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The DIVERT-CARE (Collaboration Action Research & Evaluation) Trial Protocol: A Multi-Provincial Pragmatic Cluster Randomized Trial of Cardio-Respiratory Management in Home Care

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ABSTRACT

Introduction:
Home care clients are becoming increasingly medically complex, have limited access to effective chronic disease management, and have very high emergency department (ED) visitation rates. There is a need for more appropriate and targeted supportive chronic disease management for home care clients. We aim to evaluate the effectiveness and preliminary cost-effectiveness of a targeted, person-centered cardio-respiratory management model.

Methods and analysis:
The DIVERT (Detection of Indicators and Vulnerabilities of Emergency Room Trips) – Care trial is a pragmatic, cluster-randomized, multi-center superiority trial of a flexible multi-component cardio-respiratory management model based on best-practice guidelines. The trial will be conducted in partnership with three regional, public-sector, home care providers across Canada. The primary outcome of the trial is to identify time to first unplanned ED visit within six months. Additional secondary outcomes are to identify changes in patient activation, changes in cardio-respiratory symptom frequencies, and cost-effectiveness over six months. We will also investigate the difference in the number of unplanned ED visits, number of inpatient hospitalizations, and changes in health-related quality of life. Multi-level proportional hazard and generalized linear models will be used to test the primary and secondary hypotheses. Sample size simulations indicate that enrolling 1,100 home care clients across 36 clusters (home care caseloads) will yield a power of 81% given a hazard ratio of 0.75.

Ethics and dissemination:
Ethics approval was obtained at all participating sites. Results will be submitted for publication in peer-reviewed journals and conference presentations. Home care service partners will also be informed of the study's results. The results will be used to inform future support strategies for older adults receiving home care services.

Trial registration number: ClinicalTrials.gov: NCT03012256

Keywords: Cardio-Respiratory Disease Management, Chronic Disease Management, Cluster-randomized, DIVERT Scale, Home Care

Strengths and limitations of this study

- The trial intervention addresses the growing and widespread need for better chronic disease management in the community.
- The pragmatic design will test real-world effectiveness with multi-provincial enrollment which will support generalization to other jurisdictions.
- The care model only addresses home care clients with cardio-respiratory symptoms.
- The care model is designed with general home care principles in mind but is specific to the Canadian environment.
- The care model is designed for longitudinal care environments rather than the short-term post-acute care settings.

INTRODUCTION:

Publicly-funded home care services are delivered to at least 6% of Canadians age 65-74, 15% age 75-84 and 32% age 85 or older. [1] These home care clients are increasingly medically complex, often access care across multiple settings, have very high emergency department (ED) visitation rates, and have relatively poor access to effective chronic disease management.[2–4] Their frequent ED use is rarely aligned with chronic disease management or geriatric care principles and therefore creates excess cost burdens on the health care system.[5,6]

Effective chronic disease management models employ multiple components delivered by a coordinated multidisciplinary team.[7] According to the 'chronic disease management model', home care plays a complementary function to the care medical practitioners provide.[7] Clinical and self-care support, as well as case management are among the most effective components in chronic disease management.[8–10] Self-care education and support has been shown to improve health outcomes across chronic diseases.[11,12] The provision of sustained follow-up by nurses or non-medical staff can also be effective.[13,14]

Effective home care services have been limited by insufficient targeting of clients that are most at need or most likely to benefit.[15,16] We developed and validated a prognostic case-finding tool for home care clients known as the Detection of Indicators and Vulnerabilities of Emergency Room Trips (DIVERT) Scale that has been recommended for use in the provision of home care.[17–19] It can be derived in real time from the interRAI Home Care (RAI-HC) standardized home care assessment system used in 9 Canadian provinces as well as Estonia, Finland, Hong Kong, Iceland, Ireland, Italy, Japan, the Netherlands, New Zealand, Singapore, Spain, Switzerland, and 29 U.S. states. Cardio-respiratory symptoms and conditions are prominent predictive elements of the DIVERT Scale.

Canadian home care providers, historically focused on the delivery of personal support services, have started to develop supportive chronic disease management capacity (e.g., specialist nurse monitoring).[20] Most trials, however, exclude frail seniors and are not specific to home care, which leaves little evidence to inform chronic disease management practices.[17]

From evidence-based guidelines developed – in part – by our team, extensive client profiling, and input of clients/families as well as health professionals, we developed a person-centred, multi-component cardio-respiratory management model. Our approach is based on evidence of effective implementations in other fields,[21] and includes all elements for 'person-centred care'.[22] The pilot study was recognized on the 2015 Ontario Minister of Health and Long-Term Care's Medal Honour Roll for Excellence in Health Quality.[23,24]

Recent Canadian trials have tested a 'Virtual Ward' and a 'transitional care services' model in post-acute adult patients (the latter with heart failure) and found no benefit.[25,26] The 'Virtual Ward Model' cited difficulty of hospital teams to integrate with community-based care. Community-based chronic disease management can reduce hospital use.[25,27] Our study diverges from this given that we focus on home care clients who are frail and not specifically

'post-acute'. Also, our intervention leverages a validated case finding tool based on real-time inputs from community-based providers rather than care from hospital-based teams.

The DIVERT-CARE trial will adopt a pragmatic attitude to avoid the well-documented difficulty that many clinical trials have in producing results that are generalizable to real-world conditions.[28,29] As our interest is in the effects of the intervention under realistic rather than optimal conditions, the intervention will be delivered in usual care settings by usual care providers for usual clients. Home care caseloads will be randomized to intervention or control rather than individual clients in order to mimic the process that would occur when clinical practice changes. Cluster randomized designs are commonly utilized in pragmatic trials as practice changes are implemented at levels higher than the client in real-world conditions.[30,31] The DIVERT-CARE trial will also make use of secondary data sources for outcome measurement. The use of administrative data has been shown to be more accurate than client-reported results for health services utilization and permits excellent follow-up over long periods of time without the need for intrusive follow-up procedures.[32,33] A number of pragmatic, cluster-randomized trials using administrative data have appeared in the literature.[34–37]

This paper describes the protocol and presents the rationale for a cluster-randomized study investigating the effectiveness of a cardio-respiratory disease management model in a targeted home care client population. This paper complies with the SPIRIT 2013 recommendations for clinical trial protocol reporting.[38] This study will report trial findings in accordance with CONSORT guidelines.[39]

METHODS AND ANALYSIS:

Study Population

The trial will be conducted in partnership with three regional, public-sector, home care providers across Canada: Hamilton-Niagara-Haldimand-Brant Local Health Integration Network (HNHB LHIN) in Ontario, Western Health in Newfoundland, and Island Health in British Columbia. Each health care provider or site will select a number of home care caseloads to be included in the study based on historical practice patterns from each region including caseload size, home care enrollment, and assessment patterns. A caseload represents a group of clients in a small geographical area that is served by a home care coordinator (or 'case manager'). Recruitment and randomization will occur at the level of the caseload and as such, clients were not involved in the research strategy. Each site will select enough caseloads to enroll approximately 360 long-stay home care clients, for a total of 1,100 clients over a 1.5-year time frame. We expect that over 43 distinct geographic home care caseloads will be enrolled in total.

Study Design

The DIVERT-CARE trial is a pragmatic, cluster-randomized, two-arm parallel cluster, multi-center, superiority trial with a primary outcome of time to first ED visit within 6 months of the index home care clinical assessment. The unit of randomization/intervention will be the cluster (home care caseload; Figure 1: Caseload randomization schematic), while the unit of inference/measurement/analyses will be the home care client. The cluster-randomized design

limits the potential for contamination and differential enrollment given that management and discretion over the use of resources is contained within each home care caseload. This design also supports the feasibility of the trial by reducing the number of resources (care providers) required to be trained in the intervention protocol. See Table 1 for an overview of the trial methods and design; Protocol Version 2.1 (2017-04-17).

Figure 1: Caseload Randomization Schematic <see Figure 1 attachment.>

Table 1: World Health Organization Trial Registration Data Set for DIVERT-CARE Trial (as of 11.03.2019; Protocol Version 2.1, 2017-04-17)

Data Category	**Information**
Primary registry and trial identifying number	ClinicalTrials.gov NCT03012256
Date of registration in primary registry	6 January, 2017
Secondary identifying numbers	
Source(s) of monetary or material support	Canadian Institutes of Health Research (CIHR); Hamilton Niagara Haldimand Brant Community Local Health Integration Network (Hamilton, Ontario); Western Health (Corner Brook, Newfoundland and Labrador); Island Health (Victoria, British Columbia); Canadian Frailty Network
Primary sponsor	McMaster University
Secondary sponsor(s)	N/A
Contact for public queries	Graham Campbell, MA [campbg4@mcmaster.ca]
Contact for scientific queries	Andrew Costa, PhD [acosta@mcmaster.ca] McMaster University
Public title	The DIVERT-CARE (Collaboration Action Research & Evaluation) Trial
Scientific title	The DIVERT-CARE (Collaboration Action Research & Evaluation) Trial: A Multi Provincial Pragmatic Cluster Randomized Trial of Cardio-Respiratory Management in Home Care
Countries of recruitment	Canada
Health condition(s) or problem(s) studied	Heart Failure; COPD
Intervention(s)	**Experimental:** Cardio-respiratory management model[44] **Control**: usual care / no intervention
Key inclusion and exclusion criteria	**Inclusion Criteria:** Long-stay home care clients living in a noninstitutional setting (i.e. admitted to home care and receive comprehensive clinical assessment (RAI-HC))

	Clients with DIVERT score of 9, 10, 14, or 15 (i.e. at least one cardio-respiratory symptom [chest pain, dyspnea, dizziness, irregular pulse]and at least one cardiac condition [congestive heart failure or coronary artery disease]) **Exclusion Criteria:** Clients receiving palliative care (i.e. Prognosis of less than six months to live at time of assessment [Q. K8e from RAI-HC]) Clients receiving dialysis (Q. P2g from RAI-HC)
Study type	Interventional Allocation: cluster randomized intervention model. Parallel assignment, open label Primary purpose: prevention Pragmatic
Date of first enrolment	6 February, 2018
Target sample size	1080
Recruitment status	Recruiting
Primary outcome(s)	The difference in median days to first unplanned emergency department visit [Time Frame: Up to six months from baseline]; The difference in total care costs controlling for length of stay [Time Frame: Up to six months from baseline]; Changes in patient activation (patient activation questionnaire) [Time Frame: Baseline, 2 months, 4 months, 6 months]; The difference in the number of symptoms [Time Frame: Baseline, 2 months, 4 months, 6 months]
Key secondary outcomes	The difference in the number of unplanned emergency department visits [Time Frame: Baseline, 6 months]; Description of health-related quality of life (quality of life questionnaire) [Time Frame: 4 months]

Study Objectives

Our main objective is to evaluate the effectiveness and preliminary cost-effectiveness of a targeted, person-centered cardio-respiratory management model. The sample size for the primary outcome was calculated to determine whether the cardio-respiratory disease management model is superior to standard of care in postponing unplanned ED visits. Additional outcomes include determining if the cardio-respiratory disease management model is superior to standard of care in improving client activation, reducing symptoms, and the cost-effectiveness of this model. The symptoms of interest are shortness of breath, chest pain at rest or on exertion, dizziness, perceived pain control, edema, noticeable decrease in food/fluids consumed, and unintended weight loss.

Secondary objectives include determining if the cardio-respiratory disease management model is superior to standard of care for the number of unplanned ED visits, number of unplanned

hospital admissions, and change in health-related quality of life (HRQOL). HRQOL will be assessed by the Minimal Data Set Health Status Index (MDS-HSI), which is a RAI-HC derived measure based on the Health Utilities Index Mark 2.[40,41]

Eligibility Criteria

The pragmatic attitude of the trial warrants the broadest inclusion criteria that are feasible. To be eligible for inclusion into this trial, home care clients must possess the following characteristics:

- Admitted to home care and receive comprehensive clinical assessment (RAI-HC) as part of regular home care enrolment, or reassessment;
- 19 years or older at time of assessment; and
- Categorized into DIVERT subgroups 9,10,14, or 15 (Figure 2: DIVERT Scale Target Groups). This includes:
    - those with cardio-respiratory symptoms (chest pain, dyspnea, dizziness, irregular pulse) who have a diagnosis of chronic cardiac disease and have not used an ED or hospital in the last 90 days (9, 10); OR
    - those with cardio-respiratory symptoms who have had one ED or hospital exposure in the last 90 days, regardless of if they are diagnosed with chronic cardiac disease (14, 15).

Figure 2: DIVERT Scale Target Groups <see Figure 2 attachment.>

We will exclude clients with a prognosis of less than six months to live at time of assessment (Q. K8e from RAI-HC) and clients requiring dialysis treatment (Q. P2g from RAI-HC). The exclusion of palliative and dialysis care clients is necessary as some jurisdictions place these clients on specialized caseloads.

The eligibility criteria for the trial will result in a population that is representative of non-palliative home care clients in Canada who have cardio-respiratory symptoms and are expected to need on-going care.

Recruitment and Consent

All non-palliative, non-dialysis, adult home care clients in the trial caseloads assessed using the RAI-HC (during regular home care enrollment or reassessment) who fall into one of the four target DIVERT subgroups will be enrolled into the study by a care coordinator at the time of assessment. Eligible clients will automatically be included into the intervention or 'regular care' control groups on an intent-to-treat basis. Recruitment is expected to proceed over 6-9 months for each site. Analysis of the sample size simulations that were carried out on retrospective data from the HNHB LHIN region from November 2014 to June 2015 indicates an expected enrollment of 4 clients per caseload per month.

