interact Intervention for Appropriate Care and Treatment

Study Protocol

Full title
A stepped-wedge randomised-controlled trial assessing the implementation, impact and costs of a prospective feedback loop to promote appropriate care and treatment for older patients in acute hospitals at the end-of-life.

Short title
InterACT study: **Inter**vention for **A**ppropriate **C**are and **T**reatment

Lay description
This study will work with clinical teams in three acute hospitals to trial a feedback loop approach to promoting appropriate care and treatment for older patients at the end-of-life.

Regulatory compliance
The study will be conducted in compliance with all stipulations of this protocol, the conditions of the Human Research Ethics Committee approval, the National Statement on Ethical Conduct in Human Research (NHMRC, 2007- Updated 2018), Australian Code for the Responsible Conduct of Research (NHMRC & Universities Australia, 2018), Statement on Consumer and Community Involvement in Health and Medical Research (NHMRC & CHF, 2016), the principles of Good Clinical Practice (GCP), and within Queensland and Australian laws and regulations, including the Public Health Act 2005.

Version
11.0

Date
23.11.20

AusHSI AUSTRALIAN CENTRE FOR HEALTH SERVICES INNOVATION

QUT Australian Centre for Health Law Research

STUDY INVESTIGATORS

Name	Institution	Email	Study role
CHIEF INVESTIGATORS			
Prof Adrian Barnett	Queensland University of Technology (QUT)	a.barnett@qut.edu.au	Chief Investigator A Project director
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STUDY PARTNERS

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Palliative Care Australia (PCA)	Ms Kate Reed-Cox	Kate@palliativecare.org.au	Health policy partner
Deeble Institute for Health Policy Research	Dr Rebecca Haddock	rhaddock@ahha.asn.au	Health policy partner

STUDY SYNOPSIS

TITLE	The InterACT study: **Inter**vention for **A**ppropriate **C**are and **T**reatment
TRIAL REGISTRATION	Australia New Zealand Clinical Trial Registry ACTRN12619000675123p
PROTOCOL VERSION NUMBER	11.0 23 November 2020
SPONSOR/FUNDING BODY	This project is funded by a National Health and Medical Research Council (NHMRC) partnership project grant (GNT1151923) and led by Queensland University of Technology (QUT).
STUDY AIM	To implement a prospective feedback loop intervention in three acute hospitals to increase appropriate care and treatment decisions and pathways for older patient populations at the end-of-life.
PRIMARY OBJECTIVES	To determine the impact and resource use and costs of a tailored clinical team feedback loop intervention on patient outcomes related to appropriate care and treatment at the end-of-life. To conduct a process evaluation to assess implementation, mechanisms of impact, and contextual barriers and enablers of the feedback loop intervention.
STUDY DESIGN	Multi-centre, stepped-wedge randomised controlled trial
STUDY DURATION	3 years 2018-2021 Trial: 70 weeks
STUDY PARTICIPANTS	Up to seven clinical teams at each of: Royal Brisbane & Women's Hospital (RBWH) The Prince Charles Hospital (TPCH) Gold Coast University Hospital (GCUH)
INTERVENTION	A prospective feedback loop and tailored clinical response
OUTCOME MEASURES	*Impact* Primary outcome: Proportion of patients with one or more Intensive Care Unit (ICU) admissions Outcome 2: Length of hospital stay and discharge outcome Outcome 3: Time to hospital re-admission Outcome 4: Time to first documented indications of clinician-led care review discussion Outcome 5: Time to care directive measures Outcome 6: Time to palliative care referral Outcome 7: Time to medical emergency calls *Health care resource use and costs* Outcome 8: Changes in admission and treatment costs Outcome 9: Cost of implementing the prospective feedback loop intervention *Process:* Extent and fidelity of intervention implementation, impact, and contextual barriers and enablers of the feedback loop intervention
DATA COLLECTION	*Patient record review data* No patients will be recruited. Identifiable data will be collected prospectively for record screening and feedback purposes. *Health services data*

	No patients will be recruited. Patient record review data will be linked to health services data to identify health service use for patients of the participating clinical teams aged ≥ 75 years and screened and recorded as *'*high-risk CriSTAL or SPICT-positive*'*. [CriSTAL: Criteria for Screening and Triaging to Appropriate aLternative care; SPICT: Supportive and Palliative Care Indicators Tool] *Process evaluation data* These data will be collected using a series of templates based on the Consolidated Framework for Implementation Research (CFIR) to guide the assessment of contextual barriers and enablers, an interview guide and systematic implementation planning and record keeping.
STATISTICAL ANALYSES	The primary outcome will be analysed using a Binomial regression with the patient ICU admission as the binary response variable. The key variable is the timing of the switch from usual exposure to intervention exposure phase, so the main result of this analysis will be the intervention effect on the proportion of patients with at least one ICU admission. Outcomes 2 to 7 will use competing-risk, proportional hazards survival models. Outcomes 8 and 9 will use statistical distributions to describe variability in all cost parameters. Process evaluation outcomes will be subject to thematic analysis.
KEY ETHICAL & SAFETY CONSIDERATIONS	The study has ethical approval from the Royal Brisbane and Women's Hospital Human Research Ethics Committee (HREC), HREC/2019/QRBW/51606, with mutual acceptance at The Prince Charles Hospital and Gold Coast University Hospital. A waiver of consent is approved by the HREC for access to patient and health services data. A Public Health Act (PHA) application is approved to obtain patient data in the study (Ref: QCOS/033343/RD008146).
DISSEMINATION	The study team will maintain a dissemination plan in conjunction with our study partners. Results will be directly disseminated to each participating hospital and to each participating clinical team through a series of presentations, reports and summaries. Results will be directly disseminated to our policy partners for further distribution to consumers, policy- and decision-makers in the form of evidence briefs, plain language summaries and policy recommendations. A publication plan will be established by August 2019 to inform systematic publication of results through the clinical and academic communities. We will adhere to the International Committee of Medical Journal Editors requirements for assignment of authorship and reporting the contributions of each author. All non-identifiable data sets will be available from the study statisticians (CI Barnett and CI Lee) once those data have been reported.

Contents

ADMINISTRATIVE INFORMATION

Full title

A stepped-wedge randomised-controlled trial assessing the implementation, impact and cost-consequences of a prospective feedback loop to promote appropriate care and treatment for older patients in acute hospitals at the end-of-life.

Short title

InterACT study: **Inter**vention for **A**ppropriate **C**are and **T**reatment

Trial registration

The trial is prospectively registered with the Australia New Zealand Clinical Trial Registry (ANZCTR), ACTRN12619000675123p.

Protocol version

Version 11, 23.11.2020

This protocol meets the 2013 SPIRIT Checklist for interventional trials (Appendix 3).

Version	Date	Author	Changes
2.0	23.04.19	InterACT Investigator and project team	Updated Figure 2; clarified feedback format, p.10; clarified data retention, p.22; deleted repeated paragraph, p.24
3.0	17.05.19	InterACT Investigator and project team	Updated: - administrative information - 6: Stepped wedge design (phase names and length) - 10: Intervention flow chart Expanded detail in: - 6: Study design - 9: Study populations - 12. Study procedures - 13: Statistical analysis Clarified/corrected: - 4. Objectives - 9. Study populations - 11. Study outcomes - 13. Statistical analysis
4.0	28.06.19	InterACT Investigator and project team	Updated partner contact and project team information, p.3,4. Updated exclusion criteria to allow surgical teams, p.9
5.0	13.12.19	InterACT Investigator and project team	Clarified: - CriSTAL score equal or above 6, p.12 - SPICT score equal or above 2, p.12 Updated: - Record review flow diagram, p.10, Figure 3 - Stepped-wedge time periods, Figure 2, to reflect delayed trial start date, p.7 and throughout protocol - Outcome 4: will record nature of any care change and indications of family conflict - Statistical analyses of historical data, p.26 Replaced ‘elderly’ with ‘older’
6.0	28.01.20	InterACT investigator and project team	Updated: - Names of hospital study team members, p.4 - Clinical team recruitment: p.6, p.8, Figure 2, p.7, Figure 4, p.13, - Updated sample size calculation p. 25

			- Ethical and PHA approvals, p.31-32
7.0	04.03.20	InterACT investigator and project team	Updated data collection to include coronavirus (COVID19) infection
8.0	17.03.20	InterACT investigator and project team	Updated inclusion criteria to reduce CriSTAL score to equal or above 5 Updated inclusion criteria to include CriSTAL positive **or** SPICT positive
9.0	01.07.20	InterACT investigator and project team	Updated CriSTAL score to include an additional point where the CFS score is 7 or above p. 18 Updated inclusion criteria for CriSTAL score to equal or above 6. Figure 3, p. 11, p.13 Updated roles and responsibilities and hospital study team member names, p.4 and 5 Updated Figure 2, indicating COVID-19 suspension, p.8 Statement about COVID-19 impact on data, p32.
10.0	08.10.20	InterACT investigator and project team	Update hospital study team members, p4 Updated eligibility criteria, for patients admitted under participating clinical teams at RBWH. Synopsis, p10, Figure 3, p11, p14, p20, p28 Inclusion of control hospital comparator data. p20, p21, p28
11.0	23.11.20	InterACT investigator and project team	Updated eligibility criteria, for patients admitted under participating clinical teams at RBWH. Synopsis, p10, Figure 3, p11, p14, p20

Funding, sponsors and partners

This project is funded by a National Health and Medical Research Council (NHMRC) partnership grant (GNT1151923), with financial and in-kind support from study partners. It is led by the Australian Centre for Health Services Innovation (AusHSI) and the Australian Centre for Health Law Research (ACHLR) at Queensland University of Technology (QUT). Executive advisory groups will be established at each participating hospital and will act as local trial sponsors, to support implementation.

A collaborative research agreement is established between QUT and each of the following partner institutions:

Academic investigator partners

University of New South Wales (UNSW)
University of Adelaide
Bond University

Health service partners

Metro North Hospital and Health Service (MNHHS)
Gold Coast Hospital and Health Service (GCHHS)

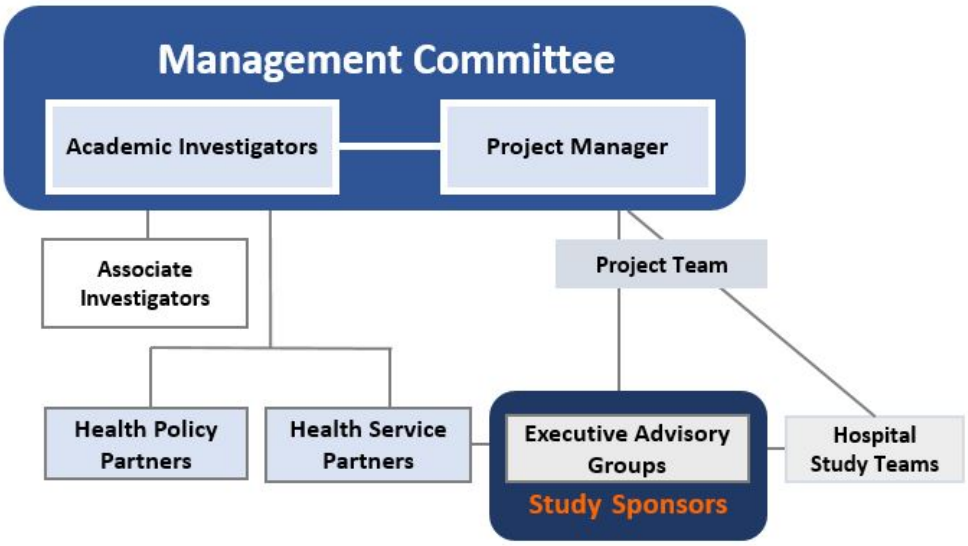
Health policy partners

Deeble Institute for Health Policy and Research
Palliative Care Australia (PCA)

Study governance

QUT is responsible for all aspects of the study management, including study design, all data associated activities, and dissemination of results. A management committee, comprising all the chief investigators and the project manager, will meet at least 3 monthly throughout the study, and additionally as required, including for data monitoring during the trial phases. Project team members and project partners will be invited to participate as required. Terms of reference are established for the management committee and require a quorum of 5 investigators for all trial related decisions.

