices/process that are available related to BEACON?	To what extent do current programs fail to meet existing needs? Will BEACON meet these needs? How will BEACON fill current gaps?
Leadership Engagement	What level of endorsement or support have you seen or heard from leaders in the hospitals? What level of involvement has leadership at the hospitals had so far with BEACON?	Who are these leaders and how has this affected things so far? Going forward? Do they know about the intention to implement BEACON? Who are these leaders? How do attitudes of different leaders vary? What kind of support have they given you? Can you provide specific examples?
Opinion Leaders	Who are the key influential individuals to get on board with this? What are influential individuals saying about BEACON?	Who are these influential individuals? To what extent will they influence others' use of the intervention? The success of the implementation?
Formally Appointed Internal	Who will lead implementation of the intervention overall and at the study sites?	How did/will this person come into this role? Appointed? Volunteered? Voluntold?

Implementation Leaders		What attributes or qualities does this person have that makes them an effective leader of this implementation? What attributes or qualities does this person lack? Does this person have sufficient authority to do what is necessary to implement the intervention?
Champions	Other than the formal implementation leader, are there people in your organization who are likely to champion (go above and beyond what might be expected) BEACON?	Were they formally appointed in this position, or was it an informal role? What position do these champions have in your organization? How do you think they will help with implementation? Getting people to use the intervention?
Key Stakeholders	Who are the key individuals to get on board with BEACON?	To encourage individuals to use the intervention? To help with implementation?
Available Resources	Do you expect to have sufficient resources at the hospitals to implement and administer BEACON?	[If Yes] What resources are you counting on? Are there any other resources that you received, or would have liked to receive? What resources will be easy to procure? [If no] What resources will not be available?
Access to Knowledge & Information	Who do you ask if you have questions about BEACON or its implementation?	How available are these individuals?
Goals & Feedback	Do you get any feedback reports about your work?	What do they look like? Content, mode, form? How helpful are those reports? How often do you get them? Where do they come from?

Appendix J:

Qualitative case study, Chapter 3 – Standards for Reporting Qualitative Research

Page/line no(s)

Title and abstract

Title - Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended	Title Page
Abstract - Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions	1

Introduction

Problem formulation - Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement	2-5
Purpose or research question - Purpose of the study and specific objectives or questions	5

Methods

Qualitative approach and research paradigm - Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended; rationale**	6
Researcher characteristics and reflexivity - Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability	8-9
Context - Setting/site and salient contextual factors; rationale**	6-7
Sampling strategy - How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale**	6-7
Ethical issues pertaining to human subjects - Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	6

Data collection methods - Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale**	7
Data collection instruments and technologies - Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection; if/how the instrument(s) changed over the course of the study	6
Units of study - Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	6 and 9
Data processing - Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/de-identification of excerpts	8
Data analysis - Process by which inferences, themes, etc., were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale**	8
Techniques to enhance trustworthiness - Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale**	8-9

Results/findings

Synthesis and interpretation - Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	9-22
Links to empirical data - Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	9-22

Discussion

Integration with prior work, implications, transferability, and contribution(s) to the field - Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/generalizability; identification of unique contribution(s) to scholarship in a discipline or field	22-28
Limitations - Trustworthiness and limitations of findings	28

Other

Conflicts of interest - Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed	29

Funding - Sources of funding and other support; role of funders in data collection, interpretation, and reporting	29

*The authors created the SRQR by searching the literature to identify guidelines, reporting standards, and critical appraisal criteria for qualitative research; reviewing the reference lists of retrieved sources; and contacting experts to gain feedback. The SRQR aims to improve the transparency of all aspects of qualitative research by providing clear standards for reporting qualitative research.

**The rationale should briefly discuss the justification for choosing that theory, approach, method, or technique rather than other options available, the assumptions and limitations implicit in those choices, and how those choices influence study conclusions and transferability. As appropriate, the rationale for several items might be discussed together.

Appendix K:

Systematic review, Chapter 5 – Protocol

Systematic review of strategies for recruiting and engaging healthcare facilities in cluster randomized controlled trials: ***A protocol for a systematic review***

Contact:

Arielle Weir, PhD Candidate

University of Ottawa, School of Epidemiology and Public Health

406 - 1919 Riverside Drive

Ottawa, ON

K1H 7W9

Background:

Randomized controlled trials (RCT) are frequently conducted as a research method[1,2] and are often deemed the gold standard of research[3,4]. Cluster RCTs (cRCTs) are trials where groups (clusters) are randomized rather than individual participants[4]. cRCTs are frequently conducted with multiple hospitals as the unit of randomization[4]. cRCTs can have advantages over non-cluster RCTs[4]. They may offer more widespread and diverse population access, with the potential for broader external generalizability of results than single site RCT. In single site non-cluster RCTs, the recruited population may be less representative of the external population that the intervention may be planned for in healthcare practice[4]. Furthermore, cRCTs can allow for a quicker recruitment rates to reach larger sample size for participants than a single site RCT may offer.