Each home care partners' process for attaining consent will apply to the trial. Individual informed consent will not be sought given that the cardio-respiratory management model is accepted, considered best practice care, and is offered – whole or in part – at the full clinical

discretion of the home care provider as per existing practice. Trial investigators have no part in the data collection, individual care decision-making, or record management during the study period beyond providing overall scientific guidance. We requested and received alteration to the requirements for consent based on satisfying the following Canadian Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2) criteria:[42]

1. The research involves no more than minimal risk to the participants.
2. The alteration to consent requirements is unlikely to adversely affect the welfare of participants.
3. It is impossible or impracticable to carry out the research and to address the research questions properly, given the research design, if the prior consent of participants is required.
4. In the case of a proposed alteration, the precise nature and extent of any proposed alteration is defined.
5. The plan to provide a debriefing (if any) which may offer participants the possibility of refusing consent and/or withdrawing data and/or human biological materials, shall be in accordance with Article 3.7B.

Our waiver of informed consent complies with existing methodological and ethical guidelines for pragmatic cluster-randomized trials. Existing guidelines state that informed consent by clients is not needed if "the intervention is to the clear advantage of every person in the cluster for the cluster to be entered in the trial"[43].

Intervention

Care planning and self-care support have been shown to be among the most effective elements of cardio-respiratory disease management[8,10] along with sustained follow-up by nurses or non-medical staff [13,14]. Care planning will be completed in a collaborative fashion amongst a care coordinator, the client, and the client's caregivers (both formal and informal). Clients in the intervention group will have their care plans guided by a multi-component cardio-respiratory disease management model in addition to receiving their usual care.[44] This comprehensive model for the intervention has been described in greater detail in a previous publication.[44] The person-centered, multi-component cardio-respiratory management model was developed based on guidelines,[17,45,46] extensive home care client profiling, and input from clients/families and health professionals. The management model contains the following components (Table 2: Description of Intervention Components): scheduled nurse-led self-management support (based on a training program and tool-kit); access to a staffed helpline; education on vaccines; advance care and goal planning; clinical pharmacist medication reconciliation; team case rounds; situation, background, assessment, and recommendation (SBAR) communication protocol with primary care; and a standardized transition package.[21,44,47] Each component has a specific objective within the model, however the manner in which it is delivered may be adapted. For example, some home care providers have clinical pharmacists on staff whereas others would rely on collaboration with community pharmacists.

Table 2: Description of intervention components

DIVERT-CARE Intervention Components	Description
Case Finding Using the DIVERT Scale	Use of the DIVERT Scale (embedded in interRAI assessment) to identify home care clients most likely to benefit.
Self-Management Education and Supports	In-home assessment of self-management goals and needs, with practical education and skills training to recognize and manage symptoms.
Access to an immediate nurse-staffed helpline	Direct phone line staffed by nurses involved in the DIVERT-CARE Intervention to aid with self-management and problem resolution.
Promotion of Vaccines	Seasonal flu vaccine and pneumococcal polysaccharide (Pneu-P-23) information and health promotion consistent with Canadian practice guidelines.
Advance Care and Goal Planning	Consultation for advance care and goals of care planning, advanced care decisions, and communication of care wishes.
Clinical Pharmacist-Led Medication Review	Review of medication for safety, efficacy and appropriate use of medications and delivery options.
Interprofessional Team Case Rounds	Weekly or biweekly care team meeting to discuss care plan, update goals, and how to support changing care needs.
SBAR Communication with Primary Care Providers	SBAR formatted communication to effectively communicate disease relevant information and care updates to primary and specialist care providers.
Standardized ED Transition Package / Personal Care Record	A succinct document to support continuity of care throughout health system. Personal care record of goals, plan of care, and community supports.

Self-management education and supports will be tailored to the needs and goals of the client. As with all home care services, clients may refuse all or any of the intervention components. The components will be delivered over 15 weeks by care coordinators and nurses who have been trained by the research team. Each component has a specific objective within the model, however, the manner in which it is delivered may be adapted by each trial partner according to their capacity and resources. Care coordinators and nurses will be provided detailed manuals explaining the components and their role in supporting clients throughout the intervention. The self-management program, based on previous pilot work[24], will use a population-based care approach pioneered by Wagner (1995) to help trial partners implement the cardio-respiratory disease management model.[48]

The intervention adheres to the following three principles: 1) multidisciplinary teams at each site will be trained on the protocols and resources related to each component of cardio-respiratory management model; 2) the teams will identify steps required to deliver the interventions; 3) the teams will plan deployment of the cardio-respiratory management model that engages clients, families, and caregivers to ensure that adequate resources are dedicated to support the interventions across the intervention caseloads, while ensuring long-term sustainability.

Clients in the control group will receive the usual set of home care services. No changes will be made to their care planning process. Depending on the jurisdiction and client needs, usual care may include personal support, nursing, physiotherapy, occupational therapy, and other services.

Allocation

Caseloads were randomized to intervention or control, and stratified by home care provider (region) and sub-region (areas with similar economic status, access to care, and geography) at a 1:2 intervention to control ratio. The uneven allocation ratio increases the power of the trial while only minimally impacting operational and research resources.

An allocation sequence was created via random number generation in collaboration with the biostatistics unit at St. Joseph's Healthcare Hamilton. The sequence features a 1:2 allocation ratio with a block of size three. Caseloads from each region were sorted by sub-region and allocated using the sequence. In the event that the end of the clusters in a sub-region did not coincide with the end of a block, the rest of the block was skipped and allocation of the next sub-region started with a new block.

Data Collection and Outcome Measures

The primary outcomes will be collected using secondary data over the six-month observation period (see Table 2: Routine Measurement). The use of routinely collected data for primary outcomes, cost, and health measures limits potential for bias from lack of blinding given that neither the care team nor the trial investigators are directly involved in the collection of outcomes. These records are accurate given that they are the basis for health care reporting systems and payments between public home care providers and contracted service providers.

Table 2: Routine Measurement

Activity	Staff Member	Approximate Time to Complete	Baseline	2 Months	4 Months	6 Months
Assess for eligibility (If intervention caseload) (RAI-HC)	Care coordinator	5 minutes	X			
Symptoms (RAI-HC)	Care coordinator	15 minutes	X	X	X	X

Health-related quality of life (RAI-HC)	Care coordinator	30 minutes			X	
Patient Activation Measure (PAM-13)	Care coordinator	5 minutes	X	X	X	X
Administrative service and billing records (CHRIS, HCC MRR, CRMS)	N/A	N/A	X	X	X	X
Emergency department and hospital records (NACRS, DAD)	N/A	N/A	X	X	X	X

Legend:
RAI-HC: Resident Assessment Instrument for Home Care (https://www.cihi.ca/en/home-care)
PAM-13: Patient Activation Measure (https://www.insigniahealth.com/products/pam-survey)
CHRIS: Client Health and Related Information System (https://hssontario.ca/Who/Pages/protecting-your-privacy.aspx)
HCC MRR: Home and Community Care Minimum Reporting Requirements (https://www2.gov.bc.ca/assets/gov/health/forms/5502datadictionary.pdf)
CRMS: Client and Referral Management System (https://www.nlchi.nl.ca/images/ProvincialCRMS_Registration_User_Guide_v2_0_2017-09-01.pdf)
NACRS: National Ambulatory Care Reporting System (https://www.cihi.ca/en/national-ambulatory-care-reporting-system-metadata
DAD: Discharge Abstract Database (https://www.cihi.ca/en/discharge-abstract-database-metadata)

The main secondary data sets include the Resident Assessment Instrument for Home Care (RAI-HC), the Patient Activation Measure (PAM-13), the Client Health and Related Information System (CHRIS), the Home and Community Care Minimum Reporting Requirements (HCC MRR), the Client and Referral Management System (CRMS), the National Ambulatory Care Reporting System (NACRS), and the Discharge Abstract Database (DAD).

The RAI-HC is a standardized comprehensive assessment containing approximately 200 items and has been found to document major domains of health reliably.[49–53]

The Patient Activation Measure (PAM-13) indicates the client's progress through four stages as they become activated (i.e., they believe their role in their own care is important, they learn enough to develop confidence to act on their own belief, they actually act, and they reach the point where they can act even under stress).

The CHRIS is the health administrative database used by Ontario's publicly-funded home care providers. It includes client assessments, documents, provider and vendor contracts, billing of services information, and medical supplies and equipment rental costs.

The HCC MRR is an information management system defining a set of data elements that are reported to the British Columbia Ministry of Health by the regional health authorities. The HCC MRR captures information on clients, income, and home and community care services.

The Client and Referral Management System (CRMS) is a health information system designed to support client and referral management for clients receiving community-based services from the regional health boards in Newfoundland. It contains information on client records and clinical activity.

The NACRS contains data from all national hospital-based and community-based ambulatory care. It is collected and maintained by the Canadian Institute for Health Information (CIHI), which conducts its own quality assurance procedures to ensure accuracy and completeness.

The DAD captures administrative, clinical, and demographic information nationally on hospital discharges (including deaths, sign-outs, and transfers). It is collected and maintained by CIHI, which conducts its own quality assurance procedures to ensure accuracy and completeness.

Sample Size Calculations

Sample size calculation assumptions:

- Primary outcome: Time to first unplanned ED visit within 6 months of baseline
- Hazard ratio of 0.75
- Mean size of a home care caseload: 120 clients
- Mean prevalence of DIVERT target group in each caseload: 30%
- Expected recruitment over 6 months per caseload: 30
- Mean cluster size: 30
- Allocation: 1:2 (intervention: control)

Simulations using retrospective secondary data sources were undertaken to explore the power of a hypothetical DIVERT-CARE trial conducted in the HNHB LHIN region of Ontario from December 2015 to June 2016. The simulations found that 36 HNHB home care caseloads randomized at a 1:2 intervention to control ratio could expect to enroll 1,100 clients across seven months. The simulation linked clients to their actual ED utilization records and extended the time to first ED visit figures for clients in 12 randomly selected intervention caseloads to achieve a hazard ratio of 0.75, a figure chosen to be more conservative than the pilot study but still clinically significant. The overall event rate was 35.5% in the intervention group and 44.8% in the control. The median time to first visit was 88 days in the intervention group and 75 days in the control. The power of the simulated DIVERT trial was 81.3% with a two-sided alpha of 0.05. Simulations with a hazard ratio of 0.80 yielded a power of 60.1%. The intraclass correlation coefficient (ICC) was estimated to be 0.005.

Based on the simulations the target sample size for the trial will be 1,100 clients, which will yield an approximate power of 81% for a hazard ratio of 0.75 and 60% for a hazard ratio of 0.80.

Statistical Analyses

Descriptive analyses will compare the treatment groups and sites on baseline demographic and clinical characteristics. Statistics on compliance, censoring, and follow-up times will also be presented.

The primary outcome will be assessed through a multi-level proportional hazards model. The dependent variable will be days until first unplanned ED visit, censored at date of home care discharge for any reason. Caseload and partner site will be included as nested random effects. Both unadjusted and adjusted results will be reported. For adjusted analysis, DIVERT subgroup, age, and sex will be included as time-independent fixed effects. The hazard ratio, 95% confidence interval, and p-value will be reported for the treatment group effect and covariates when applicable. A two-sided alpha level of 0.05 will be used to judge statistical significance.

The assumption of proportionality of hazards across treatment groups will be evaluated by a visual inspection of the hazard curves and statistical testing of a time-dependent treatment group effect. If the hazard curves cross or the time-dependent treatment group effect is significant ($p < 0.05$) then primary analysis will be modified to consider treatment group as a time-varying effect.

The economic evaluation will examine total care costs, controlling for length of stay, between treatment groups to compare incremental costs to incremental effects (i.e., cost per ED visit averted).

The other outcomes will be evaluated by multi-level generalized linear models. Four-month and six-month changes in PAM, HRQOL, number of symptoms, number of ED visits, and number of unplanned hospitalizations will be the respective dependent variables. Caseload and partner site will be included as nested random effects. Both unadjusted and adjusted results will be reported. For adjusted analysis DIVERT subgroup, age, and sex will be included as fixed effects. Unit change and rate ratios, with their associated 95% confidence interval and p-values, will be reported for the treatment group effect and covariates as applicable. A two-sided alpha level of 0.05 will be used to judge statistical significance.

Model assumptions will be evaluated by a visual inspection of residuals and the sensitivity of the results to the use of a heteroskedastic-robust variance estimator. If evidence of departure from model assumptions is present, then the analysis will be modified to utilize an empirical variance estimator.

Patient and Public Involvement

The intervention, comprehensively described elsewhere [44], was developed based on the input from clients/families and health professionals in a series of three in-person stakeholder meetings held in late 2013 and early 2014. The pilot of the study methodology was conducted in 2014 with the collaboration, input, and funding from a regional, public-sector, home care provider (HNHB LHIN). Participating clients and health professionals provided input into the intervention (and study design for health professionals) through telephone interviews using a structured questionnaire focused on the perceived benefit and utility of the interventions,

overall satisfaction, and areas for improvement. The outcomes of the pilot study were featured in the home care providers annual report to the community.

The present protocol, based on the aforementioned pilot study, received input from health professionals in each participating region through a series of in-person planning meetings in mid-2017. The general public was engaged in one region through a local radio program. Adaptations and modifications to the intervention in each region to account for their unique health service context will be described in a forthcoming implementation publication. The experience of participating clients and health professionals will be investigated in a program evaluation and qualitative study to be conducted in parallel. The results of the trial are expected to be released to the study participants and public though regional public reports.