Figure 1 Governance structure



Roles and responsibilities

Table 1 Study team responsibilities

Name	Institution	Study role	Responsibilities and contributions
Academic investigator team			
Prof Adrian Barnett	QUT	Chief Investigator A Project director	Management committee Protocol development Statistics and data analysis Data monitoring
Prof Ken Hillman	UNSW	Chief Investigator B	Management committee Protocol review Clinical care & health service delivery
Prof Lindy Willmott	QUT	Chief Investigator C	Management committee Protocol review Health law
Prof Ben White	QUT	Chief Investigator D	Management committee Protocol review Health law
Prof Gillian Harvey	University of Adelaide	Chief Investigator E	Management committee Protocol development Implementation science Qualitative data analysis
Prof Leonie Callaway	QUT	Chief Investigator F	Management committee Protocol review Clinical care & health service delivery
A/Prof Magnolia Cardona	Bond University	Chief Investigator G	Management committee Protocol development Epidemiology
Prof Nicholas Graves	QUT	Chief Investigator H	Management committee Protocol development Health economics and statistics

Dr Xing Lee	QUT	Chief Investigator I	Management committee Protocol development Statistics and data analysis Data monitoring
Prof Steven McPhail	QUT	Chief Investigator J	Management committee Protocol review Health economics and statistics
Project team			
Alison Farrington	QUT	Research project manager	Management committee Protocol development Project management Data monitoring
Carla Shield		Research coordinator	Protocol development Ethics and governance
Dr Hannah Carter		Health economist	Protocol development Health economics analysis
Christine Brown		Research assistant	Data collection and analysis Data monitoring
TBC		Statistician	Statistical analysis
TBC	QUT/ University of Adelaide	Implementation research fellow	Process evaluation analysis
Associate investigators			
Prof Jeff Lipman	University of Queensland (UQ)	Advisory role	Clinical expertise
Prof Leanne Hides	UQ	Advisory role	Qualitative research expertise
Dr Will Cairns	Queensland Health	Advisory role	Palliative care expertise
Health service partners (hospital study teams)			
Dr Liz Whiting + Dr David Rosengren	Royal Brisbane and Women's Hospital (RBWH)	Executive advisory group	Executive sponsor Advocacy and support Outcome dissemination
Dr Carol Douglas		Palliative care lead	Palliative care expertise
Rebecca Radford		Study coordinator and Auditor	Site contact Coordinate implementation Patient record reviews/data collection
Avalon Kelly-Austin		Auditor	Patient record reviews/data collection
Mary Batch		Auditor	Patient record reviews/data collection
Dr Liz Whiting Dr Jeff Rowland	The Prince Charles Hospital (TPCH)	Executive advisory group	Executive sponsor Advocacy and support Outcome dissemination
Dr James Stevenson		Palliative care lead	Palliative care expertise
Sue Mannion		Study coordinator	Site contact Coordinate implementation
Saroeun Ven		Auditor	Patient record reviews/data collection
Mark Gallagher		Auditor	Patient record reviews/data collection
Carly Ruysch		Auditor	Patient record reviews/data collection
Dr Jeremy Wellwood	Gold Coast University	Executive advisory group	Executive sponsor Advocacy and support Outcome dissemination

Dr Andrew Broadbent	Hospital (GCUH)	Palliative care lead	Palliative care expertise
David Farrant		Study coordinator	Site contact Coordinate implementation
Christine Lyall		Auditor	Patient record reviews/data collection
Vincent Sapaen		Auditor	Patient record reviews/data collection
Health policy partners			
Ms Kate Reed-Cox	Palliative Care Australia (PCA)	Advisory support (palliative care services) Knowledge translation and outcome dissemination	
Dr Rebecca Haddock	Deeble Institute for Health Policy Research	Knowledge translation Outcome dissemination (focus on policy and practice and end-of-life care workshops)	

1. INTRODUCTION

Advances in medicine mean health care professionals can prolong life, yet some treatments have a low chance of providing tangible benefit to some patients and represent a multi-million dollar cost to the public purse (1). Previous work identified reasons why doctors sometimes provide treatment they know to be non-beneficial to patients, especially elderly patients who are near the end-of-life (2, 3).

The InterACT study builds on this work and aims to promote appropriate care and treatment decisions and pathways for this patient population in three major Queensland hospitals. Specifically, it will assess the impact on patient outcomes and the cost-consequences of implementing a prospective feedback loop intervention with clinical teams. We expect to improve the capacity of clinicians to choose alternative treatments and to increase institutional support for better end-of-life care for a group of vulnerable patients.

2. BACKGROUND

Australia's health care system operates in a challenging climate of an ageing population, an increase in the number of people living with chronic disease and, most relevant for this study, an increase in elderly people living with frailty and physical and cognitive disabilities (4). This elderly population is also more likely than previously to be hospitalised, with hospitalisation rates for people aged over 85 years increasing by 35% for women and 48% for men in the decade to 2011 (5) . Further, the end-of-life phase in Australia is becoming an increasingly medicalised experience with more than half of Australian deaths now occurring in hospital, 26% in residential care and just 20% in the home (6).

There are challenges to caring for this elderly patient population in acute care settings. Specifically, there can be an inherent tension for clinicians and patients in acknowledging the limits to what medicine can provide while balancing subjective judgements about determining beneficence and addressing economic and clinical imperatives to provide appropriate and quality patient care (4).

A systematic review of 38 international studies, led by CI Cardona and CI Hillman, found 33% to 38% of patients received non-beneficial treatment at the end-of-life (7). A 2017 retrospective study of three Australian hospitals reported an observed incidence rate of non-beneficial treatment among end-of-life admissions of 12.1% (range 6.0% to 19.3%) with a mean duration of non-beneficial treatment of 15 days with one third spent in the Intensive Care Unit (ICU) (8). These types of treatments are associated with an increase in care costs, with the same study reporting an estimated annual national health system cost of $A153.1 million due to futile or non-beneficial bed days (8).

Clinicians providing end-of-life care are often tasked with preparing patients and families for a transition to less active treatment (9), however they can frequently experience a range of barriers in providing that care pathway (2, 10). These barriers are likely to lead to an increase in treatment provided that is actually not beneficial to the patient. Further, they can cause moral distress to clinicians and increase risk of a bad death by prolonging or increasing patient suffering (11).

Studies have identified evidence for why doctors provide treatment they perceive as non-beneficial, with causes broadly categorised as arising from clinician factors, hospital factors and patient factors (1-3, 12, 13). Addressing these factors is challenging, especially in large, complex acute care settings. Evidence exists for interventions to reduce non-beneficial treatment outside of acute hospitals (14-17), and an intervention study has been done in the ICU setting in the United States(18). There is, however, no published research in Australia evaluating an intervention to reduce non-beneficial treatment at the end-of-life in hospitals.

This study will use two validated tools to prospectively identify patients at the end-of-life where curative and life-sustaining interventions may be non-beneficial, or where there are predictor variables for specific potentially futile interventions. One, the Criteria for Screening and Triaging to Appropriate aLternative Care (CriSTAL) tool, was developed to identify elderly patients in the last months of life (19) and has multiple reports of its predictive validity (20, 21). The second tool, the Supportive and Palliative Care Indicators Tool (SPICT^{TM}) can be used by multidisciplinary clinical teams to identify patients at risk of deteriorating and dying (22) with recent studies reporting a significant association between a positive SPICT result and one-year mortality (23, 24).

Patient screening with these tools will form the first step in a prospective feedback loop intervention that aims to promote appropriate care and treatment for the elderly at the end-of-life. The provision of feedback to clinical teams is intended to provide a 'flag' to increase clinician awareness of the risk profile of their patients, directly addressing some of the clinician and hospital factors noted (25-27). A tailored clinical response to this information will be determined at a local clinical team level and implemented with support from a hospital executive group.

This study partnership will provide three acute hospitals with an opportunity to improve services at the end-of-life, free up hospital bed days, and improve outcomes for patients and families. The connections made with health services and policy groups by the partnership will improve the likelihood of changing practice in future.

3. AIMS OF STUDY

To implement a prospective feedback loop intervention in three acute hospitals to increase appropriate care and treatment decisions and pathways for older patient populations at the end-of-life.

4. OBJECTIVES

4.1 Primary objective

To determine the impact and the healthcare resource use and costs of a tailored clinical team feedback loop intervention on outcomes related to appropriate care and treatment at the end-of-life.

4.2 Secondary objective

To conduct a process evaluation to assess implementation, mechanisms of impact, and contextual barriers and enablers of the feedback loop intervention.

5. HYPOTHESIS

The use of a tailored feedback loop intervention in acute hospitals will improve care outcomes for older patients, specifically to increase appropriate care and treatment pathways and reduce the incidence of non-beneficial treatments.