While cRCTs offer advantages, they also present some challenges to organization and conduct of the trials[1]. They tend to be more complex and involve more personnel than what would be required for a single-site RCT. cRCTs require detailed administration and documentation to ensure that the trials are properly conducted[5]. Coordination is generally conducted through the main trial personnel, who oversee the overall study management, including randomization, monitoring of sites and centralized data management. Previous studies have emphasized the need to consider more research into the conduct of trials, to be able to provide lessons and guidance for future researchers, including these coordinating site members and stakeholders[6].

Challenges in delivery of trials can arises before patient recruitment and/or intervention launch[2,6]. Engagement and recruitment of the cluster sites themselves may prove difficult, with poor response and participation from the intended sites. Furthermore, variability between sites in the delivery fidelity of an intervention may make it difficult to launch a the full trial, as well as to assess the effectiveness of an intervention[7]. Various engagement strategies may be used to encourage a site's participation in a trial.

Our research group has conducted preliminary research surrounding the conduct of a cRCTs in hospitals. This work has consisted of a scoping review and a qualitative case study. The scoping review investigated the barriers and enablers to conducting cRCTs in hospitals. This review identified a large gap in reporting of recruitment of hospitals and implementation strategies in cRCTs. The qualitative study consisted of semi-structured interviews of the coordinating site staffs' perceptions of the conduct of the research group's cRCT they were preparing to launch in Ontario hospitals. This study identified their perceptions of potential barriers and enablers for roll out of the cRCT. A theme that frequently emerged was the difficulty in engaging the hospital sites to participate in the trial. Strategies to circumvent this perceived barrier to a cRCT may be generalizable, and identification of successful or unsuccessful techniques may be beneficial in providing guidance for future researchers in conducting their cRCT. Barriers to conduct of cRCTs may have commonalities between studies, however there is currently little widespread information or guidelines to assist research teams in identifying and circumventing these challenges. A preliminary search of the literature demonstrated limited evidence exists surrounding the use and effectiveness of strategies to engage the sites throughout the trial.

In order to describe barriers and targeted strategies, theoretical frameworks may be used[8]. Previous studies, in both the quantitative and qualitative methods, have concluded that the barriers and facilitators identified using frameworks for assessment are consistent with previous literature in which non-theory based assessments were performed[9,10]. These frameworks can allow for the more rigorous design of interventions, comparisons of results between studies and identification of successful factors in an intervention by enabling the comparison between studies[11–13]. When no framework is used, there is difficulty in comparing studies, and uncertainty as to whether comprehensive methods were used to identify all relevant aspects. The use of these frameworks in reviews could allow for the implementation strategies identified, regardless of whether the study was theory-driven or not, to be classified and better understood, consistent with the advocacy for the frameworks as previously described. It can also allow for a determination of whether previously published studies identified in the search thoroughly planned the implementation process, by determining whether the study methods were sufficient to encompass assessment of all the key domains of the framework[8].

The two previous studies by our research group were guided by the Consolidated Framework for Implementation Research (CFIR). While the CFIR may be used as a guiding framework for implementation and for barrier and facilitator assessments, it does not provide explicit strategies to use. The Expert Recommendations for Implementing Change (ERIC) compilation is a list of 73 discrete implementation strategies which can be used as building blocks to plan the implementation, and potentially address anticipated barriers[14,15]. A recently designed tool has been developed to match ERIC strategies to CFIR domains[15], allowing the capacity to build the implementation strategy with reference to identified barriers from the CFIR domains.

Objective:

Previous research by the protocol author has demonstrated a reporting gap for the conduct of cRCTs in hospitals. This is coupled with coordinating staff perceptions of some of the barriers encountered in the hospital engagement phase for the a cRCT launching in Ontario, including issues with engaging the sites. There is an apparent knowledge gap in systematically identifying and evaluating strategies to engage hospital sites to cRCTs.

The objective of this review will be to answer the following research questions: *What strategies are used to recruit healthcare facilities as clustered sites into cRCTs? Can these strategies be mapped to the ERIC compilation as a coding guide?*

As far as I am aware, there has yet to be a systematic review of strategies for engaging healthcare facilities in cRCTs. These strategies are important to identify to determine what methods are currently being used, what justification the research groups provided as to why the methods were used, and if there was any evaluation of their effectiveness. This study will potentially help to determine strategies and evidence for guiding investigators and their teams in ways to increase the efficiency and participation from the sites in cRCTs. Due to the limited literature identified in the narrow scope of hospitals, as well as the assumed similarity in strategies that would be used in different healthcare facility types, this review included any type of healthcare facility as sites randomized in a cRCT.