ETHICS AND DISSEMINATION

Harm

This trial is unlikely to cause additional risk of harm since the various components of the intervention are already available from home care agencies and service providers, though rarely offered in the standard care plan. Direct risks to the health of the client are minimal as none of the components of the intervention are novel interventions. Each element of the intervention has been shown to be safe individually. Clients in the control group will continue to receive their usual care, while clients in the intervention group will receive usual care plus increased access to additional home care services defined by the cardio-respiratory treatment model.

Ethical approval

We have received ethics approval from the Hamilton-Integrated Research Ethics Board, Health Research Ethics Authority for Western Health, and the Clinical Research Ethics Board for Vancouver Island.

Results dissemination

We aim to make the results of this study public through peer-reviewed publications, clinical trial registry, thesis manuscripts, conference publications, and notifications to our trial partners, who will include the findings in their regular newsletters and annual reports to clients, partners, and government.

DISCUSSION

In summary, this pragmatic, cluster-randomized, multi-center superiority trial will investigate the effectiveness of a cardio-respiratory disease management model in a targeted home care client population, with case finding occurring using the DIVERT scale[19]. By offering a person-centered, multi-component cardio-respiratory management model to home care clients at the highest levels of risk,[44] we hope to determine if unplanned ED visits are postponed, clients have increased activation in their care, symptoms are reduced, and that the care model is cost-effective.

This pragmatic trial will inform how multi-component cardio-respiratory care interventions are received as they are delivered in real-world conditions. Historically, trials investigating community programs have excluded frail seniors who would be at high-risk of ED services. Additionally, other trials have tended to focus on post-acute care and have not targeted high-risk clients when assessing community-based chronic disease management interventions.

The need for appropriate and targeted supportive chronic disease management is a clear and compelling health services issue, and is reflected in new provincial government investments into the sector. This trial will be an important precedent around the creation of more upstream approaches to care for home-care clients that help to take further pressure of hospitals and EDs that are already facing issues of overcrowding across Canada.

Author Contributions

APC is the principal investigator and led the conceptualization and design of the protocol, drafted, and revised the manuscript. CS, AJ, DD, and GC made contributions to the design and implementation of the study, and supported the manuscript. GA, CB, VB, SB, DF, PH, GH, JH, LL, RM, LM, and SS are co-investigators that contributed to the design of the study, and revised the manuscript. JD, TP, JR, RG, DM, and DH are trial partners who contributed to the design and implementation of the study. All authors critically revised the manuscript and approved the final version of this manuscript.

Competing interests

It should be noted that DHF has a proprietary interest in Health Utilities Incorporated, Dundas, Ontario, Canada. HUInc distributes copyrighted Health Utilities Index (HUI) materials and provides methodological advice on the use of the HUI. All others author have no competing interests.

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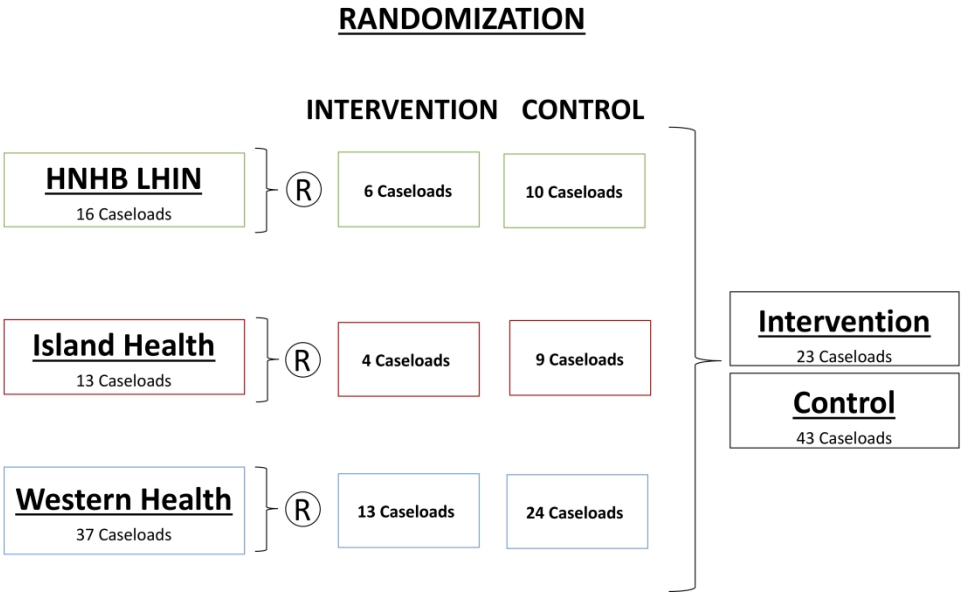

Figure 1: Caseload Randomization Schematic

368x222mm (300 x 300 DPI)

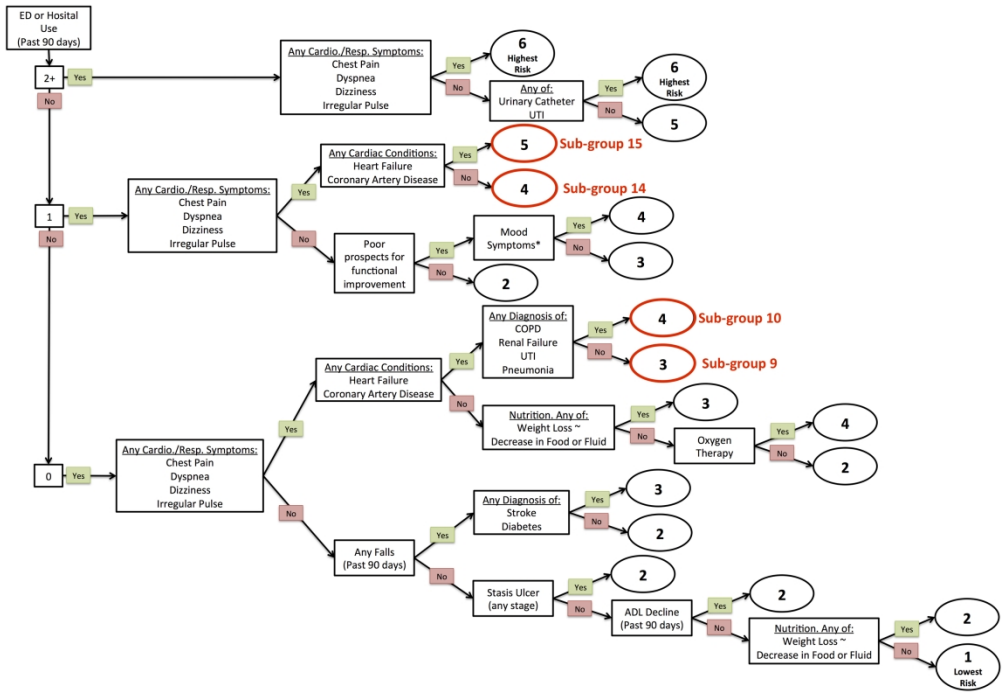

Figure 2: DIVERT Scale Target Groups

254x175mm (300 x 300 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

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		Reporting Item	Page Number
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	7-8
Protocol version	#3	Date and version identifier	7
Funding	#4	Sources and types of financial, material, and other support	17
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	17
Roles and responsibilities:	#5b	Name and contact information for the trial sponsor	17

sponsor contact information			
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	17
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	17
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	9
Objectives	#7	Specific objectives or hypotheses	8
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	6
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	9
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	10
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	10
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return;	11

		laboratory tests)	
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	11
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	12
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	12
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	14
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	9
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	9
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	9
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	9
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	9
Blinding (masking): emergency	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during	9

unblinding		the trial	
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	13
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	13
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	13
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	14
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	15
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	15
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	15
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and	15

		whether the process will be independent from investigators and the sponsor	
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	16
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	16
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	9
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	9
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	16
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	17
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	17
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	9
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	16
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	16
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	16
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	N/A

Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

BMJ Open

The DIVERT-CARE (Collaboration Action Research & Evaluation) Trial Protocol: A Multi-Provincial Pragmatic Cluster Randomized Trial of Cardio-Respiratory Management in Home Care

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Keywords:	Cardio-Respiratory Disease Management, Chronic Disease Management, Cluster-randomized, DIVERT Scale, Home Care

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The DIVERT-CARE (Collaboration Action Research & Evaluation) Trial Protocol: A Multi-Provincial Pragmatic Cluster Randomized Trial of Cardio-Respiratory Management in Home Care

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ABSTRACT

Introduction:
Home care clients are increasingly medically complex, have limited access to effective chronic disease management, and have very high emergency department (ED) visitation rates. There is a need for more appropriate and targeted supportive chronic disease management for home care clients. We aim to evaluate the effectiveness and preliminary cost-effectiveness of a targeted, person-centered cardio-respiratory management model.

Methods and analysis:
The DIVERT (Detection of Indicators and Vulnerabilities of Emergency Room Trips) – Care trial is a pragmatic, cluster-randomized, multi-center superiority trial of a flexible multi-component cardio-respiratory management model based on best-practice guidelines. The trial will be conducted in partnership with three regional, public-sector, home care providers across Canada. The primary outcome of the trial is the difference in time to first unplanned ED visit (hazard rate) within six months. Additional secondary outcomes are to identify changes in patient activation, changes in cardio-respiratory symptom frequencies, and cost-effectiveness over six months. We will also investigate the difference in the number of unplanned ED visits, number of inpatient hospitalizations, and changes in health-related quality of life. Multi-level proportional hazard and generalized linear models will be used to test the primary and secondary hypotheses. Sample size simulations indicate that enrolling 1,100 home care clients across 36 clusters (home care caseloads) will yield a power of 81% given a hazard ratio of 0.75.

Ethics and dissemination:
Ethics approval was obtained at all participating sites. Results will be submitted for publication in peer-reviewed journals and for presentation at relevant conferences. Home care service partners will also be informed of the study's results. The results will be used to inform future support strategies for older adults receiving home care services.

Trial registration number: ClinicalTrials.gov: NCT03012256

Keywords: Cardio-Respiratory Disease Management, Chronic Disease Management, Cluster-randomized, DIVERT Scale, Home Care

Strengths and limitations of this study

- The pragmatic attitude of the trial towards cluster selection, cluster assignment, participant selection, participant recruitment, informed consent, and outcome measurement supports generalization to other jurisdictions.
- Post randomization selection bias is limited by the use of existing, objective measures of eligibility.
- The use of secondary data for baseline data collection and follow-up measurement increases the accuracy of the data collection and limits the loss to follow-up compared to primary collection methods.
- It is not possible to conceal the treatment assignment, which exposes half of the primary and secondary outcomes measures to placebo and observer-expectancy effects.
- The jurisdictions included in the study used a convenience, non-probability sampling approach in cluster selection, which may limit external validity.

INTRODUCTION:

Publicly-funded home care services are delivered to at least 6% of Canadians age 65-74, 15% age 75-84 and 32% age 85 or older. [1] These home care clients are increasingly medically complex, often access care across multiple settings, have very high emergency department (ED) visitation rates, and have relatively poor access to effective chronic disease management.[2–4] Their frequent ED use is not congruent with chronic disease management or geriatric care principles and creates excess cost burdens on the health care system.[5,6]

Effective chronic disease management models employ multiple components delivered by a coordinated multidisciplinary team.[7] According to the 'chronic disease management model', home care plays a complementary function to the care medical practitioners provide.[7] Clinical and self-care support, as well as case management are among the most effective components in chronic disease management.[8–10] Self-care education and support has been shown to improve health outcomes across chronic diseases.[11,12] The provision of sustained follow-up by nurses or non-medical staff can also be effective.[13,14]

Effective home care services have been limited by insufficient targeting of clients that are most at need or most likely to benefit.[15,16] We developed and validated a prognostic case-finding tool for home care clients known as the Detection of Indicators and Vulnerabilities of Emergency Room Trips (DIVERT) Scale that has been recommended for use in the provision of home care.[17–19] It can be derived in real time from the interRAI Home Care (RAI-HC) standardized home care assessment system used in 9 Canadian provinces as well as Estonia, Finland, Hong Kong, Iceland, Ireland, Italy, Japan, the Netherlands, New Zealand, Singapore, Spain, Switzerland, and 29 U.S. states. Cardio-respiratory symptoms and conditions are prominent predictive elements of the DIVERT Scale.

Canadian home care providers, historically focused on the delivery of personal support services, have started to develop supportive chronic disease management capacity (e.g., specialist nurse monitoring).[20] Most trials, however, exclude frail seniors and are not specific to home care, which leaves little evidence to inform chronic disease management practices in this large sector of health care.[17]

From evidence-based guidelines developed – in part – by our team, extensive client profiling, and input of clients/families as well as health professionals, we developed a person-centred, multi-component cardio-respiratory management model. Our approach is based on evidence of effective implementations in other fields,[21] and includes all elements for 'person-centred care'.[22] The pilot study was recognized on the 2015 Ontario Minister of Health and Long-Term Care's Medal Honour Roll for Excellence in Health Quality.[23,24]

Recent Canadian trials have tested a 'Virtual Ward' and a 'transitional care services' model in post-acute adult patients (the latter with heart failure) and found no benefit.[25,26] The 'Virtual Ward Model' cited difficulty of hospital teams to integrate with community-based care. Community-based chronic disease management can reduce hospital use.[25,27] Our study diverges from this given that we focus on home care clients who are frail and not specifically

'post-acute'. Also, our intervention leverages a validated case finding tool based on real-time inputs from community-based providers rather than care from hospital-based teams.