6. STUDY DESIGN

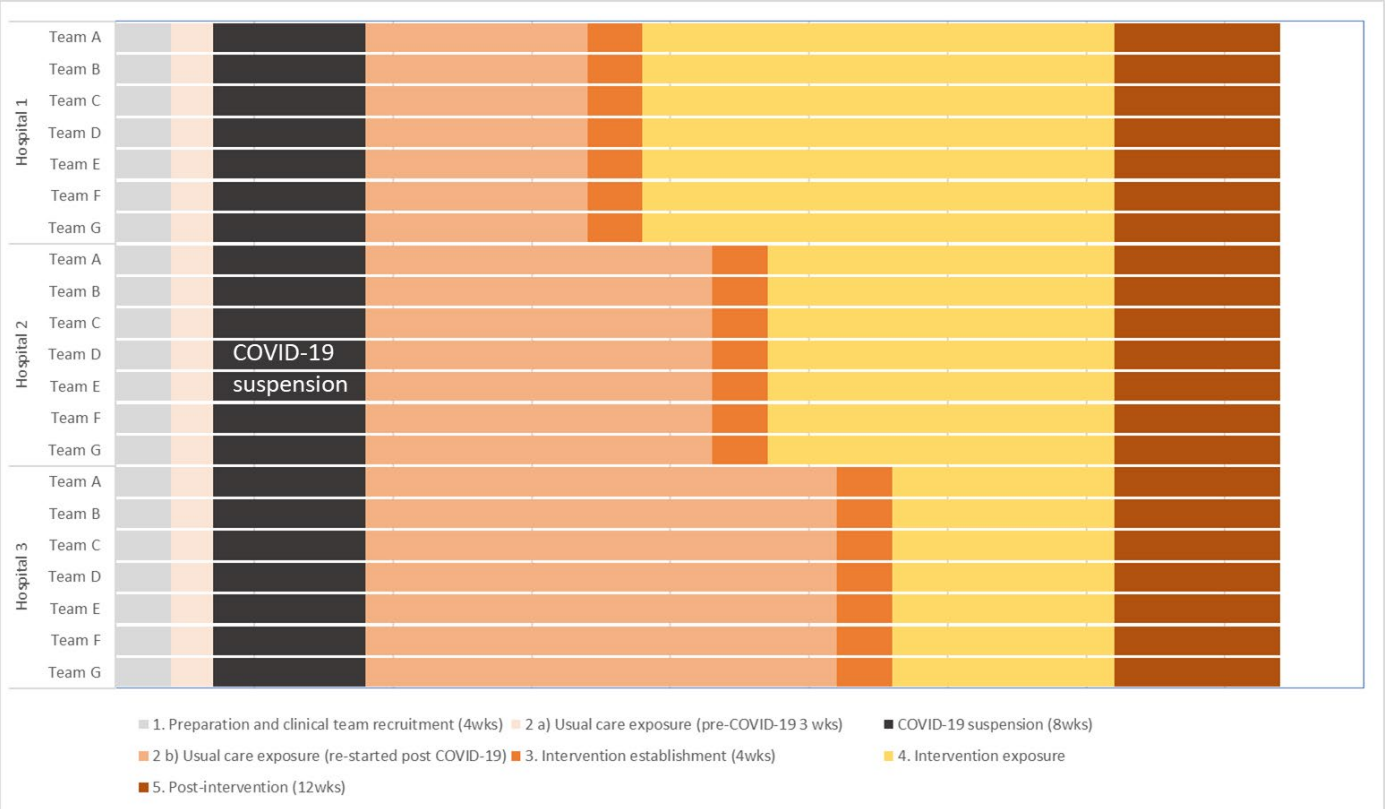
This is a randomised controlled trial using a multi-centre stepped-wedge randomised trial design (Figure 2). Five stages (site preparation, usual care exposure, intervention establishment, intervention exposure, post-intervention) will be sequentially rolled-out across the three hospitals over 70 weeks. Hospitals will be randomly allocated to one sequence of study timings. All hospitals (cluster), and their participating clinical teams (seven per hospital), complete the site preparation phase concurrently (4 weeks) and commence the usual exposure phases at the same time. The usual care exposure phase is either 16, 25 or 34 weeks, followed by a sequential

move to the four-week intervention establishment phase. This is followed by an intervention exposure phase of 16, 25 or 34 weeks.

The stepped-wedge design, with its incremental roll out, is practical to implement and mimics how the intervention might be implemented in practice at other hospitals (28) and is well-suited to the evaluation of health service delivery interventions (29). This design is also practical and feasible, allowing the study team to work with each hospital during the intervention establishment phase. Each hospital acts as their own control, avoiding issues associated with comparing heterogeneous hospitals. Temporal effects can be studied (30), with more efficiency than other cluster designs (31) as the power of the design is mainly determined by within-hospital variations.

The usual care phase was suspended for eight-weeks due to COVID-19 after only 3 weeks of data collection. The study was recommenced as week 1 of the usual care phase with allocation of phase timings as per the original stepped-wedge design.

Figure 2 Stepped-wedge study design in three hospitals with seven teams per hospital (post COVID-19)



6.1 Limitations

There are several known limitations of this stepped-wedged study design. First, there is risk of the influence of secular trends unrelated to the intervention exposure with a long study period and one-directional cross-over. Second, there is risk of unequal exposure to seasonal trends. Both of these risks will be taken into consideration in the pre-specified statistical analysis approach. Third, there is a small risk of between-site contamination occurring after the first site crossover, until the last site crossover. However, the geographical separation of

hospital sites and simultaneous cross-over of clinical teams within the same site, offers substantial protection against risk of contamination.

7. STUDY SETTING/LOCATIONS

The multi-centre trial will be undertaken at three acute, major Queensland Hospitals: Royal Brisbane and Women's Hospital (RBWH), Gold Coast University Hospital (GCUH) and The Prince Charles Hospital (TPCH). These hospitals were recruited by Chief Investigator Graves during the development of the project grant application and are part of the project partnership agreement, including financial contributions, with Metro North Hospital and Health Service (MNHHS) and Gold Coast Hospital and Health Service (GCHHS).

8. STUDY DURATION

The study will commence once all ethical and governance approvals are in place at each of the participating hospitals. The trial site preparation and recruitment component of the study will take 4 weeks; the usual care exposure, intervention establishment and intervention exposure phases will take a total of 54 weeks, and the post-intervention phase will take 12 weeks. Following this, data linkage, data analysis, publication submission and dissemination will take approximately 52 weeks.

9. STUDY POPULATION

9.1 Population 1: Intervention: clinical teams

We will aim to enrol seven clinical teams at each hospital. To trial the intervention where the most likelihood of non-beneficial treatments exists we will purposively sample in the first instance from general medicine clinical teams and from medically-oriented clinical specialities that have a regular number of patient admissions ≥ 75 years (see Figure 4 Clinical team recruitment flow chart, p. 13). The priorities for the sample of clinical teams to be invited will be decided in consultation with the hospital executive advisory group during the set up and site preparation and recruitment phase to ensure consideration of each hospital's clinical structure, work flows and other care initiatives, and to include review of patient admission rates per clinical teams.

9.1.1 Clinical team inclusion criteria

For inclusion, clinical teams must:

- be an established clinical team unit or specialty that routinely admits patients within the hospital
- include a nominated lead specialist consultant/s
- include a registrar/s and affiliated clinical nurse consultant or nurse unit manager
- have a clinical team structure and admission pattern typical of the hospital
- have a consistent history of admitting patients aged over 75 years over a sample time period in the previous year (step 2 of Figure 4)
- participate in an information session with the project team.

9.1.2 Clinical team exclusion criteria

Excluded clinical teams will be those that do not meet all the inclusion criteria and those from the emergency department, any Intensive Care Units (ICUs), mental health units, and non-acute care. While inappropriate treatment can occur in a range of settings, including emergency departments and the ICU, we are studying the InterACT intervention with clinical teams that care for patients once admitted to hospital, before they go to ICU and in medical specialties where more potential for non-beneficial treatments and older populations exists. The focus of the InterACT intervention is to prompt a clinical review of the patient's care and treatment pathways to reduce incidence of non-beneficial treatments, which could include inappropriate ICU admission. Further, as the

ICU has a different clinical and treatment focus it is less likely that the intervention can be implemented as consistently as with medically focussed clinical teams.

Clinical teams that are already implementing an intervention or initiatives related to reducing non-beneficial treatments for older patients will be excluded.

9.1.3 Potential for risk, burdens and benefits to participants

The site preparation and clinical team recruitment, usual exposure, intervention establishment and intervention exposure phases will present negligible additional risk or burden to clinician participants. In the intervention exposure phase there is a requirement for clinicians to first receive and then respond to patient record review feedback, which is the key part of the trial intervention. These processes will alter the clinician's workload, although this should be contained within the usual range of variation associated with the delivery of patient care. To minimise additional workload the feedback processes will be tailored to align as much as possible with each clinical team's existing communication workflows and patient care mechanisms.

The expected benefits are improved patient outcomes in terms of reduction in non-beneficial interventions following the clinical team response to the patient record review data, specifically the CriSTAL and SPICT scores and indicators. This should facilitate planning and delivering appropriate care and treatment to those patient groups. Cost savings may be observed due to the prevention of non-beneficial treatments.

9.2 Population 2: Patient data: Eligible patients admitted under enrolled clinical teams

9.2.1 Inclusion criteria
Patients admitted under the enrolled clinical teams **and** aged ≥75 years of age.

9.2.2 Exclusion criteria

Patients <75 years of age or not admitted under the enrolled clinical teams.

9.2.3 Potential for risk, burdens and benefits to participants

There are no potential risks or burdens to patient participants whose records are reviewed in this study. There could be benefits to patients who receive more appropriate care as clinical team care activities evolve as part of the intervention clinical response.

9.3 Population 3: Process evaluation: clinical teams, executive advisory group, site study team

9.3.1 Inclusion criteria

Enrolled clinical teams, executive advisory group and site study team members. Site study team members will include hospital employees who have a role in supporting the implementation of the study or in data collection, as determined in the site preparation phase, and may include the nurse auditor, site coordinator, palliative care team.

9.3.2 Exclusion criteria

Clinical teams not enrolled in the intervention.

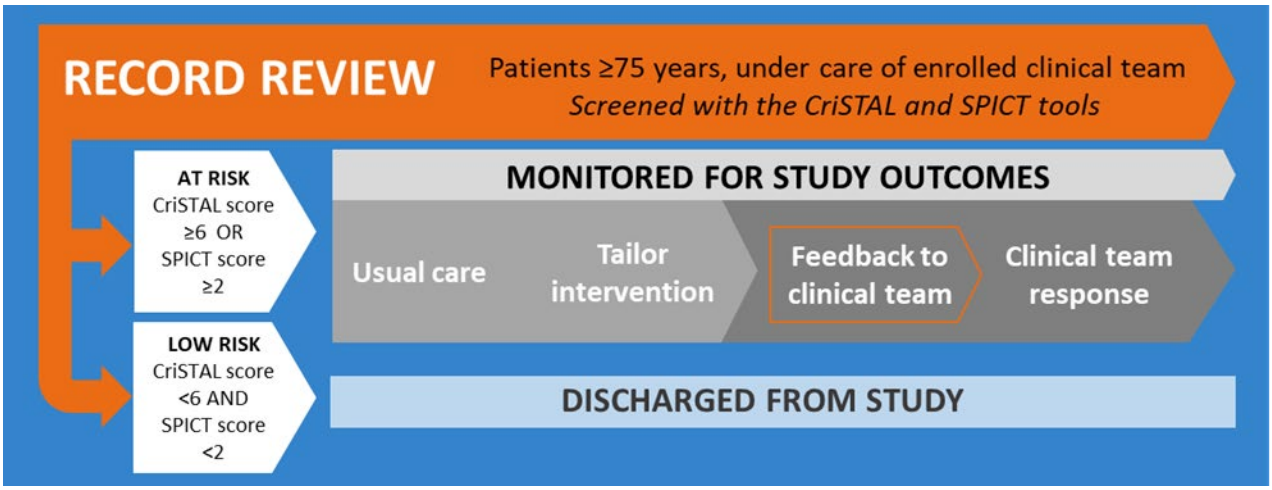
9.3.3 Potential for risk, burdens and benefits to participants

Participants may be in professional relationships with each other. If participating in a group interview, participants may express differing opinions that could potentially have negative effects on participants' relationships. Expected benefits include insights into implementation and study processes that may support the replicability of the intervention in other settings.