Methods:

Eligibility criteria

Population: The population for inclusion will be healthcare facilities participating in a cRCT. These sites will be assigned to different engagement strategies, as well as possibly randomized to different clinical interventions.

Intervention: The intervention of interest will be engagement strategies for sites to participate in a cRCT. These interventions may be targeted at various levels within the site (directors, physicians, nurses, etc.). As we are focusing on the macro hospital level, strategies targeted specifically at the patients will be excluded (although the clinical intervention may still be targeted at patients).

Comparator: No explicit strategies (eg. standard, unplanned implementation) or other implementation strategies.

Outcomes: The outcomes will be success or failure rates of the strategy. This may be participant recruitment rates by cluster, sites maintained in the cRCT, site perceptions and acceptance of the cRCT, etc. This will be mapped to the ERIC compilations.

Study design: Study design for inclusion will be cRCTs. Grey literature will also be searched. Stepped-wedge cRCTs and pragmatic cRCTs will also be eligible, if the sites are randomized, and implementation is randomized between sites. To note, the engagement strategy (intervention in this review), does not need to be randomized between clusters, however the clinical intervention does need to be as a cRCT design.

Settings: Studies must involve cRCTs of health interventions.

Language: Only studies written or translated into English will be included.

Year: There will be no restrictions based on year of study publication.

Publication Status: Published articles will be included. Abstracts, editorials and protocols will not be considered for inclusion; however, efforts will be made to determine whether the study has been published. Grey literature will also be searched on appropriate sites (eg. Clinical Trials Ontario[16], and other sites identified using CADTH's Grey Matters tool[17]).

Exclusion criteria: Studies will be excluded for the following reasons: Studies not aiming to bring about change in healthcare practice, implementation strategies aimed at the patients themselves, studies in which the intervention is paired directly with the implementation strategy (eg. site 1 gets clinical intervention A with an implementation strategy, Site 2 gets neither). Additionally, studies evaluating implementation without an accompanying clinical intervention will be excluded (eg. studies of implementation of guidelines already long in use, compared to no intervention/implementation in another site).

Search Strategy

A comprehensive literature search wa be conducted of MEDLINE, EMBASE, PsycINFO and Cochrane Central Register of Controlled Trials (CENTRAL). The search strategy has been developed with the guidance of the University of Ottawa Health Science library services [Appendix L]. The vocabulary and syntax were developed in MEDLINE and adjusted and applied to the other databases. Medical subject headings (MeSH) terms were specified and

supplemented as needed. Hand searching of the literature will be conducted from the references of relevant articles as well.

Data Management

Articles collected from the literature search will be exported to and managed in Mendeley[18]. Results will be de-duplicated prior to abstract and full text-screening. Articles will be exported to Covidence[19] for screening and data extraction.

Selection Process

Two independent reviewers will conduct title and abstract and full-text screening procedures, at each stage of the screening process prior to moving to the next stage. Conflicts will be resolved by discussion until consensus, or by consultation with a third person as required if consensus can not be reached. Results of the screening will be displayed in a Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram[20] with explanations for full text exclusions.

Data Collection

A data extraction form will be developed [Appendix O]. One reviewer will collect all the data, and an independent reviewer will check the data for accuracy.

The following information will be collected from all selected studies:

- Study information: Authors, year of publication, journal info and publication status
- Study characteristics: Study design, country, study period, implementation framework used (if any), sample size, inclusion and exclusion criteria, funding,
- Population (site characteristics): Location of site, type of healthcare facility site (eg. emergency, general, etc.))
- Population (coordinating site characteristics): Team composition, relation to the sites, member experience
- Intervention characteristics: Engagement Strategy used, length of strategy, timeline of strategy use during duration of the trial, engagement justification (ie. backed from theory/framework), clinical intervention
- Outcomes: participant recruitment rates by cluster, sites maintained in the cRCT, site perceptions and acceptance of the cRCT (qualitative or quantitative data, eg. surveys or interviews)
- Key conclusions from authors about strategy
- Miscellaneous comments from authors
- References to other relevant studies
- Potential sources of confounding

Assessing the Quality of Studies

Methodological quality of the studies is of great importance to ensure best summarization of the data. Therefore, methodological quality and risk of bias will be assessed for each of the eligible studies in the review. Risk of bias will be determined by one reviewer, and a random sample of

thirty percent of the studies will be verified by a second reviewer. Any conflicts will be resolved by consensus, or by consultation with a third person as required. Randomized control trials will be appraised by Cochrane Collaboration's tool for assessing risk of bias[21]. Cohort studies will be assessed using the SIGN Methodology Checklist 3 for cohort studies[22] . Case control studies will be assessed using the Critical Appraisal Skills Programme (CASP) checklist for case control studies[23]. Cross sectional studies will be assessed using STROBE Statement checklist for cross sectional studies[24]. Qualitative studies will be assessed using the Critical Appraisal Skills Programme (CASP) checklist for qualitative research[25] .