The DIVERT-CARE trial will adopt a pragmatic attitude to avoid the well-documented difficulty that many clinical trials have in producing results that are generalizable to real-world conditions.[28,29] As our interest is in the effects of the intervention under realistic rather than optimal conditions, the intervention will be delivered in usual care settings by usual care providers for usual clients. Home care caseloads will be randomized to intervention or control rather than individual clients in order to mimic the process that would occur when clinical practice changes. Cluster randomized designs are commonly utilized in pragmatic trials as practice changes are implemented at levels higher than the client in real-world conditions.[30,31] The DIVERT-CARE trial will also make use of secondary data sources for outcome measurement. The use of administrative data has been shown to be more accurate than client-reported results for health services utilization and permits excellent follow-up over long periods of time without the need for intrusive follow-up procedures.[32,33] A number of pragmatic, cluster-randomized trials using administrative data have appeared in the literature.[34–37]

This paper describes the protocol and presents the rationale for a cluster-randomized study investigating the effectiveness of a cardio-respiratory disease management model in a targeted home care client population. This paper complies with the SPIRIT 2013 recommendations for clinical trial protocol reporting.[38] This trial will report findings in accordance with CONSORT guidelines.[39]

METHODS AND ANALYSIS:

Study Population

The trial will be conducted in partnership with three regional, public-sector, home care providers across Canada: Hamilton-Niagara-Haldimand-Brant Local Health Integration Network (HNHB LHIN) in Ontario, Western Health in Newfoundland, and Island Health in British Columbia. These three Canadian jurisdictions were selected from 5 potential jurisdictions that expressed interest based on their geographical (West, Central, and East) and political-cultural diversity. Each health care provider will select a number of home care caseloads to be included in the study based on historical practice patterns from each sub-region including caseload size, home care enrollment, and assessment patterns. A caseload represents a group of clients in a small geographical area that is served by a home care coordinator (or 'case manager'). Recruitment and randomization will occur at the level of the caseload and as such, clients were not involved in the research strategy. Each site will select enough caseloads to enroll approximately 360 long-stay home care clients, for a total of 1,100 clients over a 1.5-year time frame. We expect that over 42 distinct geographic home care caseloads will be enrolled in total.

Study Design

The DIVERT-CARE trial is a pragmatic, cluster-randomized, two-arm parallel cluster, multi-center, superiority trial with a primary outcome of time to first ED visit within 6 months of the index home care clinical assessment. The unit of randomization/intervention will be the cluster

(home care caseload; Figure 1: Caseload randomization schematic), while the unit of inference/measurement/analyses will be the home care client. The cluster-randomized design limits the potential for contamination and differential enrollment given that management and discretion over the use of resources is contained within each home care caseload. This design also supports the feasibility of the trial by reducing the number of resources (care providers) required to be trained in the intervention protocol. See Table 1 for an overview of the trial methods and design; Protocol Version 2.1 (2017-04-17).

Figure 1: Caseload Randomization Schematic <see Figure 1 attachment.>

Table 1: World Health Organization Trial Registration Data Set for DIVERT-CARE Trial (as of 11.03.2019; Protocol Version 2.1, 2017-04-17)

Data Category	**Information**
Primary registry and trial identifying number	ClinicalTrials.gov NCT03012256
Date of registration in primary registry	6 January, 2017
Secondary identifying numbers	
Source(s) of monetary or material support	Canadian Institutes of Health Research (CIHR); Hamilton Niagara Haldimand Brant Community Local Health Integration Network (Hamilton, Ontario); Western Health (Corner Brook, Newfoundland and Labrador); Island Health (Victoria, British Columbia); Canadian Frailty Network
Primary sponsor	McMaster University
Secondary sponsor(s)	N/A
Contact for public queries	Graham Campbell, MA [campbg4@mcmaster.ca]
Contact for scientific queries	Andrew Costa, PhD [acosta@mcmaster.ca] McMaster University
Public title	The DIVERT-CARE (Collaboration Action Research & Evaluation) Trial
Scientific title	The DIVERT-CARE (Collaboration Action Research & Evaluation) Trial: A Multi Provincial Pragmatic Cluster Randomized Trial of Cardio-Respiratory Management in Home Care
Countries of recruitment	Canada
Health condition(s) or problem(s) studied	Heart Failure; COPD
Intervention(s)	**Experimental:** Cardio-respiratory management model[40] **Control**: usual care / no intervention
Key inclusion and exclusion criteria	**Inclusion Criteria:**

	Long-stay home care clients living in a non-institutional setting (i.e. admitted to home care and receive comprehensive clinical assessment (RAI-HC)) Clients with DIVERT score of 9, 10, 14, or 15 (i.e. at least one cardio-respiratory symptom [chest pain, dyspnea, dizziness, irregular pulse]and at least one cardiac condition [congestive heart failure or coronary artery disease]) **Exclusion Criteria:** Clients receiving palliative care (i.e. Prognosis of less than six months to live at time of assessment [Q. K8e from RAI-HC]) Clients receiving dialysis (Q. P2g from RAI-HC)
Study type	Interventional Allocation: cluster randomized intervention model. Parallel assignment, open label Primary purpose: prevention Pragmatic
Date of first enrolment	6 February, 2018
Target sample size	1080
Recruitment status	Recruiting
Primary outcome(s)	The difference in days to first unplanned emergency department visit (hazard rate) [Time Frame: Up to six months from baseline]; The difference in total care costs controlling for length of stay [Time Frame: Up to six months from baseline]; Changes in patient activation (patient activation questionnaire) [Time Frame: Baseline, 2 months, 4 months, 6 months]; The difference in the number of symptoms [Time Frame: Baseline, 2 months, 4 months, 6 months]
Key secondary outcomes	The difference in the number of unplanned emergency department visits [Time Frame: Up to six months from baseline]; Description of health-related quality of life (quality of life questionnaire) [Time Frame: 4 months, 6 months]

Study Objectives

Our main objective is to evaluate the effectiveness and preliminary cost-effectiveness of a targeted, person-centered cardio-respiratory management model. The sample size for the primary outcome was calculated to determine whether the cardio-respiratory disease management model is superior to standard of care in postponing unplanned ED visits. Additional outcomes include determining if the cardio-respiratory disease management model is superior to standard of care in improving client activation, reducing symptoms, and the cost-effectiveness of this model. The symptoms of interest are shortness of breath, chest pain at rest

or on exertion, dizziness, perceived pain control, edema, noticeable decrease in food/fluids consumed, and unintended weight loss.

Secondary objectives include determining if the cardio-respiratory disease management model is superior to standard of care for the number of unplanned ED visits, number of unplanned hospital admissions, and change in health-related quality of life (HRQOL). HRQOL will be assessed by the Minimal Data Set Health Status Index (MDS-HSI), which is a RAI-HC derived measure based on the Health Utilities Index Mark 2 that has demonstrated longitudinal construct validity.[41,42]

Eligibility Criteria

The pragmatic attitude of the trial warrants the broadest inclusion criteria that are feasible. To be eligible for inclusion into this trial, home care clients must possess the following characteristics:

- Admitted to home care and receive comprehensive clinical assessment (RAI-HC) as part of regular home care enrolment, or reassessment;
- 19 years or older at time of assessment; and
- Categorized into DIVERT subgroups 9,10,14, or 15 (Figure 2: DIVERT Scale Target Groups). This includes:
    - those with cardio-respiratory symptoms (chest pain, dyspnea, dizziness, irregular pulse) who have a diagnosis of chronic cardiac disease and have not used an ED or hospital in the last 90 days (9, 10); OR
    - those with cardio-respiratory symptoms who have had one ED or hospital exposure in the last 90 days, regardless of if they are diagnosed with chronic cardiac disease (14, 15).

Figure 2: DIVERT Scale Target Groups <see Figure 2 attachment.>

We will exclude clients with a prognosis of less than six months to live at time of assessment (Q. K8e from RAI-HC) and clients requiring dialysis treatment (Q. P2g from RAI-HC). The exclusion of palliative and dialysis care clients is necessary as some jurisdictions place these clients on specialized caseloads.

The eligibility criteria for the trial will result in a population that is representative of non-palliative home care clients in Canada who have cardio-respiratory symptoms and conditions. It captures approximately 1/3 of all assessed home care clients. However, we excluded individuals with cardio-respiratory symptoms with 2 or more hospital or ED episodes in the past 90 days given that they were determined in a pilot study to have exceedingly complex psycho-social needs (such as housing) that we could not address. They account for less than 4% of home care clients.

Recruitment and Consent

All non-palliative, non-dialysis, adult home care clients in the trial caseloads assessed using the RAI-HC (during regular home care enrollment or reassessment) who fall into one of the four

target DIVERT subgroups will be enrolled into the study by a care coordinator at the time of assessment. Eligible clients will automatically be included into the intervention or 'regular care' control groups on an intent-to-treat basis. Recruitment is expected to proceed over 6-9 months for each site. Analysis of the sample size simulations that were carried out on retrospective data from the HNHB LHIN region from November 2014 to June 2015 indicates an expected enrollment of 4 clients per caseload per month.

Each home care partners' process for attaining consent will apply to the trial. Individual informed consent will not be sought given that the cardio-respiratory management model is accepted, considered best practice care, and is offered – whole or in part – at the full clinical discretion of the home care provider as per existing practice. Trial investigators have no part in the data collection, individual care decision-making, or record management during the study period beyond providing overall scientific guidance. We requested and received alteration to the requirements for consent based on satisfying the following Canadian Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2) criteria:[43]

1. The research involves no more than minimal risk to the participants.
2. The alteration to consent requirements is unlikely to adversely affect the welfare of participants.
3. It is impossible or impracticable to carry out the research and to address the research questions properly, given the research design, if the prior consent of participants is required.
4. In the case of a proposed alteration, the precise nature and extent of any proposed alteration is defined.
5. The plan to provide a debriefing (if any) which may offer participants the possibility of refusing consent and/or withdrawing data and/or human biological materials, shall be in accordance with Article 3.7B.

Our waiver of informed consent complies with existing methodological and ethical guidelines for pragmatic cluster-randomized trials. Existing guidelines state that informed consent by clients is not needed if "the intervention is to the clear advantage of every person in the cluster for the cluster to be entered in the trial"[44].

Intervention

Care planning and self-care support have been shown to be among the most effective elements of cardio-respiratory disease management[8,10] along with sustained follow-up by nurses or non-medical staff [13,14]. Care planning will be completed in a collaborative fashion amongst a care coordinator, the client, and the client's caregivers (both formal and informal). Clients in the intervention group will have their care plans guided by a multi-component cardio-respiratory disease management model in addition to receiving their usual care.[39] This comprehensive model for the intervention has been described in greater detail in a previous publication.[40] The person-centered, multi-component cardio-respiratory management model was developed based on guidelines,[17,45,46] extensive home care client profiling, and input from clients/families and health professionals. The management model contains the following

components (see Table 2: Description of Intervention Components): scheduled nurse-led self-management support (based on a training program and tool-kit); access to a staffed helpline; education on vaccines; advance care and goal planning; clinical pharmacist medication reconciliation; team case rounds; situation, background, assessment, and recommendation (SBAR) communication protocol with primary care; and a standardized transition package.[21,40,47] Each component has a specific objective within the model, however the manner in which it is delivered may be adapted. For example, some home care providers have clinical pharmacists on staff whereas others would rely on collaboration with community pharmacists.

Table 2: Description of intervention components

DIVERT-CARE Intervention Components	Description
Case Finding Using the DIVERT Scale	Use of the DIVERT Scale (embedded in interRAI assessment) to identify home care clients most likely to benefit.
Self-Management Education and Supports	In-home assessment of self-management goals and needs, with practical education and skills training to recognize and manage symptoms.
Access to an immediate nurse-staffed helpline	Direct phone line staffed by nurses involved in the DIVERT-CARE Intervention to aid with self-management and problem resolution.
Promotion of Vaccines	Seasonal flu vaccine and pneumococcal polysaccharide (Pneu-P-23) information and health promotion consistent with Canadian practice guidelines.
Advance Care and Goal Planning	Consultation for advance care and goals of care planning, advanced care decisions, and communication of care wishes.
Clinical Pharmacist-Led Medication Review	Review of medication for safety, efficacy and appropriate use of medications and delivery options.
Interprofessional Team Case Rounds	Weekly or biweekly care team meeting to discuss care plan, update goals, and how to support changing care needs.
SBAR Communication with Primary Care Providers	SBAR formatted communication to effectively communicate disease relevant information and care updates to primary and specialist care providers.
Standardized ED Transition Package / Personal Care Record	A succinct document to support continuity of care throughout health system. Personal care record of goals, plan of care, and community supports.

Self-management education and supports will be tailored to the needs and goals of the client. As with all home care services, clients may refuse all or any of the intervention components. The components will be delivered over 15 weeks by care coordinators and nurses who have been trained by the research team. Care coordinators and nurses will be provided detailed manuals explaining the components and their role in supporting clients throughout the intervention. The self-management program, based on previous pilot work[24], will use a population-based care approach pioneered by Wagner (1995) to help trial partners implement the cardio-respiratory disease management model.[48]

The intervention adheres to the following three principles: 1) multidisciplinary teams at each site will be trained on the protocols and resources related to each component of cardio-respiratory management model; 2) the teams will identify steps required to deliver the interventions; 3) the teams will plan the deployment of the cardio-respiratory management model that engages clients, families, and caregivers to ensure that adequate resources are dedicated to support the interventions across the intervention caseloads, while ensuring long-term sustainability.

Clients in the control group will receive the usual set of home care services. No changes will be made to their care planning process. Depending on the jurisdiction and client needs, usual care may include personal support, nursing, physiotherapy, occupational therapy, and other services. Depending on the jurisdiction, access to the components described in the cardio-respiratory disease management model is either non-existent or otherwise very rare and inconsistent for clients receiving usual care.