10. INTERVENTION: PROSPECTIVE FEEDBACK LOOP AND TAILORED CLINICAL RESPONSE

The InterACT study intervention is a prospective feedback loop to clinical teams, based on the outcomes of a patient record review (or screening) process using the CriSTAL and SPICT tools (see Appendices 1–2). The intervention process is shown in Figure 3. Each hospital's enrolled group of clinical teams switches to the intervention exposure phase as per the randomised allocation, following a 4-week recruitment phase, a randomly allocated usual exposure phase (either 16, 25 or 34 weeks) and a 4-week intervention establishment phase.

Figure 3 InterACT intervention: Patient record review and feedback loop response



Implementation framework

We will use an implementation framework, the Consolidated Framework for Implementation Research (CFIR) (32) to inform the implementation and process evaluation of the InterACT study intervention. The intervention will be fully described in an implementation toolkit, based on CFIR. This toolkit identifies what parts of the feedback loop intervention will be fixed, what will be flexible, and the associated degree of flexibility. This will support the local tailoring of the intervention to reflect hospital context, clinical team structure and workflows.

The feedback loop

Feedback provided to the clinical teams is intended to act firstly as a flag for the clinical team to review patient care activities and pathways, and then as a stimulus for the team to implement a tailored clinical response to promote appropriate patient care and treatment outcomes (26, 33). The feedback measures will not be ascribed any meaning by the research team beyond being a predictor of possible patient outcomes; clinician expertise and autonomy will not be questioned, nor will judgements be made about the likelihood of non-beneficial treatment. The purpose is to raise awareness of the potential for non-beneficial treatment using a transparent and evidence-based outcome measure.

Tailoring the intervention

To establish a feasible and achievable feedback loop and associated clinical team response, the project team, study team, hospital executive advisory group and enrolled clinical teams will work together during the 4-week intervention establishment phase to:

- attend information sessions about the study, the tools being used, the background and evidence for non-beneficial treatment including risk factors and the range of options for responding to screened patients
- decide the process for the study team to provide the patient level screening outcomes to the clinical teams: feedback will be provided by a project team member, and could include one or a combination of text, email, database log-in or face-face notification to nominated clinical team members.
- pilot the proposed feedback mechanisms for one week with each clinical team, in the intervention establishment phase.
- decide the preferred clinical team responses to feedback. This will require agreement on how each clinical team will respond to feedback about the screening outcomes and the hospital inputs that will be provided to support this. Clinician response plans could include, but will not be limited to, palliative care referral, multidisciplinary team review, advance care planning consultation, and patient/carer meetings.

The feedback will be provided to a clinical team nominee or lead/s in the format of: Patient record review for the InterACT study on *(date)* has identified *(patient identifier)* as having a CriSTAL score of x, with *(insert CriSTAL indicators)*, and a SPICT score of x, with *(insert SPICT indicators)*. The study team will not record screening results in the patient's record.

Monitoring and evaluating implementation

Process evaluation is an essential part of designing and testing complex interventions (34). The real-world setting and length of this trial will require a pragmatic approach to intervention adherence, reach and fidelity. The project team will systematically monitor the implementation process as part of the process evaluation, using templates and approaches based on the CFIR constructs. This embedded approach will aim to provide direct support for implementing the InterACT intervention and will inform understanding of how the actual implementation process contributed to the study outcomes.

The InterACT intervention is mapped to the 'Template for Intervention Description and Replication' (TIDieR) checklist and guide (35) to promote the replicability of this research.

11. STUDY OUTCOMES

A summary of project outcomes and outcome measures are in Table 2. The denominator group for Outcomes 1 to 9 are patients admitted under the enrolled clinical teams and who, following screening with the CriSTAL tool and the SPICT, are identified and recorded as *high-risk CriSTAL (*at high risk of death within 3 months), defined by the CriSTAL tool as having a score equal to or above 6, **or** *SPICT-positive* (presence of indicators of potential deterioration within 12 months), with a SPICT general indicator score equal to or greater than 2.

Table 2 Project outcomes and outcome measures

Impact outcomes		
Primary outcome	Proportion of patients with one or more Intensive Care Unit (ICU) admissions	ICU admissions during the current hospital stay from the date first recorded as *high-risk CriSTAL or SPICT-positive*.
Outcome 2	Length of hospital stay and discharge outcome	Length of hospital stay, with the transition endpoints of 'discharged alive' and 'death in hospital', from the date first recorded as *high-risk CriSTAL or SPICT-positive.*
Outcome 3	Time to hospital re-admission	The time in days to re-admission to any Queensland public hospital for re-admissions within 12 weeks from date of discharge.
Outcome 4	Time to first documented indications of clinician-led care review discussion	The time in days from the date first recorded as *high-risk CriSTAL or SPICT-positive* to documentation of a clinician-led care review activity. The type of care review activity, nature of any care change and indications of family conflict will also be recorded.
Outcome 5	Time to first care directive measure	The time in days from the date first recorded as *high-risk CriSTAL or SPICT-positive* to documentation of any care directive (including discussion outcomes, advance care plan, statement of choices, acute resuscitation plan). The type of care directive will also be recorded.
Outcome 6	Time to first palliative care referral	The time in days to first documented palliative care referral from the date first recorded as *high-risk CriSTAL or SPICT-positive* during the current hospital stay.
Outcome 7	Time to first medical emergency call	The time in days to first medical emergency call during the current hospital stay.
Health care resource use and costs		
Outcome 8	Changes in admission and treatment costs	Costs of treatment will be taken from routinely collected information and will begin accumulating from the date first recorded as *high-risk CriSTAL or SPICT positive*. All costs will be stratified by the acute and palliative care phases. This ensures that treatment costs reflect only those costs that relate to care provided at the end-of-life phase.
Outcome 9	Cost of implementing the prospective feedback loop intervention	The cost of implementing the study intervention will be measured by the duration and unit costs of staff time associated with completing direct study activities (including document review and clinical team feedback activities).
Process outcomes		
Extent and fidelity of intervention implementation, impact, and contextual barriers and enablers of the feedback loop intervention		

12. STUDY PROCEDURES

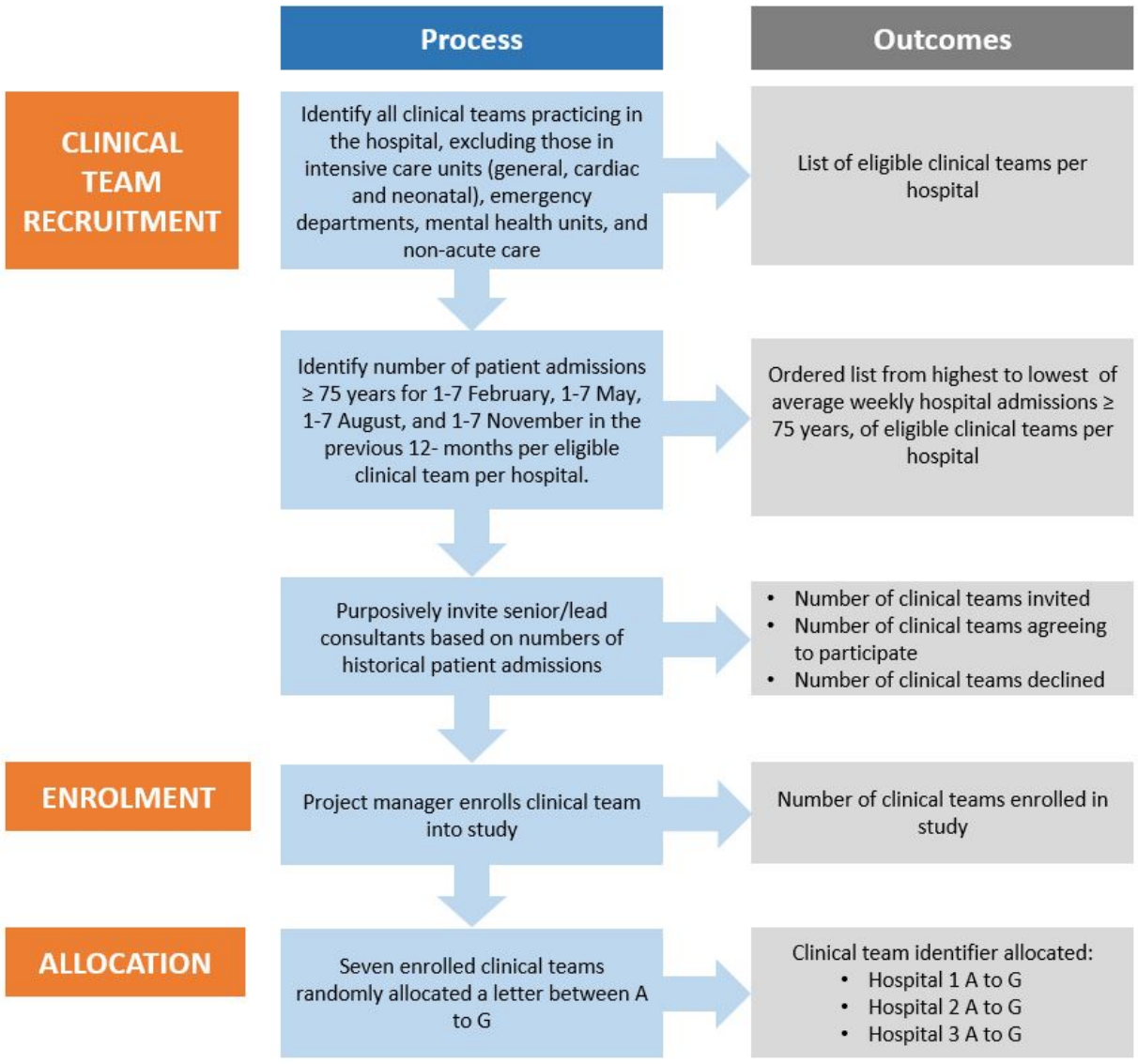
12.1 Recruitment and consent

12.1.1 Recruitment

Lead clinicians in each hospital will be made aware of the hospital's role as a partner in the InterACT study in the pre-trial period. Once all written governance and ethical approvals are in place, a start date for the trial will be advised to all hospitals. Meetings and information sessions will then be arranged for the recruitment period, in conjunction with each hospital executive advisory group.

We have chosen to study the effects of the intervention in a patient cohort aged ≥ 75 years and with clinical specialties that are more likely than other specialities to have patient cohorts at risk of non-beneficial treatment. The clinical team recruitment flow chart is shown in Figure 4.

Figure 4 Clinical team recruitment flow chart



To inform a stratified ordering of clinical teams for purposive sampling that will maximise a sample of patients aged ≥ 75 years, we will firstly identify the number of patient admissions ≥ 75 years for 1 to 7 February, 1 to7 May, 1 to 7 August, and 1 to 7 November in the previous 12 month period per eligible clinical team per hospital. Based on this information, we will develop an ordered sampling list that considers the average number of admissions per clinical team and prioritises medical specialties. A purposive sampling approach will be followed until the study team has recruited seven clinical teams at each participating hospital during the four-week recruitment phase.