Data Analysis

Data will be analysed using the ERIC compilation. The ERIC compilation has been used in retrospective analysis of strategies for implementation[26,27], supporting its use in data analysis for this systematic review. Qualitative data will be analyzed using directed content analysis[28]. The ERIC compilation will inform the coding. The frequency and potential success (as defined in the studies) will be described. One reviewer will code all data, and a subset will be verified by an independent coder. Quantitative data (eg. number of sites approached for inclusion vs number of sites included in the trial) will be represented as a proportion where appropriate. As there is likely to be a large degree of heterogeneity in identified studies (ie. clinical intervention type, target population of the engagement strategy), there is unlikely to be data that would be beneficially included in a meta-analysis. Outcome data (as described in the methods) will be summarized and displayed in appropriate tables. If comparable strategies are found in multiple studies, they will be contrasted to compare outcomes and difference between studies.

Quality assurance

The protocol has been developed using Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 checklist[29]. The systematic review will be conducted using the Measurement Tool to Assess the Methodological Quality of Systematic Reviews (AMSTAR) tool[30] to assess the strength of the body of evidence. Any modifications to the protocol will be reported and justified and included in the final report.

PRISMA-P 2015 checklist[29]

Administrative Information

2. Title:
    a. Identification: Identify the report as a protocol of a systematic review [Y]
    b. If the protocol is for an update of a previous systematic review, identify as such [N/A]
2. Registration: If registered, provide the name of the registry and registration number [N/A]
3. Authors:
    c. Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author [to be added in subsequent version of protocol]
    d. Describe contributions of protocol authors and identify the guarantor of the review. [to be added in the subsequent version of the protocol]

4. Amendments: If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments [Y]

5. Support: [to be addressed in subsequent version of the protocol]

    d. Indicate sources of financial support for the review
    e. Provide the name of the review funder and/or sponsor
    f. Describe the roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol

Introduction

6. Rationale: Describe the rationale for the review in the context of what is already known [Y]

7. Objectives: Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO) [Y]

Methods

8. Eligibility Criteria: Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review [Y]

9. Information Sources: Describe all intended information sources (such as electronic database, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage [Y]

10. Search Strategy: Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated [Y]

11. Study Records:

    d. Data Management: describe the mechanism(s) that will be used to manage records and data throughout the review [Y]
    e. Selection Process: State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis) [Y]
    f. Data Collection Process: Described planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators [Y]

12. Data Items: List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications [Y]

13. Outcomes and Prioritization: List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale [Y]

14. Risk of Bias in Individual Studies: Describe anticipated methods for assessing risk of bias of individuals studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis [Y]

15. Data Synthesis:

e. Describe criteria under which study data will be quantitatively synthesized [N/A]
f. If data are appropriately for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency [N/A]
g. Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression) [N/A]
h. If quantitative synthesis is not appropriate, describe the type of summary planned [Y]

16. Meta-bias(es): Specify any planned assessment of meta-bias(es) (such as publication bias, selective outcome reporting within studies) [N/A]

17. Confidence in Cumulative Evidence: Describe how the strength of the body of evidence will be assessed (such as GRADE) [Y]

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Appendix L:

Systematic review, Chapter 5 – Search strategy

MEDLINE

1. exp randomized controlled trial/
2. exp Randomized Controlled Trials as Topic/
3. 1 or 2
4. exp cluster analysis/
5. Cluster*.ti,ab,kf.
6. 4 or 5
7. 3 and 6
8. ((cluster* or multi-cent* or group-randomi?ed or place-randomi?ed) adj4 trial*).ti,ab,kf.
9. cRCT*.ti,ab,kf.
10. 7 or 8 or 9
11. ((acceptabilit* or engag* or collaborat* or participat* or commit* or undertak* or organiz* or organis* or recruit* or implementat*) adj4 (site* or centre* or center*)).ti,ab,kf.
12. ((implement* or engag* or participat* or recruit*) adj3 (strateg* or intervention*)).ti,ab,kf.
13. ((engag* or involv* or participat* or collaborat* or commit*) adj3 (physician* or doctor* or clinician* or nurse* or director* or administrator* or hospital*)).ti,ab,kf.
14. "process evaluation".ti,ab,kf.
15. lesson* learn*.ti,ab,kf.
16. 11 or 12 or 13 or 14 or 15
17. exp Hospitals/
18. health facilities/ or academic medical centers/ or exp hospitals, teaching/ or exp outpatient clinics, hospital/ or surgicenters/
19. (hospital or hospitals).ti,ab,kf.
20. ((healthcare or health care) adj3 facilit*).ti,ab,kf.
21. (medical* adj3 (center* or centre*)).ti,ab,kf.
22. 17 or 18 or 19 or 20 or 21
23. 10 and 16 and 22