Allocation

Caseloads were randomized to intervention or control, and stratified by home care provider (region) and sub-region (areas with similar economic status, access to care, and geography) at a 1:2 intervention to control ratio. The uneven allocation ratio increases the power of the trial while only minimally impacting operational and research resources.

A blocked allocation sequence was created via random number generation in collaboration with the biostatistics unit at St. Joseph's Healthcare Hamilton. The sequence features a 1:2 allocation ratio with a block of size three. Caseloads from each region were sorted by sub-region and allocated using the sequence. In the event that the end of the clusters in a sub-region did not coincide with the end of a block, the rest of the block was skipped and allocation of the next sub-region started with a new block.

Data Collection and Outcome Measures

The primary outcomes will be collected using secondary data over the six-month observation period (see Table 3: Routine Measurement). The use of routinely collected data for primary outcomes, cost, and health measures limits potential for bias from lack of blinding given that neither the care team nor the trial investigators are directly involved in the collection of outcomes. These records are accurate given that they are the basis for health care reporting systems and payments between public home care providers and contracted service providers.

Table 3: Routine Measurement

Activity	Staff Member	Approximate Time to Complete	Baseline	2 Months	4 Months	6 Months
Assess for eligibility (If intervention caseload) (RAI-HC)	Care coordinator	5 minutes	X			
Symptoms (RAI-HC)	Care coordinator	15 minutes	X	X	X	X
Health-related quality of life (RAI-HC)	Care coordinator	30 minutes	X		X	X
Patient Activation Measure (PAM-13)	Care coordinator	5 minutes	X	X	X	X
Administrative service and billing records (CHRIS, HCC MRR, CRMS)	N/A	N/A	X	X	X	X
Emergency department and hospital records (NACRS, DAD)	N/A	N/A	X	X	X	X

Legend:
RAI-HC: Resident Assessment Instrument for Home Care (https://www.cihi.ca/en/home-care)
PAM-13: Patient Activation Measure (https://www.insigniahealth.com/products/pam-survey)
CHRIS: Client Health and Related Information System (https://hssontario.ca/Who/Pages/protecting-your-privacy.aspx)
HCC MRR: Home and Community Care Minimum Reporting Requirements (https://www2.gov.bc.ca/assets/gov/health/forms/5502datadictionary.pdf)
CRMS: Client and Referral Management System (https://www.nlchi.nl.ca/images/ProvincialCRMS_Registration_User_Guide_v2_0_2017-09-01.pdf)
NACRS: National Ambulatory Care Reporting System (https://www.cihi.ca/en/national-ambulatory-care-reporting-system-metadata
DAD: Discharge Abstract Database (https://www.cihi.ca/en/discharge-abstract-database-metadata)

The main secondary data sets include the Resident Assessment Instrument for Home Care (RAI-HC), the Patient Activation Measure (PAM-13), the Client Health and Related Information System (CHRIS), the Home and Community Care Minimum Reporting Requirements (HCC MRR), the Client and Referral Management System (CRMS), the National Ambulatory Care Reporting System (NACRS), and the Discharge Abstract Database (DAD).

The RAI-HC is a standardized comprehensive assessment containing approximately 200 items and has been found to document major domains of health reliably.[49–53]

The Patient Activation Measure (PAM-13) [54] indicates the client's progress through four stages as they become activated (i.e., they believe their role in their own care is important, they learn enough to develop confidence to act on their own belief, they actually act, and they reach the point where they can act even under stress). The PAM is a widely used measure of patient activation that has demonstrated sensitivity to health-related outcomes, including health service use.[55,56]

The CHRIS is the health administrative database used by Ontario's publicly-funded home care providers. It includes client assessments, documents, provider and vendor contracts, billing of services information, and medical supplies and equipment rental costs.

The HCC MRR is an information management system defining a set of data elements that are reported to the British Columbia Ministry of Health by the regional health authorities. The HCC MRR captures information on clients, income, and home and community care services.

The Client and Referral Management System (CRMS) is a health information system designed to support client and referral management for clients receiving community-based services from the regional health boards in Newfoundland. It contains information on client records and clinical activity.

The NACRS contains data from all national hospital-based and community-based ambulatory care. It is collected and maintained by the Canadian Institute for Health Information (CIHI), which conducts its own quality assurance procedures to ensure accuracy and completeness.

The DAD captures administrative, clinical, and demographic information nationally on hospital discharges (including deaths, sign-outs, and transfers). It is collected and maintained by CIHI, which conducts its own quality assurance procedures to ensure accuracy and completeness.

Sample Size Calculations

Sample size calculation assumptions:

- Primary outcome: Time to first unplanned ED visit within 6 months of baseline
- Hazard ratio of 0.75
- Mean size of a home care caseload: 120 clients
- Mean prevalence of DIVERT target group in each caseload: 30%
- Expected recruitment over 6 months per caseload: 30
- Mean cluster size: 30
- Allocation: 1:2 (intervention: control)

Simulations using retrospective secondary data sources were undertaken to explore the power of a hypothetical DIVERT-CARE trial conducted in the HNHB LHIN region of Ontario from December 2015 to June 2016. The simulations found that 36 HNHB home care caseloads randomized at a 1:2 intervention to control ratio could expect to enroll 1,100 clients across

seven months. The simulation linked clients to their actual ED utilization records and extended the time to first ED visit figures for clients in 12 randomly selected intervention caseloads to achieve a hazard ratio of 0.75, a figure chosen to be more conservative than the pilot study but still clinically significant. The overall event rate was 35.5% in the intervention group and 44.8% in the control. The median time to first visit was 88 days in the intervention group and 75 days in the control. The power of the simulated DIVERT trial was 81.3% with a two-sided alpha of 0.05. Simulations with a hazard ratio of 0.80 yielded a power of 60.1%. The intraclass correlation coefficient (ICC) was estimated to be 0.005.

Based on the simulations the target sample size for the trial will be 1,100 clients, which will yield an approximate power of 81% for a hazard ratio of 0.75 and 60% for a hazard ratio of 0.80.

Statistical Analyses

Descriptive analyses will compare the treatment groups and sites on baseline demographic and clinical characteristics. Statistics on compliance, censoring, and follow-up times will also be presented.

The primary outcome will be assessed through a multi-level proportional hazards model on an intent-to-treat basis. The dependent variable will be days until first unplanned ED visit, censored at date of home care discharge for any reason. Caseload and partner site will be included as nested random effects. Both unadjusted and adjusted results will be reported. For adjusted analysis, DIVERT subgroup, age, and sex will be included as time-independent fixed effects. The hazard ratio, 95% confidence interval, and p-value will be reported for the treatment group effect and covariates when applicable. A two-sided alpha level of 0.05 will be used to judge statistical significance.

The assumption of proportionality of hazards across treatment groups will be evaluated by a visual inspection of the hazard curves and statistical testing of a time-dependent treatment group effect. If the hazard curves cross or the time-dependent treatment group effect is significant ($p < 0.05$) then primary analysis will be modified to consider treatment group as a time-varying effect.

The economic evaluation will examine total care costs, controlling for length of stay, between treatment groups to compare incremental costs to incremental effects (i.e., cost per ED visit averted). Total care costs are defined as direct costs incurred by the home care provider in the provision of home care services, including: human resources and equipment. We will use a micro-costing approach based on the listed/billed service cost consumed by each patient.

The other outcomes will be evaluated by multi-level generalized linear models. Four-month and six-month changes in PAM, HRQOL, number of symptoms, number of ED visits, and number of unplanned hospitalizations will be the respective dependent variables. Caseload and partner site will be included as nested random effects. Both unadjusted and adjusted results will be reported. For adjusted analysis DIVERT subgroup, age, and sex will be included as fixed effects. Unit change and rate ratios, with their associated 95% confidence interval and p-values, will be

reported for the treatment group effect and covariates as applicable. A two-sided alpha level of 0.05 will be used to judge statistical significance.

Model assumptions will be evaluated by a visual inspection of residuals and the sensitivity of the results to the use of a heteroskedastic-robust variance estimator. If evidence of departure from model assumptions is present, then the analysis will be modified to utilize an empirical variance estimator.

Patient and Public Involvement

The intervention, comprehensively described elsewhere [40], was developed based on the input from clients/families and health professionals in a series of three in-person stakeholder meetings held in late 2013 and early 2014. The pilot of the study methodology was conducted in 2014 with the collaboration, input, and funding from a regional, public-sector, home care provider (HNHB LHIN). Participating clients and health professionals provided input into the intervention (and study design for health professionals) through telephone interviews using a structured questionnaire focused on the perceived benefit and utility of the interventions, overall satisfaction, and areas for improvement. The outcomes of the pilot study were featured in the home care providers annual report to the community.

The present protocol, based on the aforementioned pilot study, received input from health professionals in each participating region through a series of in-person planning meetings in mid-2017. The general public was engaged in one region through a local radio program. Adaptations and modifications to the intervention in each region to account for their unique health service context will be described in a forthcoming implementation publication. The experience of participating clients and health professionals will be investigated in a program evaluation and qualitative study to be conducted in parallel. The results of the trial are expected to be released to the study participants and public though regional public reports.

ETHICS AND DISSEMINATION

Harm

This trial is unlikely to cause additional risk of harm since the various components of the intervention are already available from home care agencies and service providers, though rarely offered in the standard care plan. Direct risks to the health of the client are minimal as none of the components of the intervention are novel interventions. Each element of the intervention has been shown to be safe individually. Clients in the control group will continue to receive their usual care, while clients in the intervention group will receive usual care plus increased access to additional home care services defined by the cardio-respiratory treatment model. A Data Monitoring and Ethics (or equivalent) Committee was not required, and formal stopping rules or interim analyses are not planned.

Ethical approval

We have received ethics approval from the Hamilton-Integrated Research Ethics Board, Health Research Ethics Authority for Western Health, and the Clinical Research Ethics Board for Vancouver Island.

Results dissemination

We aim to make the results of this study public through peer-reviewed publications, clinical trial registry, thesis manuscripts, conference publications, and notifications to our trial partners, who will include the findings in their regular newsletters and annual reports to clients, partners, and government.

DISCUSSION

In summary, this pragmatic, cluster-randomized, multi-center superiority trial will investigate the effectiveness of a cardio-respiratory disease management model in a targeted home care client population, with case finding occurring using the DIVERT scale[19]. By offering a person-centered, multi-component cardio-respiratory management model to home care clients at the highest levels of risk,[40] we hope to determine if unplanned ED visits are postponed, clients have increased activation in their care, symptoms are reduced, and that the care model is cost-effective.

This pragmatic trial will inform how multi-component cardio-respiratory care interventions are received as they are delivered in real-world conditions. Historically, trials investigating community programs have excluded frail seniors who would be at high-risk of ED services. Additionally, other trials have tended to focus on post-acute care and have not targeted high-risk clients when assessing community-based chronic disease management interventions.

The need for appropriate and targeted supportive chronic disease management is a clear and compelling health services issue, and is reflected in new provincial government investments into the sector. This trial will be an important precedent around the creation of more upstream approaches to care for home-care clients that help to take further pressure of hospitals and EDs that are already facing issues of overcrowding across Canada.

Author Contributions

APC is the principal investigator and led the conceptualization and design of the protocol, drafted, and revised the manuscript. CS, AJ, DD, MJ, and GC made contributions to the design and implementation of the study, and supported the manuscript. GA, CB, VB, SB, DF, PH, GH, JH, LL, RM, LM, and SS are co-investigators that contributed to the design of the study, and revised the manuscript. JD, TP, JR, RG, DM, and DH are trial partners who contributed to the design and implementation of the study. All authors critically revised the manuscript and approved the final version of this manuscript.

Competing interests

It should be noted that DHF has a proprietary interest in Health Utilities Incorporated, Dundas, Ontario, Canada. HUInc distributes copyrighted Health Utilities Index (HUI) materials and provides methodological advice on the use of the HUI. All others author have no competing interests.