The project manager will invite eligible clinical teams to participate at routine meetings in the hospital. The project manager, an executive sponsor and site-based study coordinator will explain the study and what is involved. A study participant information sheet will be provided and the study protocol will be available to all interested clinicians. Clinicians will be given two weeks to distribute participant information sheets and to discuss participation with their clinical teams. The project manager and site team will follow up clinicians via email, phone or follow-up meeting. Clinical team composition will reflect the usual clinical team structure at each hospital, and minimally include two senior clinical consultants who agree to participate.

12.1.2 Consent

The clinical team is the unit of enrolment into the study. A nominated lead clinician will provide agreement on behalf of their clinical team by contacting the project manager and expressing their verbal agreement for the team to participate and comply with the study requirements.

The clinical team unit members, hospital executive advisory groups and site-based study teams will be invited to participate in the process evaluation activities. The clinical team membership will be confirmed according to the enrolled clinical teams per hospital, the hospital's usual workflow and team structure as part of tailoring the intervention in the establishment phase. A summary of consent processes is in Table 3.

Table 3 Consent requirements

Phases	Activity	Participant Information	Consent
Site preparation and clinical team recruitment	Clinical team enrolment	Participant Information Sheet (PIS): InterACT study Intervention	Project manager to enrol the team following receipt of verbal agreement to participate from a nominated clinical team lead.
Usual care exposure Intervention establishment Intervention exposure	Patient record review	Not applicable	Clinical team: Recruitment agreement applies Patient data: Public Health Act (PHA) approval
Intervention establishment Intervention exposure	Clinical team feedback Semi-structured individual and group interviews	Not applicable PIS: Interviews *Flyers and PISs distributed via email and at relevant clinical team*	Clinical team: Recruitment agreement applies Patient data: Public Health Act (PHA) approval Clinical teams, study team, advisory group: Signed consent form

		and advisory group meetings by project team	
Post-intervention	Existing patient data sets Semi-structured individual and group interviews	Not applicable PIS: Interviews *Flyers and PISs distributed via email and at relevant clinical team and advisory group meetings by project team*	Patient data: Public Health Act (PHA) approval Clinical teams, study team, advisory group: Signed consent form

12.1.3 Enrolment

Clinical teams will be enrolled by the project manager.

12.2 Withdrawal

12.2.1 Participant withdrawal from study activities

As the unit of study enrolment is the clinical team, if an individual clinician participant, including a lead clinician who provided agreement to participate on behalf of their clinical team, withdraws from the interventional study procedures, for example due to a change of employment, then data collection and clinical team participation will continue unchanged. Other clinical team members would continue to be provided with the patient screening feedback. This is explained in the participant information sheet. The dates and reasons (if given) of all withdrawals will be recorded and reported.

12.2.2 Discontinuation of study or study site

Once enrolled, clinical team participation in the study will only be discontinued in consultation with their hospital executive advisory group and only if ongoing participation is untenable or negatively impacting patient care. Data collected on study participants up to the time of withdrawal will remain in the study database in order for the study to be scientifically valid. This is explained in the Participant Information Sheet (PIS).

The study will only be discontinued if a regulatory body, funding body, or Human Research Ethics Committee (HREC) judges it necessary for medical, safety, regulatory, or other reasons consistent with applicable laws, regulations and good clinical practice.

12.3 Randomisation, allocation and blinding

Statistician CI Lee will be responsible for computer generation of the study timing randomisation and the intra-hospital clinical team identifiers once all ethical and governance approvals are in place and all teams are enrolled at each of the three participating hospitals.

12.3.1 Allocation to stepped-wedge design timing

The three participating hospitals will be randomly allocated to intervention timing through the allocation of hospital identifiers from 1 to 3 prior to commencement of the trial. These identifiers will dictate the allocation to the stepped-wedge design, as per Figure 1. There will be sequential roll-out of the intervention over 40 weeks. All three hospitals receive the intervention, with the timing randomised.

Delayed switchover to the intervention establishment and/or intervention exposure phase could only be considered if, in the view of the investigator team and hospital executive advisory group, there is a major hospital situation that would impact capacity to complete the study phases in a timely or correct manner. The study completion date would be unchanged.

12.3.2 Allocation of clinical team identifiers

Clinical teams at each hospital will be randomly allocated a letter from A to G. These identifiers will help anonymise the data storage and reporting and does not change how the teams will receive the intervention.

12.3.3 Blinding and concealment of allocation

Given the nature of the intervention, and the fact that each hospital receives the intervention, it is not possible to blind the clinical teams to the intervention. Concealment of allocation will occur in relation to the cross-over timing to the intervention phases. During the site preparation and clinical team recruitment phase, the date the intervention exposure phase is commencing will be concealed from the hospital teams (including enrolled clinical teams, employed auditors, advisory group and site study team members). The project team will notify the hospital's advisory group, auditor and clinical team participants of their intervention establishment and intervention exposure start dates about eight weeks prior to allow time to plan for the intervention establishment phase activities. From this time point, the particular hospital's clinical teams will be aware of their allocation in the study.

Commencing the intervention establishment phase could impact clinical practice as it will naturally highlight the study focus and the potential for risks of patients receiving non-beneficial treatment. To reduce the impact of this change on the analysis, patient record screening data collection will continue through the intervention establishment phase but will not be part of the data analysis. These data will be used in the qualitative analysis.

12.4 Measurement tools used

Table 4 Measurement tools

Tools	Origin/ validation history	Data quality requirements
CriSTAL	(19-21)	Project team trained, hospital-employed registered nurse auditors Inter-rater reliability checks: as part of training, twice during each phase
SPICT	(22-24)	
Semi-structured group and individual interviews outline	Adapted from Consolidated Framework for Implementation Research (CFIR) (32)	Two project team members to conduct all group interviews; one project team member to conduct individual interviews
Time and activity tracking template	Excel spreadsheet, tailored to study requirements	Review monthly
Implementation record templates	Adapted from CFIR	Review monthly

We use a modified version of the CriSTAL tool by including an additional point on the CriSTAL score if the Clinical Frailty Scale is 7 or above. The original tool uses a point for 5 or above, and we keep that point together with the additional point at 7 or above. This modification is based on two recent papers (36, 37) showing an increasing risk of death with increasing Clinical Frailty Scale scores.

12.5 Study involvement by participants

This is summarised in Table 5.

12.5.1 Site preparation and clinical team recruitment phase

The hospital executive advisory group and site-based study teams will be formalised, and communication plans decided. In this phase, eligible clinical teams will be informed of the study and invited to participate during existing work team meetings and/or specific information sessions. One senior clinical team member will be required to verbally indicate their team's agreement to participate to the project manager.

12.5.2 Usual care exposure phase

Patient record review

Active involvement by clinical teams will not be required during this phase. Medical records of patients under the care of recruited clinical teams will be screened by a trained study team member using the CriSTAL and SPICT tools, as per Figure 3 Patient record review flow chart.

The hospital executive advisory group and site-based study teams will meet at least twice through this phase.

12.5.3 Intervention establishment phase

Patient record review

Continue as for the baseline phase.

Feedback loop and clinical team response

To prepare for the intervention phase, the project team, study team, hospital executive advisory group and the clinical teams will work together to:

- participate in confidential clinical team level review of their baseline patient screening outcomes
- tailor each clinical teams' process for and response to patient screening feedback
- pilot the feedback and response process for one week per clinical team, in the intervention establishment phase.

Clinicians will be invited to voluntarily participate in a 15 to 20-minute group or individual interview after the pilot.

12.5.4 Intervention exposure phase

Patient record review and score feedback

During this phase clinical team nominees or leads will be required to be available to receive feedback twice weekly about their patients who are identified as being *high-risk CriSTAL or SPICT-positive*.

Clinical team response

The clinical team leads with support from their clinical team members will be responsible for implementing a pre-established response to their patients identified in the CriSTAL and SPICT screening process. The parameters for this response, including timing, will be those determined during the intervention establishment phase.

Implementation monitoring

Clinical team members will be invited at least once to voluntarily participate in a 15 to 20-minute group or individual interview based on the CFIR constructs. Members of the clinical team and the site-based study team will also be asked to meet with the project and study team to complete monitoring documents, including capturing time spent on intervention activities. The purpose of this tool will be to assess the adherence to the feedback loop and fidelity of the feedback clinical response.

12.5.5 Post-intervention phase

Semi-structured interviews

The following groups will be asked to voluntarily participate in a 15 to 20-minute group or individual interview based on the CFIR constructs:

- members of enrolled clinical teams (consultants, registrars, residents, nurse managers and nurse and allied health specialists)
- members of each hospital's advisory group
- members of the site-based study teams, e.g. palliative care team leads, ICU directors, advance care planning facilitators, auditors, and study coordinators.

The interview will discuss how the intervention was introduced, any adaptations that were made, how staff responded, what changes in practice were implemented, and contextual factors that influenced implementation.

Table 5 Participant involvement summary

TIME IN WEEKS	PHASE	PARTICIPANT INVOLVEMENT: Clinical team	PARTICIPANT INVOLVEMENT: Advisory group and site study team
-	**Pre-trial**	Awareness raising of hospital partnership in the study	Awareness raising of hospital partnership in the study
4	**Site preparation and clinical team recruitment**	See recruitment flow chart Attend information sessions	Meet 2 to 3 times to progress recruitment
16, 25 or 34	**Usual care exposure**	No active involvement	Meet 2 to 3 times to plan for establishment phase
4	**Intervention establishment**	Participate in activities to: - Introduce the trial to teams - Support local context assessment - Tailor the clinician feedback response - Prepare for intervention phase Complete one-week pilot of prospective feedback response Participate in voluntary interviews	Participate in activities to: - Introduce the trial to teams - Support local context assessment - Support clinical team participation and tailored intervention activities
16, 25 or 34	**Intervention exposure**	Be available for record review feedback Implement agreed clinical team response Participate in a voluntary interview	Convene 4 to 6 weekly to support ongoing participation and engagement
12	**Post-intervention**	Participate in a voluntary interview Review and disseminate trial outcomes	Participate in a voluntary interview Review and disseminate trial outcomes

12.6 Data management

12.6.1 Data collection

Data collection and implementation will be commenced at each hospital only after written ethical and governance approvals have been obtained. Data collection methods at each site are summarised in Table 6 and the data collection schedule is shown in Table 7.

Patient record review data

No patients will be recruited. Identifiable data will be collected prospectively for record screening and feedback purposes.

Health services data

No patients will be recruited. Patient record review data will be linked to health services data to identify health service use for eligible patients of the participating clinical teams recorded as high-risk CriSTAL or SPICT-positive. Data will be linked by the relevant data custodian and supplied to the QUT-based project team in a non-identifiable format at the patient level. Non-identifiable whole of hospital data will be obtained from existing data sources via the relevant data custodians as per a PHA approval.

To review for seasonality and potential confounders over time, we will access historical routinely collected data, which will consist of non-identifiable data sets for patients ≥75 years of age admitted under the enrolled clinical teams for the historical data collection period (trial start date less two years). If the enrolled clinical team data is not available (due to change in team or hospital structure) a comparable clinical team data set will be sourced.

To assess impacts on hospital use due to long-term trends or the COVID-19 pandemic, data will be collected for all patients aged ≥ 75 years admitted to any clinical team in study hospitals and from three other large/major South-East Queensland hospitals who will not receive the InterACT intervention (comparator hospitals). These data will consist of non-identifiable data sets for patients aged ≥ 75 years admitted during the historical and trial periods of the study.