Appendix M:

Systematic review, Chapter 5 – PRESS Review

***PRESS Guideline* — Search Submission & Peer Review Assessment**

SEARCH SUBMISSION: THIS SECTION TO BE FILLED IN BY THE SEARCHER

Searcher's Name: Arielle Weir
Date Submitted: 2019-12-03

Email: Click or tap here to enter text.
Date Needed By: December 15, 2019 (if possible)

Systematic Review Title

Systematic review of strategies for recruiting and engaging hospitals in cluster randomized controlled trials (cRCTs)

This search strategy is: (Highlight the appropriate response)

A. My PRIMARY (core) database strategy — First time submitting a strategy for search question and database

B. My PRIMARY (core) strategy — Follow-up review NOT the first time submitting a strategy for search question and database. If this is a response to peer review, itemize the changes made to the review suggestions

C. SECONDARY search strategy— First time submitting a strategy for search question and database

D. SECONDARY search strategy – NOT the first time submitting a strategy for search question and database. If this is a response to peer review, itemize the changes made to the review suggestions.

Database (ie, Medline, Cinahl)

MEDLINE, EMBASE, PsycINFO and Cochrane Central Register of Controlled Trials (CENTRAL)

Interface (Ovid, Ebsco)

Ovid

Research Question. Describe the purpose of the search

Question: How do the strategies used in cRCTs of hospitals affect hospital site-engagement in the trial and the uptake of the intervention? Can these strategies be mapped to the ERIC compilation as a coding guide?

There has yet to be a systematic review of strategies for engaging hospitals in cRCTs. These strategies are important to identify to determine what methods are currently being used, what justification the research groups provided as to why the methods were used, and if there was any evaluation of their effectiveness. This study will potentially help to determine strategies and evidence for guiding investigators and their teams in ways to increase the efficiency and participation from the sites in cRCTs

PICO Format (Outline the PICOs for your question – ie. Patient, Intervention, Comparison, Outcome and Study Design – as applicable)

P	The population for inclusion will be hospitals participating in a cRCT. These sites will be assigned to different engagement strategies, as well as possibly randomized to different clinical interventions.
I	The intervention of interest will be engagement strategies for sites to participate in a cRCT. These interventions may be targeted at various levels within the site (directors, physicians, nurses, etc.). As we are focusing on the macro hospital level, strategies targeted specifically at the patients will be excluded (although the clinical intervention may still be targeted at patients).
C	No explicit strategies (eg. standard, unplanned implementation) or other implementation strategies.
O	The outcomes will be success or failure rates of the strategy. This may be participant recruitment rates by cluster, sites maintained in the cRCT, site perceptions and acceptance of the cRCT, etc. This will be mapped to the ERIC compilations.

Inclusion Criteria (List criteria such as age groups, study designs, etc, to be included) [optional]

Study design for inclusion will be cRCTs or reports on cRCTs. Grey literature will also be searched. Stepped-wedge cRCTs and pragmatic cRCTs will also be eligible, if the sites are randomized, and implementation is randomized between sites. To note, the engagement strategy (intervention in this review), does not need to be randomized between clusters, however the clinical intervention does need to be as a cRCT design.

Exclusion Criteria (List criteria such as study designs, date limits, etc., to be excluded) *[optional]*

Studies will be excluded for the following reasons: Studies not aiming to bring about change in healthcare practice, implementation strategies aimed at the patients themselves, studies in which the intervention is paired directly with the implementation strategy (eg. site 1 gets clinical intervention A with an implementation strategy, Site 2 gets neither). Additionally, studies evaluating implementation without an accompanying clinical intervention will be excluded (eg. studies of implementation of guidelines already long in use, compared to no intervention/implementation in another site).

Was a search filter applied?