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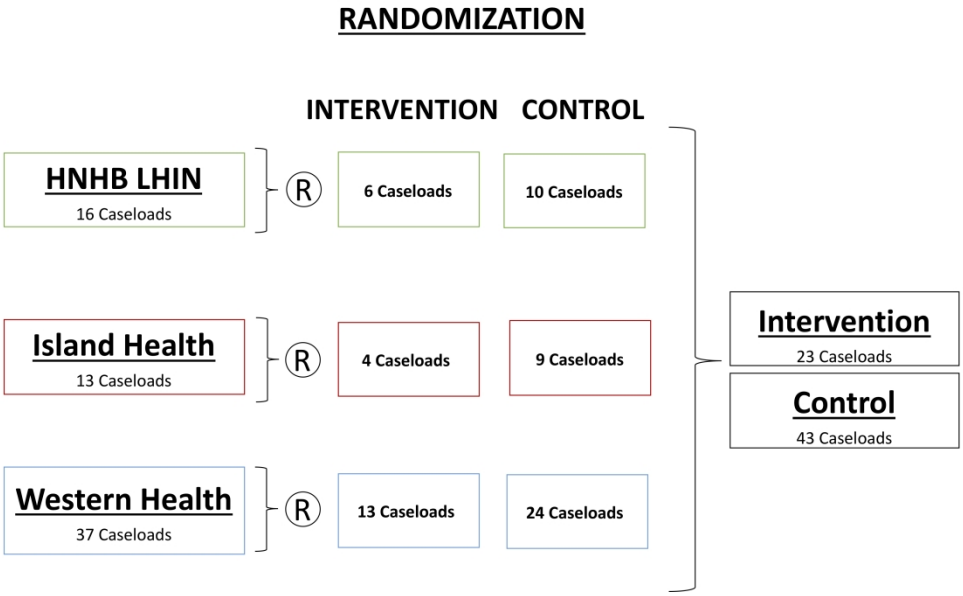

Figure 1: Caseload Randomization Schematic

368x222mm (300 x 300 DPI)

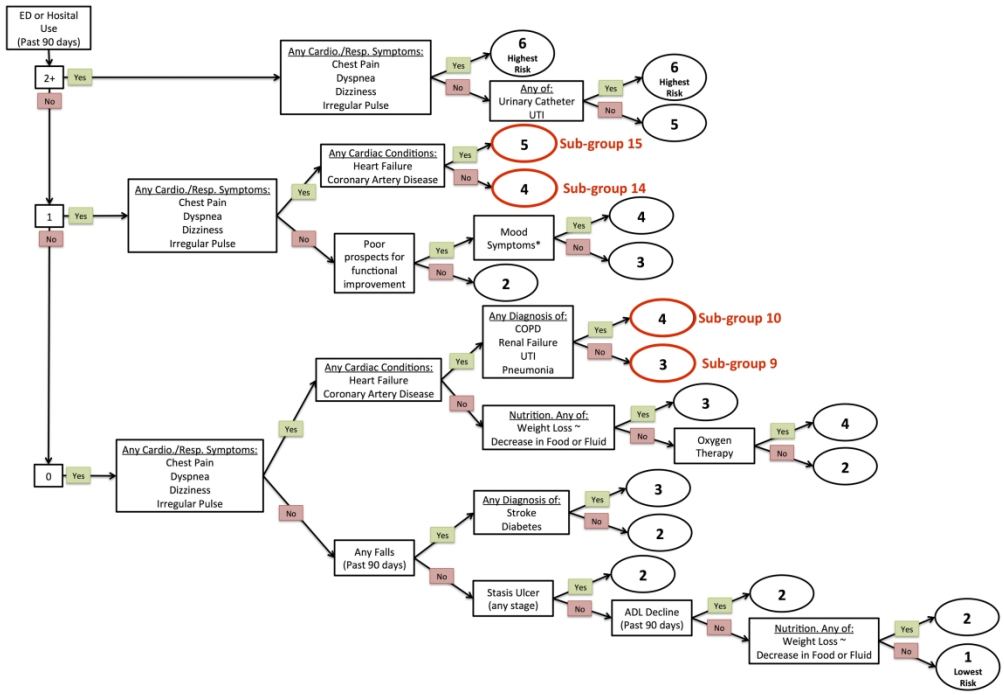

Figure 2: DIVERT Scale Target Groups

254x175mm (300 x 300 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

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		Reporting Item	Page Number
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	7-8
Protocol version	#3	Date and version identifier	7
Funding	#4	Sources and types of financial, material, and other support	17
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	17
Roles and responsibilities:	#5b	Name and contact information for the trial sponsor	17

sponsor contact information			
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	17
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	17
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	9
Objectives	#7	Specific objectives or hypotheses	8
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	6
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	9
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	10
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	10
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return;	11

		laboratory tests)	
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	11
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	12
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	12
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	14
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	9
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	9
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	9
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	9
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	9
Blinding (masking): emergency	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during	9

unblinding		the trial	
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	13
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	13
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	13
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	14
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	15
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	15
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	15
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and	15

		whether the process will be independent from investigators and the sponsor	
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	16
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	16
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	9
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	9
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	16
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	17
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	17
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	9
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	16
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	16
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	16
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	N/A

Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

BMJ Open

The DIVERT-CARE (Collaboration Action Research & Evaluation) Trial Protocol: A Multi-Provincial Pragmatic Cluster Randomized Trial of Cardio-Respiratory Management in Home Care

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Version: 6.5(AC)
Date: November, 2019

The DIVERT-CARE (Collaboration Action Research & Evaluation) Trial Protocol: A Multi-Provincial Pragmatic Cluster Randomized Trial of Cardio-Respiratory Management in Home Care

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ABSTRACT

Introduction:
Home care clients are increasingly medically complex, have limited access to effective chronic disease management, and have very high emergency department (ED) visitation rates. There is a need for more appropriate and targeted supportive chronic disease management for home care clients. We aim to evaluate the effectiveness and preliminary cost-effectiveness of a targeted, person-centered cardio-respiratory management model.

Methods and analysis:
The DIVERT (Detection of Indicators and Vulnerabilities of Emergency Room Trips) – Care trial is a pragmatic, cluster-randomized, multi-center superiority trial of a flexible multi-component cardio-respiratory management model based on best-practice guidelines. The trial will be conducted in partnership with three regional, public-sector, home care providers across Canada. The primary outcome of the trial is the difference in time to first unplanned ED visit (hazard rate) within six months. Additional secondary outcomes are to identify changes in patient activation, changes in cardio-respiratory symptom frequencies, and cost-effectiveness over six months. We will also investigate the difference in the number of unplanned ED visits, number of inpatient hospitalizations, and changes in health-related quality of life. Multi-level proportional hazard and generalized linear models will be used to test the primary and secondary hypotheses. Sample size simulations indicate that enrolling 1,100 home care clients across 36 clusters (home care caseloads) will yield a power of 81% given a hazard ratio of 0.75.

Ethics and dissemination:
Ethics approval was obtained from the Hamilton Integrated Research Ethics Board as well as each participating site's ethics board. Results will be submitted for publication in peer-reviewed journals and for presentation at relevant conferences. Home care service partners will also be informed of the study's results. The results will be used to inform future support strategies for older adults receiving home care services.

Trial registration number: ClinicalTrials.gov: NCT03012256

Keywords: Cardio-Respiratory Disease Management, Chronic Disease Management, Cluster-randomized, DIVERT Scale, Home Care

Strengths and limitations of this study

- The pragmatic attitude of the trial towards cluster selection, cluster assignment, participant selection, participant recruitment, informed consent, and outcome measurement supports generalization to other jurisdictions.
- Post randomization selection bias is limited by the use of existing, objective measures of eligibility.
- The use of secondary data for baseline data collection and follow-up measurement increases the accuracy of the data collection and limits the loss to follow-up compared to primary collection methods.
- It is not possible to conceal the treatment assignment, which exposes half of the primary and secondary outcomes measures to placebo and observer-expectancy effects.
- The jurisdictions included in the study used a convenience, non-probability sampling approach in cluster selection, which may limit external validity.

INTRODUCTION:

Publicly-funded home care services are delivered to at least 6% of Canadians age 65-74, 15% age 75-84 and 32% age 85 or older. [1] These home care clients are increasingly medically complex, often access care across multiple settings, have very high emergency department (ED) visitation rates, and have relatively poor access to effective chronic disease management.[2–4] Their frequent ED use is not congruent with chronic disease management or geriatric care principles and creates excess cost burdens on the health care system.[5,6]

Effective chronic disease management models employ multiple components delivered by a coordinated multidisciplinary team.[7] According to the 'chronic disease management model', home care plays a complementary function to the care medical practitioners provide.[7] Clinical and self-care support, as well as case management are among the most effective components in chronic disease management.[8–10] Self-care education and support has been shown to improve health outcomes across chronic diseases.[11,12] The provision of sustained follow-up by nurses or non-medical staff can also be effective.[13,14]

Effective home care services have been limited by insufficient targeting of clients that are most at need or most likely to benefit.[15,16] We developed and validated a prognostic case-finding tool for home care clients known as the Detection of Indicators and Vulnerabilities of Emergency Room Trips (DIVERT) Scale that has been recommended for use in the provision of home care.[17–19] It can be derived in real time from the interRAI Home Care (RAI-HC) standardized home care assessment system used in 9 Canadian provinces as well as Estonia, Finland, Hong Kong, Iceland, Ireland, Italy, Japan, the Netherlands, New Zealand, Singapore, Spain, Switzerland, and 29 U.S. states. Cardio-respiratory symptoms and conditions are prominent predictive elements of the DIVERT Scale.

Canadian home care providers, historically focused on the delivery of personal support services, have started to develop supportive chronic disease management capacity (e.g., specialist nurse monitoring).[20] Most trials, however, exclude frail seniors and are not specific to home care, which leaves little evidence to inform chronic disease management practices in this large sector of health care.[17]

From evidence-based guidelines developed – in part – by our team, extensive client profiling, and input of clients/families as well as health professionals, we developed a person-centred, multi-component cardio-respiratory management model. Our approach is based on evidence of effective implementations in other fields,[21] and includes all elements for 'person-centred care'.[22] The pilot study was recognized on the 2015 Ontario Minister of Health and Long-Term Care's Medal Honour Roll for Excellence in Health Quality.[23,24]

Recent Canadian trials have tested a 'Virtual Ward' and a 'transitional care services' model in post-acute adult patients (the latter with heart failure) and found no benefit.[25,26] The 'Virtual Ward Model' cited difficulty of hospital teams to integrate with community-based care. Community-based chronic disease management can reduce hospital use.[25,27] Our study diverges from this given that we focus on home care clients who are frail and not specifically

'post-acute'. Also, our intervention leverages a validated case finding tool based on real-time inputs from community-based providers rather than care from hospital-based teams.

The DIVERT-CARE trial will adopt a pragmatic attitude to avoid the well-documented difficulty that many clinical trials have in producing results that are generalizable to real-world conditions.[28,29] As our interest is in the effects of the intervention under realistic rather than optimal conditions, the intervention will be delivered in usual care settings by usual care providers for usual clients. Home care caseloads will be randomized to intervention or control rather than individual clients in order to mimic the process that would occur when clinical practice changes. Cluster randomized designs are commonly utilized in pragmatic trials as practice changes are implemented at levels higher than the client in real-world conditions.[30,31] The DIVERT-CARE trial will also make use of secondary data sources for outcome measurement. The use of administrative data has been shown to be more accurate than client-reported results for health services utilization and permits excellent follow-up over long periods of time without the need for intrusive follow-up procedures.[32,33] A number of pragmatic, cluster-randomized trials using administrative data have appeared in the literature.[34–37]

This paper describes the protocol and presents the rationale for a cluster-randomized study investigating the effectiveness of a cardio-respiratory disease management model in a targeted home care client population. This paper complies with the SPIRIT 2013 recommendations for clinical trial protocol reporting.[38] This trial will report findings in accordance with CONSORT guidelines.[39]

METHODS AND ANALYSIS:

Study Population

The trial will be conducted in partnership with three regional, public-sector, home care providers across Canada: Hamilton-Niagara-Haldimand-Brant Local Health Integration Network (HNHB LHIN) in Ontario, Western Health in Newfoundland, and Island Health in British Columbia. These three Canadian jurisdictions were selected from 5 potential jurisdictions that expressed interest based on their geographical (West, Central, and East) and political-cultural diversity. Each health care provider will select a number of home care caseloads to be included in the study based on historical practice patterns from each sub-region including caseload size, home care enrollment, and assessment patterns. A caseload represents a group of clients in a small geographical area that is served by a home care coordinator (or 'case manager'). Recruitment and randomization will occur at the level of the caseload and as such, clients were not involved in the research strategy. Each site will select enough caseloads to enroll approximately 360 long-stay home care clients, for a total of 1,100 clients over a 1.5-year time frame. We expect that over 42 distinct geographic home care caseloads will be enrolled in total.

Study Design

The DIVERT-CARE trial is a pragmatic, cluster-randomized, two-arm parallel cluster, multi-center, superiority trial with a primary outcome of time to first ED visit within 6 months of the index home care clinical assessment. The unit of randomization/intervention will be the cluster

(home care caseload; Figure 1: Caseload randomization schematic), while the unit of inference/measurement/analyses will be the home care client. The cluster-randomized design limits the potential for contamination and differential enrollment given that management and discretion over the use of resources is contained within each home care caseload. This design also supports the feasibility of the trial by reducing the number of resources (care providers) required to be trained in the intervention protocol. See Table 1 for an overview of the trial methods and design; Protocol Version 2.1 (2017-04-17).