Process evaluation data

These data will be collected using a series of templates based on the CFIR to guide the assessment of contextual barriers and enablers, an interview guide and systematic implementation planning and record keeping.

Table 6 Data collection summary

Data	Method	Timing	Responsibility
Objective 1 - To determine the impact and health-care resource use and costs of a tailored clinical team feedback loop intervention on patient outcomes related to appropriate care and treatment at the end-of-life.			
COMMON DATA SET			
Number admitted under care of enrolled clinical team aged ≥ 75 years. Number of patients identified as high-risk CriSTAL **or** SPICT positive	The site auditor will screen patient records using the CriSTAL and SPICT tool and will record: Date and time of screening Indicators present and scores for CriSTAL and SPICT tools Date and time of ward admission	Twice weekly: Week 5 to week 58: Datasets to be extracted from REDCap weekly in weeks 1 to 8 of each of the usual exposure and intervention exposure phases; fortnightly	Site-based trained auditors

For high-risk CriSTAL or SPICT positive patients: presence, type and date of care directive document/documentation of discussion Coronavirus (COVID-19) infected (date)	Type and date of care directive document/documentation Coronavirus (COVID-19) infected (date) Date of feedback to clinical team All common data will be recorded in a spreadsheet in REDCap	otherwise, for data monitoring purposes. Intervention exposure phase	Project team nominee
COMPARATOR DATA SET			
For all patients ≥ 75 years admitted to TPCH, RBWH, GCUH, and 3 comparator hospitals, for 2 years prior to week 1: Age, Sex, Admission type (elective patient status, source of referral / admission, transferring from facility), length of stay, admission date and time, ICU admission and discharge date and time for all ICU transfers, separation date and time, and discharge destination	Project team to source patient data from relevant data custodians.	Once: when all ethical and governance approvals in place	Project staff
For all patients ≥ 75 years admitted to TPCH, RBWH, GCUH, for the trial period: Age, Sex, Admission type (elective patient status, source of referral / admission, transferring from facility), length of stay, admission date and time, ICU admission date and discharge date and time for all ICU transfers, separation date and discharge destination	Project team to source patient data from relevant data custodians.	Once: after week 70	Project staff
HISTORICAL DATA SET			
For all patients ≥ 75 years admitted under enrolled clinical teams for the 2 years prior to week 1:	Project team to source patient data from relevant data custodians.	Once: Week 5	Project staff

Length of hospital stay, location and discharge outcome			
Primary outcome: Proportion of patients with one or more Intensive Care Unit (ICU) admissions			
For identified high-risk CriSTAL or SPICT positive patients: Time in hours from time of first positive record review to time of ICU admissions from week 5 to week 58	Project team to source patient data from relevant data custodians to include date/time of event.	Once: After week 58	Project staff
Outcome 2: Length of hospital stay and discharge outcome			
For identified high-risk CriSTAL or SPICT positive patients: Length of hospital stay in hours and location of hospital stay from date/time of first positive record review, and discharge outcome from week 5 to week 58	Project team to source patient data from relevant data custodians to include date/time and outcome of event.	Once: After week 58	Project staff
Outcome 3: Time to hospital re-admission			
For identified high-risk CriSTAL or SPICT positive patients: Time in days since first positive record review, and location, of hospital re-admissions during weeks 5 to week 58, with follow-up to 12 weeks from discharge from screened admission (up to week 70)	Project team to source patient data from relevant data custodians to include date/time of event, location.	Once: After week 70	Project staff
Outcome 4: Time to first documented indications of clinician-led care review discussion			
For identified high-risk CriSTAL or SPICT positive patients: Time in hours from first positive record review to documentation of first clinician-led activity that considers care pathways from week 5 to week 58	Review of patient records Date/time, type of event, nature of any care change and indications of family conflict will be recorded onto a spreadsheet in REDCap	Twice weekly: Week 5 to week 58	Site-based trained auditors
Outcome 5: Time to documented care directive measures (including outcomes of an oral discussion, advance care plan, statement of choices, acute resuscitation plan)			
For identified high-risk CriSTAL or SPICT positive patients: Time in hours from first positive record review to documentation of a care directive, from week 5 to week 58, including	Review of patient records Date/time, type and content of care directive will be recorded onto a spreadsheet in REDCap	Twice weekly: Week 5 to week 58	Site-based trained auditors

documentation of an oral discussion or a written directive, to: - reduce/cease active treatment - increase comfort care - continue active treatment. -			
Outcome 6: Time to first palliative care referral			
For identified high-risk CriSTAL or SPICT positive patients: Time in hours from first positive record review to palliative care referral, from week 5 to week 58	Review of patient records Date/time of referral will be recorded onto a spreadsheet in REDCap.	Twice weekly: Week 5 to week 58	Site-based trained auditors
Outcome 7: Time to first medical emergency call			
For identified high-risk CriSTAL or SPICT positive patients: Time in hours from first positive record review to medical emergency calls during screened admission from week 5 to week 58	Project team to source patient data from data custodian of Medical Emergency Response Team database to include date/time of event.	Once: Post-intervention	Project staff
Outcome 8: Changes in admission and treatment costs			
For identified high-risk CriSTAL or SPICT positive patients: Admission costs for ICU admissions (primary outcome) Length of stay costs (outcome 2) Treatment costs since first date of positive screening (e.g. pathology tests, diagnostics, medications, procedures)	Project team to source data from literature estimates combined with change from baseline to intervention of primary outcome and outcome 2 Project team to source patient data from hospital-based Transition II data custodians to include date/time of event	Once: Post-intervention	Project staff
Outcome 9: Cost of implementing the prospective feedback loop intervention			
Number and unit costs of resources used in direct study related implementation activities: document review and clinical team feedback activities, including staff time for training, meetings, record reviews, giving and receiving feedback	Site-based study staff to prospectively record patient record review time spent on an Excel spreadsheet. Site study coordinator and project team to prospectively complete Excel spreadsheet tracking tool of time spent on all other intervention activities	Monthly: Week 1 to week 58	Project staff Study team

Objective 2 - To conduct a process evaluation to assess implementation, mechanisms of impact, and contextual barriers and enablers of the feedback loop intervention.			
Outcome: Extent and fidelity of implementation, impact, and contextual barriers and enablers of the feedback loop intervention			
Systematic assessment of the hospital site context, including readiness for implementation Monitoring of implementation Evaluation of implementation	Collect and monitor information using documents based on Consolidated Framework for Implementation Research (CFIR): - context assessment - hospital specific implementation plan - implementation record (including feedback and clinical response records) Semi-structured group or individual interviews based on CFIR. Clinical team, study team and executive advisory group meeting records (attendees, time, key points) Maintain records of communication and feedback using OneNote REDCap records of clinical team feedback: Date provided To whom	Ongoing: Week 1 to week 62 Week 1 to 4 of intervention establishment phase At least once during intervention exposure phase. Post-intervention, week 59 to week 62 Ongoing: Week 1 to week 62 Ongoing: Week 1 to week 62 Intervention exposure phase	Project team

Table 7 Data collection schedule

Method	Site preparation and clinical team recruitment phase Week 1 to 4	Usual care exposure phase Week 5 to weeks 20/29/38	Establishment phase Week 21 to 24 Week 30 to 33 Week 39 to 42	Intervention phase Week 25 to 58 Week 34 to 58 Week 43 to 58	Post-intervention phase Week 59 to 70
Objective 1 Impact and resource use					
Historical data					
Comparator data					
Patient record screening (CriSTAL and SPICT tools)					
Routinely collected hospital data sets					
Review of patient records					
Implementation cost records					
Objective 2 Process evaluation					
Site context assessment					
Implementation records					
Semi-structured interviews					

12.6.2 Access to existing data

A Public Health Act (PHA) approval will be in place to enable access to existing data sets and for data linkage between those datasets.

Table 8 Existing dataset access

Name of data set	Data custodian	Agency type	Data collection format	Variable	Justification
Queensland Hospital Admitted Patient Data Collection (QHAPDC)	Statistical Services Branch	State	Non-identifiable	Length of stay ICU admission Re-admissions Discharge outcomes/death Referrals	Primary outcome, outcomes 2, 3, 6, 8
Transition II Clinical Costing Database, MNHHS	Director, Clinical Health Information Services	Institutional	Non-identifiable	Costs LOS Referrals	Outcome 8
Transition II Clinical Costing Database, GCUH	Manager, Health Analytics Team	Institutional	Non-identifiable	Costs LOS Referrals	Outcome 8
Medical Emergency Response Team (MERT) database	Safety and Quality Unit, TPCH Safety and Quality Unit, RBWH TBA, GCUH	Institutional	Non-identifiable	Medical emergency response calls	Outcome 7

12.6.3 Data storage

The project manager will maintain a list of appropriately qualified persons to whom the chief investigator has delegated study duties. The project manager, investigators and other QUT-based project staff are responsible for maintaining a comprehensive and centralised bibliographic filing system of all study-related (essential) documentation, suitable for inspection at any time by the approving HREC or applicable regulatory authorities.

A detailed data management plan will be completed, in line with QUT policy. This will direct that all document data will be stored on hard disk drives. These computers will be networked to a file storage server, where an automated batch file copy procedure will back up the entire hard disk drive of each computer on a daily basis. Data will be shared via a password protected file storage server at QUT that only members of the research team can access. All references will be stored in one bibliographic database that can be accessed by the research team.

12.6.4 Data retention

Study records will be retained as per the Queensland Government University Sector Retention and Disposal Schedule. Data will be retained for a minimum of 15 years. At the end of the study, final non-identifiable data sets will be deposited in QUT's Research Data Storage System (RDSS). In line with publication embargoes and requirements, we will generate a document object identifier (DOI) for each non-identifiable data set and make this record publicly accessible.

12.7 Safety Evaluations

The following will be used to evaluate the safety of staff involved in the study:

- protocol deviation and adverse events reporting
- incident and unanticipated problem monitoring.

12.7.1 Protocol deviations/adverse event reporting

Participating hospital staff and clinical teams are required to report all protocol deviations and adverse events to the project manager. The project manager is responsible for ensuring that all protocol deviations and adverse events observed by the investigator/s, project team or reported by sites are collected, reviewed with CI Barnett, recorded in the source documents, and reported to the approving HREC and site Research Governance Officers.

A protocol deviation is any noncompliance with the study protocol or HREC requirements. The noncompliance may be either on the part of the participant, the investigator, project team or the study site staff. As a result of deviations or adverse events, corrective actions are to be implemented promptly.

12.7.2 Incident and unanticipated problem monitoring and reporting

The project manager is responsible for ensuring that all incidents and unanticipated problems observed by the investigator/s, project team or reported by sites are collected, reviewed and recorded in the source documents. Incidents could require reporting to the approving HREC and site Research Governance Officers.

12.8 Monitoring

A data monitoring group will be established for the trial period. This group, led by the project manager and including the project team and at least two investigators, will convene regularly through the trial period to monitor data collection and trial processes for each site. This will include weekly review by the project team

in weeks 1 to 8 of the usual care exposure phase and weeks 1 to 8 of each hospitals' intervention exposure phase; in other periods it will be at least fortnightly by the project team. Data will be reviewed to ensure correct collection of the usual care exposure and intervention exposure data sets and to monitor implementation of the study intervention. This group will not monitor the study outcomes.