No

If YES, which one(s) (e.g., Cochrane RCT filter, PubMed Clinical Queries filter)? Provide the source if this is a published filter. [mandatory if YES to previous question — textbox]

Other notes or comments you feel would be useful for the peer reviewer? [optional]

Please copy and paste your search strategy here, exactly as run, including the number of hits per line. [mandatory]

1 exp randomized controlled trial/ 496070

2 exp Randomized Controlled Trials as Topic/ 131549

3 1 or 2 620136

4 exp cluster analysis/ 63355

5 3 and 42970

6 ((cluster* or multi-cent* or group-randomi?ed or place-randomi?ed) adj4 trial*).ti,ab,kf. 16429

7 cRCT*.ti,ab,kf. 207

8 5 or 6 or 7 17381

9 "process evaluation".ti,ab,kf. 3347

10 8 and 9511

11 lesson* learn*.ti,ab,kf. 20928

12 8 and 11 103

13 8 or 10 or 12 17381

14 ((acceptabilit* or engag* or collaborat* or participat* or commit* or undertak* or organiz* organis* or recruit* or implementat*) adj4 (site* or centre* or center*)).ti,ab,kf. 31830

15 ((implement* or engag* or participat*) adj3 (strateg* or intervention*)).ti,ab,kf. 40487

16 ((engag* or involv* or participat* or collaborat* or commit*) adj3 (physician* or doctor* or clinician* or nurse* or director* or administrator*)).ti,ab,kf. 29991

17 14 or 15 or 16 100383

18 exp Hospitals/ 267581

19 health facilities/ or academic medical centers/ or exp hospitals, teaching/ or exp outpatient clinics, hospital/ or surgicenters/ 99212

20 (hospital or hospitals).ti,ab,kf. 1093716

21 ((healthcare or health care) adj3 facilit*).ti,ab,kf. 13583

22 (medical* adj3 (center* or centre*)).ti,ab,kf. 79794

23 18 or 19 or 20 or 21 or 22 1285160

24 13 and 17 and 23 344

PEER REVIEW ASSESSMENT: THIS SECTION TO BE FILLED IN BY THE REVIEWER

Reviewer: Amanda Hodgson Email: Amanda.hodgson@uottawa.ca Date Completed:2019-12-06

Translation

C - Revision Required

If "B' or "C", please provide and explanation or example
In your first set of terms for cRCTs, I would strongly suggest including a text term for cluster*.ti,ab,kf along with your cluster analysis/ mesh heading when you AND these terms with the RCT mesh terms (line 5), as there is a risk in limiting by this one mesh term:
Exp cluster analysis/
Cluster*.ti,ab,kf.

Boolean and Proximity Operators

C - Revision Required

If "B' or "C", please provide and explanation or example

Missing an OR in line 14:

organiz* OR organis*

Subject Headings

B - Revision suggestion

If "B' or "C", please provide and explanation or example

For the cRCT set of terms, there are some additional subject headings that may be appropriate to include. As you have done with the mesh terms for RCT, you would then "AND" these with your "cluster" term limiters.

Multicenter study as topic/
(Multicenter study or randomized controlled trial).pt.
["pt" means "publication type" which is an indexed "field" in Medline]
Placebos/
Random allocation/

You could also investigate/explore some additional MeSH subject headings for the engagement/recruitment set of terms, in particular:

exp "Outcome and Process Assessment (Health Care)"/
exp Hospital Administration/
Hospital Information systems/
exp Communication/
*patient selection/
*[the *asterisk denotes a focused term, you could try *focusing many of these terms if you get too many hits]*
*sample size/
*patient dropouts/
Planning techniques/
Eligibility determination/
State medicine/
Implementation research/
Intracluster correlation/
Researcher-subject relations/

Text Word Searching

B - Revision suggestion

If "B' or "C", please provide and explanation or example

Line 15 – recruit?
((implement* or engag* or participat* or recruit*) adj3 (strateg* or intervention*)).ti,ab,kf.

Line 16 – hospital?
((engag* or involv* or participat* or collaborat* or commit*) adj3 (physician* or doctor* or clinician* or nurse* or director* or administrator* or hospital*)).ti,ab,kf.

Spelling, Syntax and Line Numbers

C - Revision Required

If "B' or "C", please provide and explanation or example

It appears that **lines 10 and 12** are redundant when OR'ed in with line #13 – your core cRCT set. I wonder if these terms would be better placed within your engagement recruitment set? If not, they should be AND'ed directly with the Hospitals set, and omit the engagement/recruitment set, if you wished to highlight this info**.**

Limits and Filters

B - Revision suggestion

If "B' or "C", please provide and explanation or example

- There are many established RCT filters available, which may be easier to apply then starting from scratch. InterTASC Filter Resource
- McMaster / HIRU Hedges
- PubMed Clinical Queries
- University of Alberta Search Filters

Overall Evaluation

C - Revision Required

Additional Comments: Some additional mesh terms should be applied to the engagement/recruitment set, and in the cRCT set. You have suggested additional databases, and this should be easy to do by using the Ovid platform for all of the searches. To translate to Embase, you will need to find alternate subject headings from the EMTREE subject headings list for that database.