Figure 1: Caseload Randomization Schematic <see Figure 1 attachment.>

Table 1: World Health Organization Trial Registration Data Set for DIVERT-CARE Trial (as of 11.03.2019; Protocol Version 2.1, 2017-04-17)

Data Category	**Information**
Primary registry and trial identifying number	ClinicalTrials.gov NCT03012256
Date of registration in primary registry	6 January, 2017
Secondary identifying numbers	
Source(s) of monetary or material support	Canadian Institutes of Health Research (CIHR); Hamilton Niagara Haldimand Brant Community Local Health Integration Network (Hamilton, Ontario); Western Health (Corner Brook, Newfoundland and Labrador); Island Health (Victoria, British Columbia); Canadian Frailty Network
Primary sponsor	McMaster University
Secondary sponsor(s)	N/A
Contact for public queries	Graham Campbell, MA [campbg4@mcmaster.ca]
Contact for scientific queries	Andrew Costa, PhD [acosta@mcmaster.ca] McMaster University
Public title	The DIVERT-CARE (Collaboration Action Research & Evaluation) Trial
Scientific title	The DIVERT-CARE (Collaboration Action Research & Evaluation) Trial: A Multi Provincial Pragmatic Cluster Randomized Trial of Cardio-Respiratory Management in Home Care
Countries of recruitment	Canada
Health condition(s) or problem(s) studied	Heart Failure; COPD
Intervention(s)	**Experimental:** Cardio-respiratory management model[40] **Control**: usual care / no intervention
Key inclusion and exclusion criteria	**Inclusion Criteria:**

	Long-stay home care clients living in a non-institutional setting (i.e. admitted to home care and receive comprehensive clinical assessment (RAI-HC)) Clients with DIVERT score of 9, 10, 14, or 15 (i.e. at least one cardio-respiratory symptom [chest pain, dyspnea, dizziness, irregular pulse]and at least one cardiac condition [congestive heart failure or coronary artery disease]) **Exclusion Criteria:** Clients receiving palliative care (i.e. Prognosis of less than six months to live at time of assessment [Q. K8e from RAI-HC]) Clients receiving dialysis (Q. P2g from RAI-HC)
Study type	Interventional Allocation: cluster randomized intervention model. Parallel assignment, open label Primary purpose: prevention Pragmatic
Date of first enrolment	6 February, 2018
Target sample size	1080
Recruitment status	Recruiting
Primary outcome(s)	The difference in days to first unplanned emergency department visit (hazard rate) [Time Frame: Up to six months from baseline]; The difference in total care costs controlling for length of stay [Time Frame: Up to six months from baseline]; Changes in patient activation (patient activation questionnaire) [Time Frame: Baseline, 2 months, 4 months, 6 months]; The difference in the number of symptoms [Time Frame: Baseline, 2 months, 4 months, 6 months]
Key secondary outcomes	The difference in the number of unplanned emergency department visits [Time Frame: Up to six months from baseline]; Description of health-related quality of life (quality of life questionnaire) [Time Frame: 4 months, 6 months]

Study Objectives

Our main objective is to evaluate the effectiveness and preliminary cost-effectiveness of a targeted, person-centered cardio-respiratory management model. The sample size for the primary outcome was calculated to determine whether the cardio-respiratory disease management model is superior to standard of care in postponing unplanned ED visits. Additional outcomes include determining if the cardio-respiratory disease management model is superior to standard of care in improving client activation, reducing symptoms, and the cost-effectiveness of this model. The symptoms of interest are shortness of breath, chest pain at rest

or on exertion, dizziness, perceived pain control, edema, noticeable decrease in food/fluids consumed, and unintended weight loss.

Secondary objectives include determining if the cardio-respiratory disease management model is superior to standard of care for the number of unplanned ED visits, number of unplanned hospital admissions, and change in health-related quality of life (HRQOL). HRQOL will be assessed by the Minimal Data Set Health Status Index (MDS-HSI), which is a RAI-HC derived measure based on the Health Utilities Index Mark 2 that has demonstrated longitudinal construct validity.[41,42]

Eligibility Criteria

The pragmatic attitude of the trial warrants the broadest inclusion criteria that are feasible. To be eligible for inclusion into this trial, home care clients must possess the following characteristics:

- Admitted to home care and receive comprehensive clinical assessment (RAI-HC) as part of regular home care enrolment, or reassessment;
- 19 years or older at time of assessment; and
- Categorized into DIVERT subgroups 9,10,14, or 15 (Figure 2: DIVERT Scale Target Groups). This includes:
    - those with cardio-respiratory symptoms (chest pain, dyspnea, dizziness, irregular pulse) who have a diagnosis of chronic cardiac disease and have not used an ED or hospital in the last 90 days (9, 10); OR
    - those with cardio-respiratory symptoms who have had one ED or hospital exposure in the last 90 days, regardless of if they are diagnosed with chronic cardiac disease (14, 15).

Figure 2: DIVERT Scale Target Groups <see Figure 2 attachment.>

We will exclude clients with a prognosis of less than six months to live at time of assessment (Q. K8e from RAI-HC) and clients requiring dialysis treatment (Q. P2g from RAI-HC). The exclusion of palliative and dialysis care clients is necessary as some jurisdictions place these clients on specialized caseloads.

The eligibility criteria for the trial will result in a population that is representative of non-palliative home care clients in Canada who have cardio-respiratory symptoms and conditions. It captures approximately 1/3 of all assessed home care clients. However, we excluded individuals with cardio-respiratory symptoms with 2 or more hospital or ED episodes in the past 90 days given that they were determined in a pilot study to have exceedingly complex psycho-social needs (such as housing) that we could not address. They account for less than 4% of home care clients.

Recruitment and Consent

All non-palliative, non-dialysis, adult home care clients in the trial caseloads assessed using the RAI-HC (during regular home care enrollment or reassessment) who fall into one of the four

target DIVERT subgroups will be enrolled into the study by a care coordinator at the time of assessment. Eligible clients will automatically be included into the intervention or 'regular care' control groups on an intent-to-treat basis. Recruitment is expected to proceed over 6-9 months for each site. Analysis of the sample size simulations that were carried out on retrospective data from the HNHB LHIN region from November 2014 to June 2015 indicates an expected enrollment of 4 clients per caseload per month.

Each home care partners' process for attaining consent will apply to the trial. Individual informed consent will not be sought given that the cardio-respiratory management model is accepted, considered best practice care, and is offered – whole or in part – at the full clinical discretion of the home care provider as per existing practice. Trial investigators have no part in the data collection, individual care decision-making, or record management during the study period beyond providing overall scientific guidance. We requested and received alteration to the requirements for consent based on satisfying the following Canadian Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2) criteria:[43]

1. The research involves no more than minimal risk to the participants.
2. The alteration to consent requirements is unlikely to adversely affect the welfare of participants.
3. It is impossible or impracticable to carry out the research and to address the research questions properly, given the research design, if the prior consent of participants is required.
4. In the case of a proposed alteration, the precise nature and extent of any proposed alteration is defined.
5. The plan to provide a debriefing (if any) which may offer participants the possibility of refusing consent and/or withdrawing data and/or human biological materials, shall be in accordance with Article 3.7B.

Our waiver of informed consent complies with existing methodological and ethical guidelines for pragmatic cluster-randomized trials. Existing guidelines state that informed consent by clients is not needed if "the intervention is to the clear advantage of every person in the cluster for the cluster to be entered in the trial"[44].

Intervention

Care planning and self-care support have been shown to be among the most effective elements of cardio-respiratory disease management[8,10] along with sustained follow-up by nurses or non-medical staff [13,14]. Care planning will be completed in a collaborative fashion amongst a care coordinator, the client, and the client's caregivers (both formal and informal). Clients in the intervention group will have their care plans guided by a multi-component cardio-respiratory disease management model in addition to receiving their usual care.[39] This comprehensive model for the intervention has been described in greater detail in a previous publication.[40] The person-centered, multi-component cardio-respiratory management model was developed based on guidelines,[17,45,46] extensive home care client profiling, and input from clients/families and health professionals. The management model contains the following

components (see Table 2: Description of Intervention Components): scheduled nurse-led self-management support (based on a training program and tool-kit); access to a staffed helpline; education on vaccines; advance care and goal planning; clinical pharmacist medication reconciliation; team case rounds; situation, background, assessment, and recommendation (SBAR) communication protocol with primary care; and a standardized transition package.[21,40,47] Each component has a specific objective within the model, however the manner in which it is delivered may be adapted. For example, some home care providers have clinical pharmacists on staff whereas others would rely on collaboration with community pharmacists.

Table 2: Description of intervention components

DIVERT-CARE Intervention Components	Description
Case Finding Using the DIVERT Scale	Use of the DIVERT Scale (embedded in interRAI assessment) to identify home care clients most likely to benefit.
Self-Management Education and Supports	In-home assessment of self-management goals and needs, with practical education and skills training to recognize and manage symptoms.
Access to an immediate nurse-staffed helpline	Direct phone line staffed by nurses involved in the DIVERT-CARE Intervention to aid with self-management and problem resolution.
Promotion of Vaccines	Seasonal flu vaccine and pneumococcal polysaccharide (Pneu-P-23) information and health promotion consistent with Canadian practice guidelines.
Advance Care and Goal Planning	Consultation for advance care and goals of care planning, advanced care decisions, and communication of care wishes.
Clinical Pharmacist-Led Medication Review	Review of medication for safety, efficacy and appropriate use of medications and delivery options.
Interprofessional Team Case Rounds	Weekly or biweekly care team meeting to discuss care plan, update goals, and how to support changing care needs.
SBAR Communication with Primary Care Providers	SBAR formatted communication to effectively communicate disease relevant information and care updates to primary and specialist care providers.
Standardized ED Transition Package / Personal Care Record	A succinct document to support continuity of care throughout health system. Personal care record of goals, plan of care, and community supports.

Self-management education and supports will be tailored to the needs and goals of the client. As with all home care services, clients may refuse all or any of the intervention components. The components will be delivered over 15 weeks by care coordinators and nurses who have been trained by the research team. Care coordinators and nurses will be provided detailed manuals explaining the components and their role in supporting clients throughout the intervention. The self-management program, based on previous pilot work[24], will use a population-based care approach pioneered by Wagner (1995) to help trial partners implement the cardio-respiratory disease management model.[48]

The intervention adheres to the following three principles: 1) multidisciplinary teams at each site will be trained on the protocols and resources related to each component of cardio-respiratory management model; 2) the teams will identify steps required to deliver the interventions; 3) the teams will plan the deployment of the cardio-respiratory management model that engages clients, families, and caregivers to ensure that adequate resources are dedicated to support the interventions across the intervention caseloads, while ensuring long-term sustainability.

Clients in the control group will receive the usual set of home care services. No changes will be made to their care planning process. Depending on the jurisdiction and client needs, usual care may include personal support, nursing, physiotherapy, occupational therapy, and other services. Depending on the jurisdiction, access to the components described in the cardio-respiratory disease management model is either non-existent or otherwise very rare and inconsistent for clients receiving usual care.

Allocation

Caseload randomization was designed and completed centrally and not revealed to prospective sites until after all site caseloads were enrolled. Caseloads were randomized to intervention or control, and stratified by home care provider (region) and sub-region (areas with similar economic status, access to care, and geography) at a 1:2 intervention to control ratio. The uneven allocation ratio increases the power of the trial while only minimally impacting operational and research resources.

A blocked allocation sequence was created via random number generation in collaboration with the biostatistics unit at St. Joseph's Healthcare Hamilton. The sequence features a 1:2 allocation ratio with a block of size three. After enrollment, caseloads from each region were sorted by sub-region and allocated using the sequence. In the event that the end of the clusters in a sub-region did not coincide with the end of a block, the rest of the block was skipped and allocation of the next sub-region started with a new block.

Data Collection and Outcome Measures

The primary outcomes will be collected using secondary data over the six-month observation period (see Table 3: Routine Measurement). The use of routinely collected data for primary outcomes, cost, and health measures limits potential for bias from lack of blinding given that neither the care team nor the trial investigators are directly involved in the collection of

outcomes. These records are accurate given that they are the basis for health care reporting systems and payments between public home care providers and contracted service providers.

Table 3: Routine Measurement

Activity	Staff Member	Approximate Time to Complete	Baseline	2 Months	4 Months	6 Months
Assess for eligibility (If intervention caseload) (RAI-HC)	Care coordinator	5 minutes	X			
Symptoms (RAI-HC)	Care coordinator	15 minutes	X	X	X	X
Health-related quality of life (RAI-HC)	Care coordinator	30 minutes	X		X	X
Patient Activation Measure (PAM-13)	Care coordinator	5 minutes	X	X	X	X
Administrative service and billing records (CHRIS, HCC MRR, CRMS)	N/A	N/A	X	X	X	X
Emergency department and hospital records (NACRS, DAD)	N/A	N/A	X	X	X	X

Legend:
RAI-HC: Resident Assessment Instrument for Home Care (https://www.cihi.ca/en/home-care)
PAM-13: Patient Activation Measure (https://www.insigniahealth.com/products/pam-survey)
CHRIS: Client Health and Related Information System (https://hssontario.ca/Who/Pages/protecting-your-privacy.aspx)
HCC MRR: Home and Community Care Minimum Reporting Requirements (https://www2.gov.bc.ca/assets/gov/health/forms/5502datadictionary.pdf)
CRMS: Client and Referral Management System (https://www.nlchi.nl.ca/images/ProvincialCRMS_Registration_User_Guide_v2_0_2017-09-01.pdf)
NACRS: National Ambulatory Care Reporting System (https://www.cihi.ca/en/national-ambulatory-care-reporting-system-metadata
DAD: Discharge Abstract Database (https://www.cihi.ca/en/discharge-abstract-database-metadata)

The main secondary data sets include the Resident Assessment Instrument for Home Care (RAI-HC), the Patient Activation Measure (PAM-13), the Client Health and Related Information System (CHRIS), the Home and Community Care Minimum Reporting Requirements (HCC MRR), the Client and Referral Management System (CRMS), the National Ambulatory Care Reporting System (NACRS), and the Discharge Abstract Database (DAD).

The RAI-HC is a standardized comprehensive assessment containing approximately 200 items and has been found to document major domains of health reliably.[49–53]

The Patient Activation Measure (PAM-13) [54] indicates the client's progress through four stages as they become activated (i.e., they believe their role in their own care is important, they learn enough to develop confidence to act on their own belief, they actually act, and they reach the point where they can act even under stress). The PAM is a widely used measure of patient activation that has demonstrated sensitivity to health-related outcomes, including health service use.[55,56]

The CHRIS is the health administrative database used by Ontario's publicly-funded home care providers. It includes client assessments, documents, provider and vendor contracts, billing of services information, and medical supplies and equipment rental costs.

The HCC MRR is an information management system defining a set of data elements that are reported to the British Columbia Ministry of Health by the regional health authorities. The HCC MRR captures information on clients, income, and home and community care services.

The Client and Referral Management System (CRMS) is a health information system designed to support client and referral management for clients receiving community-based services from the regional health boards in Newfoundland. It contains information on client records and clinical activity.