13. SAMPLE SIZE AND STATISTICAL ANALYSES

13.1. Sample size and statistical power

The sample size calculations were performed to ensure the study has sufficient statistical power for the analysis of the primary outcome measure, the difference in the proportion of high-risk CriSTAL or SPICT-positive patients who had one or more ICU admissions (primary outcome). Simulation-based sample size calculations (38) were used to determine adequate sample to power the analyses. Information used in the patient hospital episode simulation procedure was obtained from a previous study estimating the incidence and impact of non-beneficial treatment in three tertiary public hospitals in the same state (8). In particular, we calculated the proportion of patients aged 75 years or older who had one or more ICU admissions during their hospitalisation, stratified by their retrospectively identified non-beneficial treatment status.

Weekly chart review and identification of at least three patients aged 75 years or over with high-risk CriSTAL or SPICT-positive status in each of the 21 clinical teams across the 3 hospitals will give a statistical power of 95% to detect a reduction in the proportions of patients with ICU admissions from 0.20 in the usual care exposure period to 0.113 in the intervention exposure period. The sample size calculations were based on a 5% statistical significance level for a two-sided z-test of the intervention coefficient, within-ward correlation of 0.1, and a stepped-wedge design as shown in Figure 1. We performed a sensitivity analysis with an alternative within-ward correlation of 0.01 and estimated the corresponding power to be 79.3%.

13.2 Data analysis – overall considerations

All data analyses presented in the following subsections will be adjusted for potential confounders of patient age and sex, unless specified otherwise. Additionally, the fitted models will be assessed for adequacy of model fit to data and tested for violations of model assumptions.

Censoring will be used in the survival analyses to avoid contamination of the estimated intervention effect from patients exposed to multiple study phases. Specifically,

- Usual care exposure period patient data will only include patients admitted to a clinical team and identified as high-risk CriSTAL or SPICT-positive during the usual care exposure period
- Data collected in the intervention establishment phase will not be included in the statistical analysis. Patients who remain in the wards at the change-over time to the establishment phase are censored on the day prior to the change-over.
- Only patients admitted and identified as high-risk CriSTAL or SPICT-positive in the intervention exposure phase will be included as data for the intervention exposure phase.
- Patients who remain in the hospital at the end of the intervention exposure phase will be censored on the last study day.

There is a potential risk that the censoring will be statistically informative as it is more likely to affect patients with long hospital stays. We will compare patient characteristics, notably their length of stay and other study outcomes listed below, of those who were censored with those who were not censored. If large differences are detected, the survival models will be adapted to use inverse probability censoring weighting estimators to explicitly account for the informative censoring.

For the binomial regression analysis of the primary outcome, censored patients will be excluded from the analysis. We do not anticipate too many patients to be excluded from the analysis. If the proportion of censored patients that will be excluded exceeds 5% of the data set, we will perform a planned sensitivity analysis where the primary outcome is analysed using a survival model instead.

We plan to perform a sensitivity analysis on the time scale used in the survival analyses for Outcomes 2 to 7. The proposed sensitivity analysis will reanalyse the data, using calendar time in conjunction with, and in place of, time since admission to enrolled medical team (39). The use of multiple time scales is expected to present useful additional information on the time-dependent outcome measures and intervention effect, as well as be better able to control for risk patterns that vary over calendar time, e.g., seasonal effects.

A separate sensitivity analysis is proposed to include a weekend and after-hours time-varying indicator covariate in the survival analyses. It is plausible that hospitals have different routine clinical practices and run at a reduced capacity during these times, which would impact the outcome measures (e.g., reduced risk of discharge on weekends). This analysis will create multiple observations per patient and hence the survival models will include a patient-cluster to adjust for correlated data using robust sandwich variance estimators.

As an exploratory data analysis, we will compare the time between patient admission to the recruited clinical team to first high-risk CriSTAL or SPICT-positive identification in the usual care period with the corresponding duration in the intervention period. This analysis serves to provide a more complete description of patient hospitalisations during the study, but findings of this analysis are not expected to affect the proposed analyses below as the CriSTAL and SPICT screening frequencies are identical in both periods. As such, we anticipate this duration to be similar across both periods. If a large difference is detected, the investigator team will deliberate the addition of this duration in the survival analysis as a potential transient model transition in the corresponding survival models. A similar partition will also be applied to the Outcome 8 to investigate if there are potential differences in admission and treatment costs in this time between the usual care and intervention exposure periods.

We will review historical data on the primary outcome (ICU admission) as well as secondary outcomes where historical data is able to be extracted from administrative databases prior to performing the statistical analyses proposed. These secondary outcomes are length of hospital stay and discharge (Outcome 2) and time to hospital readmission within 12 weeks from index discharge date (Outcome 3). We will investigate the historical data and comparator hospital data for potential seasonality, for changes to hospital use in the study cohort due to the COVID-19 pandemic and other time trends that should be incorporated into the statistical analyses, if any. Additionally, we will compare historical data with baseline exposure data for these outcomes to investigate if there was a notable Hawthorne effect from the trial and if it is possible to quantify the effect.

For most analyses we examine the time to the first event rather than the total number of events, for example, the time to first medical emergency team (MET) call rather than the total number of MET calls during the patient's hospital admission. This is because the first event is often crucial and potentially sets patients down a very different care pathway. If the intervention is successful, then we would expect it to have a positive impact on the time to first event. We note that our planned survival analyses examine both the time and number of first events.

Subgroup analyses of the primary outcome and outcomes 2 to 9 will be performed for each individual hospital separately.

We will use EQUATOR guidelines to write-up our results, using the CONSORT guidelines for randomised trials, the extension for stepped-wedge trials and TIDIER guidelines for intervention descriptions (35, 40, 41). Results will be presented as means with 95% confidence intervals. We will create p-values but will preference confidence intervals over p-values and only include p-values in papers if journals insist on them.

An initial analysis will be created using a scrambled intervention group by randomly allocating each patient to the usual care exposure or intervention exposure. A complete statistical report will be created using this scrambled data and sent to all investigators for discussion. This allows investigators to query the methods and approaches used prior to the final report. It can also uncover errors in the code or data. Changes can be made prior to seeing the main results, which helps avoid the bias of only making changes where results are perceived as unfavourable.

13.2.1 Analysis primary outcome: Proportion of patients with at least one Intensive Care Unit (ICU) admission

The primary outcome will be analysed using a Binomial regression with the patient ICU admission as the binary response variable. The question is: does the patient have at least one ICU admission in their relevant hospital admission episode? The key variable is the timing of the switch from usual care exposure to intervention exposure phase, so the main result of this analysis will be the intervention exposure effect on the proportion of patients with at least one ICU admission. A linear time covariate will be included to capture any potential calendar time trend throughout the 58 week data collection period. The model will also adjust for potential confounders of patient age and sex.

The model will include a random intercept for each enrolled clinical team to account for any underlying differences in the proportion of patients with ICU admissions between the teams. Experience with similar data and models has found that these intercepts will often be close to zero and the model may not converge. If this occurs we will simply leave out the intercept and run a standard binomial regression model.

13.2.2 Analysis outcome 2: Length of hospital stay and discharge outcome

Length of hospital stay of outcome 2 refers to the time spent in hospital beginning from the patient's admission to care of an enrolled medical team.

Outcome 2 will be investigated using a competing risk, proportional hazards survival model with 'discharged alive' (separated by discharge location, e.g., to palliative care, nursing home) and 'in-hospital death' as competing endpoints for each patient's hospital stay in hours. Use of the competing risk survival model provides an estimate of the intervention effect which appropriately accounts for the competing and time-varying nature of the two transitions on a patient's length of stay (42). Cumulative incidence curves will be used to compare the event rates over time between the usual care exposure and intervention exposure phases. The survival analysis will adjust for potential confounders of patient age, sex and time spent in hospital for identified hospital episode prior to admission to enrolled clinical team. Additionally, the survival analysis will stratify by clinical teams to account for underlying differences between clinical teams.

13.2.3 Analysis outcome 3: Time to hospital re-admission

Analysis of outcome 3 will use a proportional hazards survival model for time to re-admission to any Queensland public hospital within the first 12 weeks after the discharge of the index hospital episode. The analysis will only include patients discharged alive from their index episode. Patients who died after leaving hospital or were not re-admitted within the 12 weeks are treated as censored observations at day of death, or at the end of the 12 weeks follow-up period, respectively. The estimated cumulative incidence curves will be

compared to investigate differences in re-admission rates over time between the usual care exposure and intervention exposure phases. Each clinical team will be a separate stratum in the survival analysis.

13.2.4 Analysis outcome 4: Time to event and type of documented care review activity

A competing-risk, proportional hazards survival model, stratified by clinical teams, will be fitted to the time until first documented care review activity with hospital discharge and in-hospital death as competing events. The time will begin from when the patient came under the care of the clinical team. The model will have a binary variable indicating if patients were in the usual care exposure or intervention exposure phase. An estimated cause-specific hazard ratio of greater than one for this variable will indicate a decrease in time to the particular care review activity. Cumulative incidence curves will be examined to investigate differences in rates of first documented care review activity over time between the usual care exposure and intervention exposure phases.

We will examine the impact of time to documentation of continuing active treatment or family conflict, which could be a strong competing risk for documentation of care review activities. We will examine the interplay between these events using data from the usual care exposure period only, and consider whether and how to add continuing active treatment to the survival model.

13.2.5 Analysis outcome 5: Time to first care directive measure

Analysis for outcome 5 will use a competing-risk, proportional hazards survival model fitted to the time until first care directive measure, treating hospital discharge and in-hospital deaths as competing events, stratified by clinical team. The time will begin from when the patient came under the care of the clinical team. A binary variable indicating if the patient was part of the usual care exposure or intervention exposure phase will be included in the model to estimate the associated cause-specific hazard ratio associated with the intervention, and will investigate the difference in cumulative incidence curves between event rates in the usual care exposure and intervention exposure phases.

13.2.6 Analysis outcome 6: Time to first palliative care referrals

Analysis of outcome 6 will use a competing-risk, proportional hazards survival model to time to first palliative care referral with hospital discharge and in-hospital death as competing events. Each clinical team will be a separate stratum in the survival analysis. The intervention effect will be estimated from a binary indicator of study phases (usual care exposure or intervention exposure) as a cause-specific hazard ratio for palliative care referral hazard. Cumulative incidence curves will be used to examine event rate differences over time between the usual care exposure and intervention exposure phases.

13.2.7 Analysis outcome 7: Time to first medical emergency calls

Outcome 7 will be analysed using a competing-risk, proportional hazards model for time to first medical emergency calls with hospital discharge and in-hospital deaths as competing events, stratified by clinical teams. An indicator variable of study phase (usual care exposure or intervention exposure) will be used to estimate the intervention effect on the time to first medical emergency call. We will compare the cumulative incidence curves to assess for differences in rates over time across the two phases.