Appendix N:

Systematic review, Chapter 5 – PRISMA Reporting Guidelines

		Reporting Item	Page Number
Title			
	#1	Identify the report as a systematic review, meta-analysis, or both.	1
Abstract			
Structured summary	#2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number	2
Introduction			
Rationale	#3	Describe the rationale for the review in the context of what is already known.	3
Objectives	#4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
Methods			
Protocol and registration	#5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address) and, if available, provide registration information including the registration number.	4
Eligibility criteria	#6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rational	4
Information sources	#7	Describe all information sources in the search (e.g., databases with dates of coverage, contact with study authors to identify additional studies) and date last searched.	4
Search	#8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	20
Study selection	#9	State the process for selecting studies (i.e., for screening, for determining eligibility, for inclusion in the systematic review, and, if applicable, for inclusion in the meta-analysis).	4

Data collection process	#10	Describe the method of data extraction from reports (e.g., piloted forms, independently by two reviewers) and any processes for obtaining and confirming data from investigators.	4
Data items	#11	List and define all variables for which data were sought (e.g., PICOS, funding sources), and any assumptions and simplifications made.	21
Risk of bias in individual studies	#12	Describe methods used for assessing risk of bias in individual studies (including specification of whether this was done at the study or outcome level, or both), and how this information is to be used in any data synthesis.	4
Summary measures	#13	State the principal summary measures (e.g., risk ratio, difference in means).	4-5
Planned methods of analyis	#14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis.	4-5
Risk of bias across studies	#15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	4
Additional analyses	#16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a
Results			
Study selection	#17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5
Study characteristics	#18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citation.	6
Risk of bias within studies	#19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).	8
Results of individual studies	#20	For all outcomes considered (benefits and harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot.	n/a
Synthesis of results	#21	Present the main results of the review. If meta-analyses are done, include for each, confidence intervals and measures of consistency.	8
Risk of bias across studies	#22	Present results of any assessment of risk of bias across studies (see Item 15).	8

Additional analysis	#23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
Discussion			
Summary of Evidence	#24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policy makers	12
Limitations	#25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	14
Conclusions	#26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	14
Funding			
Funding	#27	Describe sources of funding or other support (e.g., supply of data) for the systematic review; role of funders for the systematic review.	14

Appendix O:

Systematic review, Chapter 5 – Data Extraction Form

Reviewer Initials:

Study ID:

Study Title:

Study information

Author(s):

Year:

Journal, Volume, Page Number:

Publication Status:

Study Characteristic	
Article design	
Country	
Settings	
Study period	
Implementation Framework used (if any)	
Sample size	
Inclusion/exclusion criteria (for cRCT)	
Funding	
Population (Coordinating Site) Characteristic	
Team Composition	
Relation to the site	
Member experience	
Intervention (Recruitment) Characteristic	
Strategy used	
Recruitment justification (eg. implementation framework)	
Outcome Characteristic	
Study authors' definition of outcome success	
Success of strategies (for example, sites retained, or participation rates)	
Reasons for not participating	
Miscellaneous outcome information	
Miscellaneous Item	
Key Conclusions about strategy use	
Miscellaneous comments from authors	
References to other relevant studies	

Appendix P:

Systematic review, Chapter 5 – Quality Appraisal of Literature Using Squire 2.0

Title and Abstract		Walker[23]	Ersek[24]	Johnson[5]	Maxwell[32]	Funkhouser[25]	Hundley[27]	Ellis[30]	Fairhurst[31]	Hanson[26]	Gravenstein[28]	Grazier[29]
1. Title	Indicate that the manuscript concerns an initiative to improve healthcare (broadly defined to include the quality, safety, effectiveness, patient-centeredness, timeliness, cost, efficiency, and equity of healthcare)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2. Abstract	a. Provide adequate information to aid in searching and indexing	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
	b. Summarize all key information from various sections of the text using the abstract format of the intended publication or a structured summary such as: background, local problem, methods, interventions, results, conclusions	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Introduction	*Why did you start?*											
3. Problem Description	Nature and significance of the local problem	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y
4. Available knowledge	Summary of what is currently known about the problem, including relevant previous studies	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
5. Rationale	Informal or formal frameworks, models, concepts, and/or theories used to explain the problem, any reasons or assumptions that were used to develop the intervention(s), and reasons why the intervention(s) was expected to work	N	Y	N	N	N	N	N	N	N	N	N
6. Specific aims	Purpose of the project and of this report	N	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
Methods	*What did you do?*											
7. Context	Contextual elements considered important at the outset of introducing the intervention(s)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
8. Intervention(s)	a. Description of the intervention(s) in sufficient detail that others could reproduce it	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y
	b. Specifics of the team involved in the work	N	N	Y	N	N	N	N				
9. Study of the Intervention(s)	a. Approach chosen for assessing the impact of the intervention(s)	Y	N	Y	Y	N	N	Y	Y	Y	Y	Y
	b. Approach used to establish whether the observed outcomes were due to the intervention(s)	N	N	N	Y	N	N	Y	N	N	N	N
10. Measures	a. Measures chosen for studying processes and outcomes of the intervention(s), including rationale for choosing them, their operational definitions, and their validity and reliability	N	N	N	Y	N	N	N	N	N	Y	N
	b. Description of the approach to the ongoing assessment of contextual elements that contributed to the success, failure, efficiency, and cost	N	N	N	N	N	N	Y	N	N	N	N
	c. Methods employed for assessing completeness and accuracy of data	N	N	Y	Y	N	N	N	N	N	N	N

11. Analysis	a. Qualitative and quantitative methods used to draw inferences from the data	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y
	b. Methods for understanding variation within the data, including the effects of time as a variable	N	Y	Y	N	N	n/a	N	N	N	N	N
12. Ethical Considerations	Ethical aspects of implementing and studying the intervention(s) and how they were addressed, including, but not limited to, formal ethics review and potential conflict(s) of interest	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Results	*What did you find?*											
13. Results	a. Initial steps of the intervention(s) and their evolution over time (e.g., time-line diagram, flow chart, or table), including modifications made to the intervention during the project	Y	Y	Y	Y	Y	Y	n/a	Y	Y	Y	Y
	b. Details of the process measures and outcome	Y	N	Y	Y	Y	N	Y	N	N	N	N
	c. Contextual elements that interacted with the intervention(s)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	d. Observed associations between outcomes, interventions, and relevant contextual elements e. Unintended consequences such as unexpected benefits, problems, failures, or costs associated with the intervention(s).	N	N	N	N	N	N	N	N	N	N	N
	f. Details about missing data	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Discussion	*What does it mean?*											
14. Summary	a. Key findings, including relevance to the rationale and specific aims	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	b. Particular strengths of the project	N	N	N	Y	N	N	Y	N	N	N	Y
15. Interpretation	a. Nature of the association between the intervention(s) and the outcomes	N	N	N	N	Y	N	Y	N	N	N	N
	b. Comparison of results with findings from other publications	N	N	Y	Y	Y	Y	Y	N	N	Y	Y
	c. Impact of the project on people and systems	Y	N	N	N	N	N	Y	Y	N	N	N
	d. Reasons for any differences between observed and anticipated outcomes, including the influence of context	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	e. Costs and strategic trade-offs, including opportunity costs	Y	N	N	N	N	N	Y	Y	N	N	N
16. Limitations	a. Limits to the generalizability of the work	N	N	N	Y	N	N	Y	N	N	N	Y
	b. Factors that might have limited internal validity such as confounding, bias, or imprecision in the design, methods, measurement, or analysis	N	N	N	Y	N	N	N	N	N	N	Y
	c. Efforts made to minimize and adjust for limitations	N	N	N	N	N	N	N	N	N	N	N
17. Conclusions	a. Usefulness of the work	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	b. Sustainability	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
	c. Potential for spread to other contexts	N	N	N	Y	Y	N	Y	N	N	N	Y
	d. Implications for practice and for further study in the field	Y	N	Y	Y	N	N	Y	Y	N	Y	Y
	e. Suggested next steps											
18. Funding	Sources of funding that supported this work. Role, if any, of the funding organization in the	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

	design, implementation, interpretation, and reporting											

The SQUIRE guidelines provide a framework for reporting new knowledge about how to improve healthcare · The SQUIRE guidelines are intended for reports that describe system level work to improve the quality, safety, and value of healthcare, and used methods to establish that observed outcomes were due to the intervention(s). · A range of approaches exists for improving healthcare. SQUIRE may be adapted for reporting any of these. · Authors should consider every SQUIRE item, but it may be inappropriate or unnecessary to include every SQUIRE element in a particular manuscript. · The SQUIRE Glossary contains definitions of many of the key words in SQUIRE. · The Explanation and Elaboration document provides specific examples of well-written SQUIRE items, and an in-depth explanation of each item.