The NACRS contains data from all national hospital-based and community-based ambulatory care. It is collected and maintained by the Canadian Institute for Health Information (CIHI), which conducts its own quality assurance procedures to ensure accuracy and completeness.

The DAD captures administrative, clinical, and demographic information nationally on hospital discharges (including deaths, sign-outs, and transfers). It is collected and maintained by CIHI, which conducts its own quality assurance procedures to ensure accuracy and completeness.

Sample Size Calculations

Sample size calculation assumptions:

- Primary outcome: Time to first unplanned ED visit within 6 months of baseline
- Hazard ratio of 0.75
- Mean size of a home care caseload: 120 clients
- Mean prevalence of DIVERT target group in each caseload: 30%
- Expected recruitment over 6 months per caseload: 30
- Mean cluster size: 30
- Allocation: 1:2 (intervention: control)

Simulations using retrospective secondary data sources were undertaken to explore the power of a hypothetical DIVERT-CARE trial conducted in the HNHB LHIN region of Ontario from December 2015 to June 2016. The simulations found that 36 HNHB home care caseloads

randomized at a 1:2 intervention to control ratio could expect to enroll 1,100 clients across seven months. The simulation linked clients to their actual ED utilization records and extended the time to first ED visit figures for clients in 12 randomly selected intervention caseloads to achieve a hazard ratio of 0.75, a figure chosen to be more conservative than the pilot study but still clinically significant. The overall event rate was 35.5% in the intervention group and 44.8% in the control. The median time to first visit was 88 days in the intervention group and 75 days in the control. The power of the simulated DIVERT trial was 81.3% with a two-sided alpha of 0.05. Simulations with a hazard ratio of 0.80 yielded a power of 60.1%. The intraclass correlation coefficient (ICC) was estimated to be 0.005.

Based on the simulations the target sample size for the trial will be 1,100 clients, which will yield an approximate power of 81% for a hazard ratio of 0.75 and 60% for a hazard ratio of 0.80.

Statistical Analyses

Descriptive analyses will compare the treatment groups and sites on baseline demographic and clinical characteristics. Statistics on compliance, censoring, and follow-up times will also be presented.

The primary outcome will be assessed through a multi-level proportional hazards model on an intent-to-treat basis. The dependent variable will be days until first unplanned ED visit, censored at date of home care discharge for any reason. Caseload and partner site will be included as nested random effects. Both unadjusted and adjusted results will be reported. For adjusted analysis, DIVERT subgroup, age, and sex will be included as time-independent fixed effects. The hazard ratio, 95% confidence interval, and p-value will be reported for the treatment group effect and covariates when applicable. A two-sided alpha level of 0.05 will be used to judge statistical significance.

The assumption of proportionality of hazards across treatment groups will be evaluated by a visual inspection of the hazard curves and statistical testing of a time-dependent treatment group effect. If the hazard curves cross or the time-dependent treatment group effect is significant ($p < 0.05$) then primary analysis will be modified to consider treatment group as a time-varying effect.

The economic evaluation will examine total care costs, controlling for length of stay, between treatment groups to compare incremental costs to incremental effects (i.e., cost per ED visit averted). Total care costs are defined as direct costs incurred by the home care provider in the provision of home care services, including: human resources and equipment. We will use a micro-costing approach based on the listed/billed service cost consumed by each patient.

The other outcomes will be evaluated by multi-level generalized linear models. Four-month and six-month changes in PAM, HRQOL, number of symptoms, number of ED visits, and number of unplanned hospitalizations will be the respective dependent variables. Caseload and partner site will be included as nested random effects. Both unadjusted and adjusted results will be reported. For adjusted analysis DIVERT subgroup, age, and sex will be included as fixed effects.

Unit change and rate ratios, with their associated 95% confidence interval and p-values, will be reported for the treatment group effect and covariates as applicable. A two-sided alpha level of 0.05 will be used to judge statistical significance.

Model assumptions will be evaluated by a visual inspection of residuals and the sensitivity of the results to the use of a heteroskedastic-robust variance estimator. If evidence of departure from model assumptions is present, then the analysis will be modified to utilize an empirical variance estimator.

Patient and Public Involvement

The intervention, comprehensively described elsewhere [40], was developed based on the input from clients/families and health professionals in a series of three in-person stakeholder meetings held in late 2013 and early 2014. The pilot of the study methodology was conducted in 2014 with the collaboration, input, and funding from a regional, public-sector, home care provider (HNHB LHIN). Participating clients and health professionals provided input into the intervention (and study design for health professionals) through telephone interviews using a structured questionnaire focused on the perceived benefit and utility of the interventions, overall satisfaction, and areas for improvement. The outcomes of the pilot study were featured in the home care providers annual report to the community.

The present protocol, based on the aforementioned pilot study, received input from health professionals in each participating region through a series of in-person planning meetings in mid-2017. The general public was engaged in one region through a local radio program. Adaptations and modifications to the intervention in each region to account for their unique health service context will be described in a forthcoming implementation publication. The experience of participating clients and health professionals will be investigated in a program evaluation and qualitative study to be conducted in parallel. The results of the trial are expected to be released to the study participants and public though regional public reports.

ETHICS AND DISSEMINATION

Harm

This trial is unlikely to cause additional risk of harm since the various components of the intervention are already available from home care agencies and service providers, though rarely offered in the standard care plan. Direct risks to the health of the client are minimal as none of the components of the intervention are novel interventions. Each element of the intervention has been shown to be safe individually. Clients in the control group will continue to receive their usual care, while clients in the intervention group will receive usual care plus increased access to additional home care services defined by the cardio-respiratory treatment model. A Data Monitoring and Ethics (or equivalent) Committee was not required, and formal stopping rules or interim analyses are not planned.

Ethical approval

We have received ethics approval from the Hamilton-Integrated Research Ethics Board, Health Research Ethics Authority for Western Health, and the Clinical Research Ethics Board for Vancouver Island (see supplementary file).

Results dissemination

We aim to make the results of this study public through peer-reviewed publications, clinical trial registry, thesis manuscripts, conference publications, and notifications to our trial partners, who will include the findings in their regular newsletters and annual reports to clients, partners, and government.

DISCUSSION

In summary, this pragmatic, cluster-randomized, multi-center superiority trial will investigate the effectiveness of a cardio-respiratory disease management model in a targeted home care client population, with case finding occurring using the DIVERT scale[19]. By offering a person-centered, multi-component cardio-respiratory management model to home care clients at the highest levels of risk,[40] we hope to determine if unplanned ED visits are postponed, clients have increased activation in their care, symptoms are reduced, and that the care model is cost-effective.

This pragmatic trial will inform how multi-component cardio-respiratory care interventions are received as they are delivered in real-world conditions. Historically, trials investigating community programs have excluded frail seniors who would be at high-risk of ED services. Additionally, other trials have tended to focus on post-acute care and have not targeted high-risk clients when assessing community-based chronic disease management interventions.

The need for appropriate and targeted supportive chronic disease management is a clear and compelling health services issue, and is reflected in new provincial government investments into the sector. This trial will be an important precedent around the creation of more upstream approaches to care for home-care clients that help to take further pressure of hospitals and EDs that are already facing issues of overcrowding across Canada.

Author Contributions

APC is the principal investigator and led the conceptualization and design of the protocol, drafted, and revised the manuscript. CS, AJ, DD, MJ, and GC made contributions to the design and implementation of the study, and supported the manuscript. GA, CB, VB, SB, DF, PH, GH, JH, LL, RM, LM, and SS are co-investigators that contributed to the design of the study, and revised the manuscript. JD, TP, JR, RG, DM, and DH are trial partners who contributed to the design and implementation of the study. All authors critically revised the manuscript and approved the final version of this manuscript.

Competing interests

It should be noted that DHF has a proprietary interest in Health Utilities Incorporated, Dundas, Ontario, Canada. HUInc distributes copyrighted Health Utilities Index (HUI) materials and provides methodological advice on the use of the HUI. All others author have no competing interests.

Funding statement

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Acknowledgements

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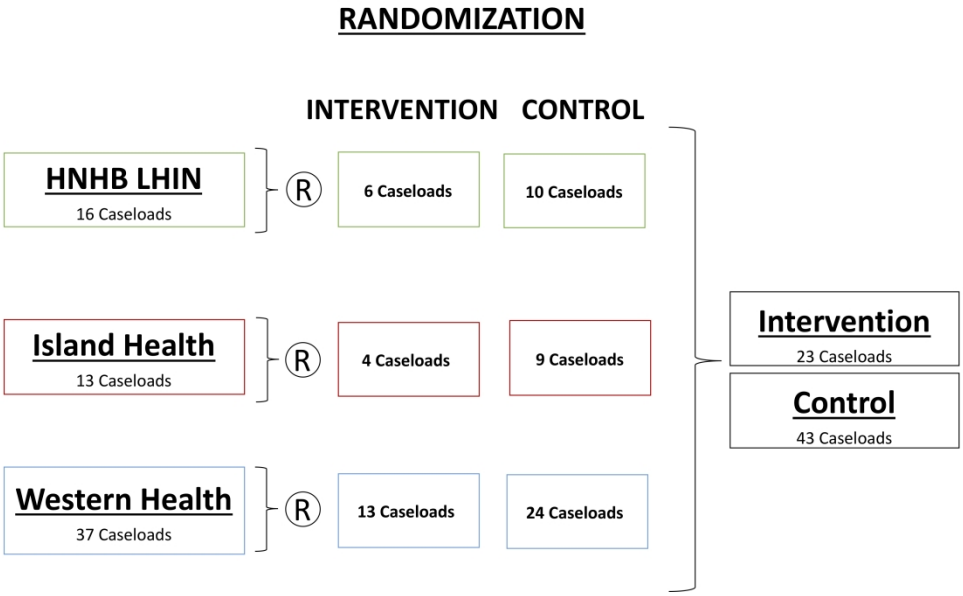

Figure 1: Caseload Randomization Schematic

368x222mm (300 x 300 DPI)

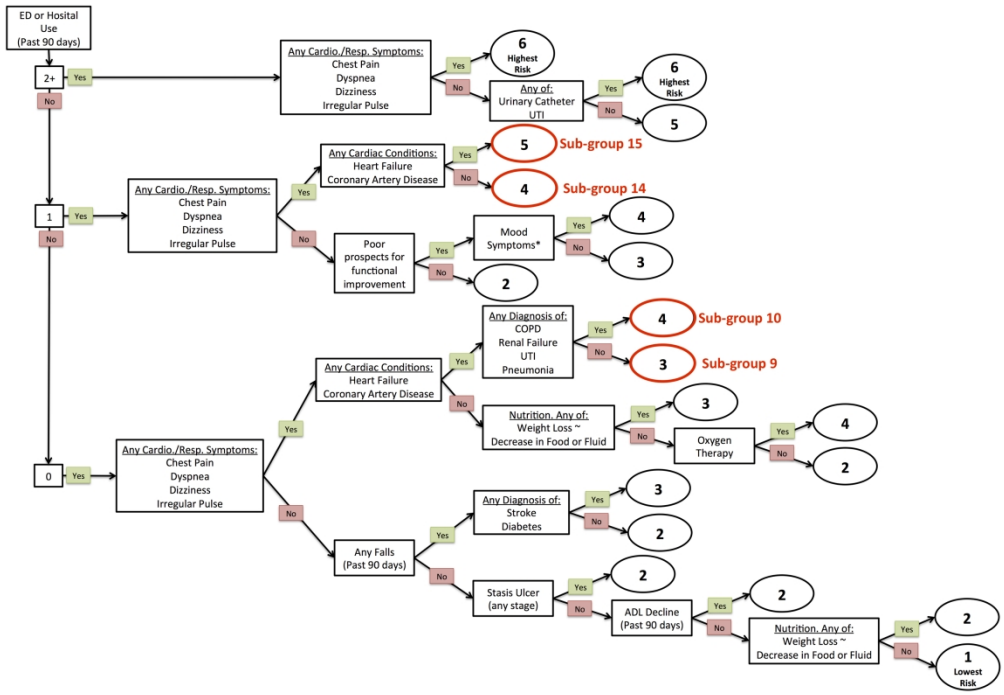

Figure 2: DIVERT Scale Target Groups

254x175mm (300 x 300 DPI)

Ethical approval – detailed supplement.

DIVERT CARE Site:	Haldimand Brant Community Local Health Integration Network (Hamilton, Ontario) & McMaster University– **LEAD SITE**	Island Health (Victoria, British Columbia)	Western Health (Corner Brook, Newfoundland and Labrador)
Full name of the ethical committee:	Hamilton-Integrated Research Ethics Board	Clinical Research Ethics Board for Vancouver Island	Health Research Ethics Authority for Western Health
Reference Number:	# 2651	C2017-014	# 20171652

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

		Reporting Item	Page Number
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	7-8
Protocol version	#3	Date and version identifier	7
Funding	#4	Sources and types of financial, material, and other support	17
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	17
Roles and responsibilities:	#5b	Name and contact information for the trial sponsor	17

sponsor contact information			
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	17
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	17
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	9
Objectives	#7	Specific objectives or hypotheses	8
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	6
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	9
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	10
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	10
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return;	11

		laboratory tests)	
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	11
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	12
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	12
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	14
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	9
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	9
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	9
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	9
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	9
Blinding (masking): emergency	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during	9

unblinding		the trial	
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	13
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	13
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	13
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	14
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	14
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	15
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	15
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	15
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and	15

		whether the process will be independent from investigators and the sponsor	
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	16
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	16
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	9
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	9
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	16
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	17
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	17
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	9
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	16
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	16
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	16
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	N/A

Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A