13.2.8 Analysis outcome 8: Changes in admission and treatment costs

For outcome 8, data on the health services used by patients in the trial will be retrieved. Patient level information available from the 'Transition II Clinical Costing Database' include: emergency department, admission to hospital and transfer to ICU, surgery, pharmacy use, diagnostics and imaging and pathology and referral to palliative care and duration of admission. This database is updated with a notification of in-hospital death from Queensland's Death Registry. Cost savings from intervention effects could arise from fewer non-

beneficial treatments on the ward, reduced referrals to ICU, and earlier discharge at the end-of-life from acute care to community-based settings.

Any costs that occurred before the patient was reviewed and recorded as *high-risk CriSTAL or SPICT-positive* will be excluded.

Statistical distributions will be used to describe variability in all cost parameters. The normal, uniform, beta and gamma could be used depending on the type of parameter. Fitted distributions will be randomly re-sampled and the economic outcomes of 'change to total costs' simulated 10,000 times. This approach propagates uncertainty in prior parameters forward to the total cost outcomes. The key outcome will be the average cost per patient together with 95% bootstrap confidence intervals to estimate the uncertainty in this average.

13.2.9 Analysis outcome 9: Cost of implementing the prospective feedback loop intervention

The costs of implementing the intervention, outcome 9, will be measured by the duration of staff time associated with collecting, interpreting and providing the feedback, and for all activities required to establish the intervention at 'Stage One'. Prospective weekly activity and time diaries will be completed by the research teams to record minutes of staff time and grade of health care worker. The economic opportunity costs of healthcare workers' time will be valued by Queensland Health wage rates to include the full costs of employment. Quantities and types of consumables and incidentals used will be recorded by the research team and valued in dollar terms by market price. The key outcome will be the estimated total cost of the intervention together with a bootstrap 95% confidence interval for the total.

13.2.10 Additional information

Residual checks

For all regression models, the residuals will be used to assess if the model provides an adequate fit to the data, if there are unaccounted seasonal and temporal trends to be incorporated the model assumptions are violated, and if there are any outlying or influential observations.

Planned sensitivity analyses

The first planned sensitivity analysis will investigate the impact of using a different time scale in the survival analyses for Outcomes 2 to 7 by reanalysing the data using calendar time in place of time since admission to enrolled clinical team as the time scale(s). This investigation will highlight any potential differences or similarities in the intervention effect size using the two different time scales and provide a richer interpretation of the effect of the intervention.

The second planned sensitivity analysis investigates the addition of a weekend and after-hours indicator covariate in the survival models on the estimated intervention effect sizes. It is plausible that there are different routine clinical practices and staffing capacities during regular working hours, and weekends and after hours, which could impact the outcomes of interest. This sensitivity analysis aims to quantify this difference and determine if it impacts the estimated intervention effect for the outcomes measured. This analysis will create multiple observations per patient and hence the survival models will include a patient-cluster to adjust for correlated data using robust sandwich variance estimators.

The third planned sensitivity analysis evaluates the interaction between SPICT and CriSTAL scores with the outcomes and intervention effect. It is plausible that patients with higher scores might have poorer outcomes, and a stronger intervention effect. This sensitivity analysis involves the addition of the SPICT and CriSTAL scores, and interaction terms between the scores and intervention indicator covariate, as covariates in the statistical models.

The fourth planned sensitivity analysis is conditional on the proportion of censored patient data. If greater than 5% of the patient data is censored, the primary outcome data will be analysed using a survival model instead as survival models readily handles censored data. Comparison of the estimated intervention effect under the two approach would highlight the impact of excluding censored patient data in the binomial regression.

Planned subgroup analyses

All analyses will be repeated for each hospital. Results will be presented using the blinded hospital identifier. The aim is to examine whether there was a large heterogeneity between the three hospitals in terms of the intervention effect.

COVID-19 impact
It is currently unclear the full immediate and long-term impact of COVID-19 on the study's patient cohort hospital presentations, as well as hospital staffing and processes. As such, we will assess the clinical and statistical comparability of the pre-COVD-19 usual care exposure data with the post-COVID-19 usual care exposure data prior to deciding whether it would be appropriate to retain the pre-COVID-19 data in for the analysis. We will assess the comparator hospital data to identify potential COVID-19 impacts.

Cost adjustment

As the study will run over two financial years, costs will be adjusted to the latest year.

Software

We will use R for data management, modelling and graphics (43). We will make all our R code publicly available via Github (https://github.com/agbarnett/InterACT) or a similar coding site.

13.3 Data analysis - Objective 2 Process evaluation

Interview notes and transcripts, and monitoring and field records will be subject to thematic analysis. A project team member with implementation science and qualitative research expertise will complete this process, under the guidance of CI Harvey. Analysis will be iterative: firstly identifying emerging themes, then comparing and refining these. Analysis will continue until no new themes emerge and agreement on themes is achieved.

14. ETHICAL CONSIDERATIONS AND REGULATORY OBLIGATIONS

14.1 Human Research Ethics Committee

The project team will submit an ethics application and obtain written approval from a Queensland Health Human Research Ethics Committee (HREC) at one participating hospital, with mutual acceptance for the other two participating hospitals. A copy of the protocol, proposed informed consent forms, other written participant information, and any other relevant study material will be submitted to the HREC. All subsequent protocol amendments, once approved by the InterACT management committee, will be submitted as a variation to the approving ethics committee. An administrative review will be submitted to the QUT HREC.

The project manager will notify the HREC of deviations from the protocol or serious adverse events occurring at the hospital in accordance with local procedures. The investigators and project manager will be responsible for adhering to ethics committee requirements throughout the study.

14.2 Informed consent

Informed consent will be required where a trial site staff member participates in study-related survey activities where individual staff data is collected, such as interviews. Concerns about consent will be addressed by the project manager in accordance with governance and ethical requirements.

Patient audit data

A waiver of consent is approved from the HREC for access to patient data (HREC/2019/QRBW/51606).

Health services data

A waiver of consent is approved from the HREC for access to health services data (HREC/2019/QRBW/51606).

Patient chart screening and feedback

Clinical teams invited to participate will be provided with a participant information sheet. One nominated lead and representative clinician must indicate directly to the project manager their team's willingness to participate. Verbal consent from the lead clinician implies consent to participate in the review and feedback activity for the whole clinical team.

Interviews

Clinicians and hospital staff invited to participate in interviews will be provided with a participant information sheet. Prior to any such study-related activity, the QUT study team member will ensure that each participant is fully informed about the nature and objectives of the project and possible risks associated with participation, including answering any questions the participant may have throughout the study. A written informed consent must be signed and personally dated by the participant and the QUT study team member who performed the informed consent. The original signed informed consent form will be retained in accordance with QUT policy, and a copy of the participant information sheet retained by the participant.

14.3 Waiver of consent

A waiver of consent will be sought for access to patient health information, as this research is low risk and has benefits for the patient that justify any risks associated with not asking consent. Further, in the conduct of this research:

- it would be impracticable to obtain individual patient consent due to the quantity of records and sensitivity of the audit focus (identifying patients at risk of dying within three months, and patients with potential for receiving non-beneficial treatment)
- there is no known reason to expect that patients would not have consented if they had been asked
- there are plans and processes in place for protection of patient privacy and confidentiality of the data
- a plan will be in place to support the dissemination of results and ensure other information arising from the research is available to the participating clinical teams and hospital staff and stakeholder groups, including health consumer groups
- the possibility of commercial exploitation of derivatives of the data will not deprive the participants of financial benefits
- the waiver is not prohibited by State, federal or international law.

The lead institution (QUT) will make a summary description of this research publicly accessible via annual research reports and publications.

Health services and patient data

A Public Health Act (PHA) application is approved to obtain patient data in the study, (Ref: QCOS/033343/RD008146) as shown in Table 8, p. 21.

14.4 Site/governance review

In accordance with the Queensland Health Research Governance requirements, Site Specific Assessment (SSA) approval will be in place from the three participating public hospital sites (GCUH, RBWH, TPCH) prior to the study commencing.

14.5 Confidentiality

Hospital identifiers will be assigned to all sites; a letter identifier will be assigned to each clinical team. All data and information generated by the hospital as part of the study will be kept confidential by the research study team as per the *Australian Code for the Responsible Conduct of Research.* The investigators, project team, hospital-based study team and other hospital personnel will not use this information and data for any purpose other than conducting the study. These restrictions do not apply to information which it is necessary to disclose in confidence to HREC solely for the evaluation of the study.

Audio recordings taken from discussion group and interview sessions will be kept for fifteen years after transcription. Transcription will be reported in non-identifiable format.

15. DISSEMINATION OF RESULTS & PUBLICATIONS

The study team will maintain a dissemination plan in conjunction with our study partners.

15.1 Intellectual property

Intellectual property requirements will be informed by the collaborative research agreements and hospital site agreements.

15.2 Dissemination of results to participants

Results will be directly disseminated to each participating hospital and to each participating clinical team through a series of presentations, reports and summaries.

15.3 Dissemination of results to health consumers, policy makers and other stakeholders

Results will be directly disseminated to our policy partners for further distribution to consumers, policy- and decision-makers in the form of evidence briefs, plain language summaries and policy recommendations.

A publication plan will be established by August 2019 to inform systematic publication of results through the clinical and academic communities. We will adhere to the International Committee of Medical Journal Editors requirements for assignment of authorship and reporting the contributions of each author.

All final non-identifiable data sets will be available from the study statisticians (CIs Barnett and Lee) once those data have been reported.

16. OUTCOMES AND SIGNIFICANCE

This intervention evolved from the previous work completed by the CIs on non-beneficial treatments (1, 2, 8). The emphasis of this study is to support clinicians to recognise the potential for non-beneficial treatment at the end-of-life as part of a feedback loop that relays objective information about a patient's risk profile in relation to death and deterioration. The tailored clinical response promotes communication, engagement and awareness.

Within the Australian healthcare system there are economic and clinical imperatives to reduce non-beneficial treatments. By concurrently completing a process evaluation of the study intervention we will identify the barriers and enablers to using objective data to promote appropriate patient care pathways. This research will be useful for implementation of similar interventions in other hospital settings.

17. ABBREVIATIONS

ACHLR	Australian Centre for Health Law Research
ANZCTR	Australian and New Zealand Clinical Trial Registry
AusHSI	Australian Centre for Health Service Innovation
CFIR	Consolidated Framework for Implementation Research
CI	Chief Investigator
CONSORT	Consolidated Standards of Reporting Trials
CriSTAL	Criteria for Screening and Triaging to Appropriate aLternative Care
HREC	Human Research Ethics Committee
ICU	Intensive Care Unit
GCHHS	Gold Coast Hospital and Health Service
GCUH	Gold Coast University Hospital
MET	Medical Emergency Team
MNHHS	Metro North Hospital and Health Service
NHMRC	National Health and Medical Research Council
PCA	Palliative Care Australia
PHA	Public Health Act
QUT	Queensland University of Technology
RBWH	Royal Brisbane and Women's Hospital
SPICT	Supportive and Palliative Care Indicators Tool
SPIRIT	Standard Protocol Items: Recommended for Interventional Trials
SSA	Site Specific Assessment
TIDieR	Template for Intervention Description and Replication
TPCH	The Prince Charles Hospital
UNSW	University of New South Wales
UQ	University of Queensland

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APPENDICES

Appendix 1

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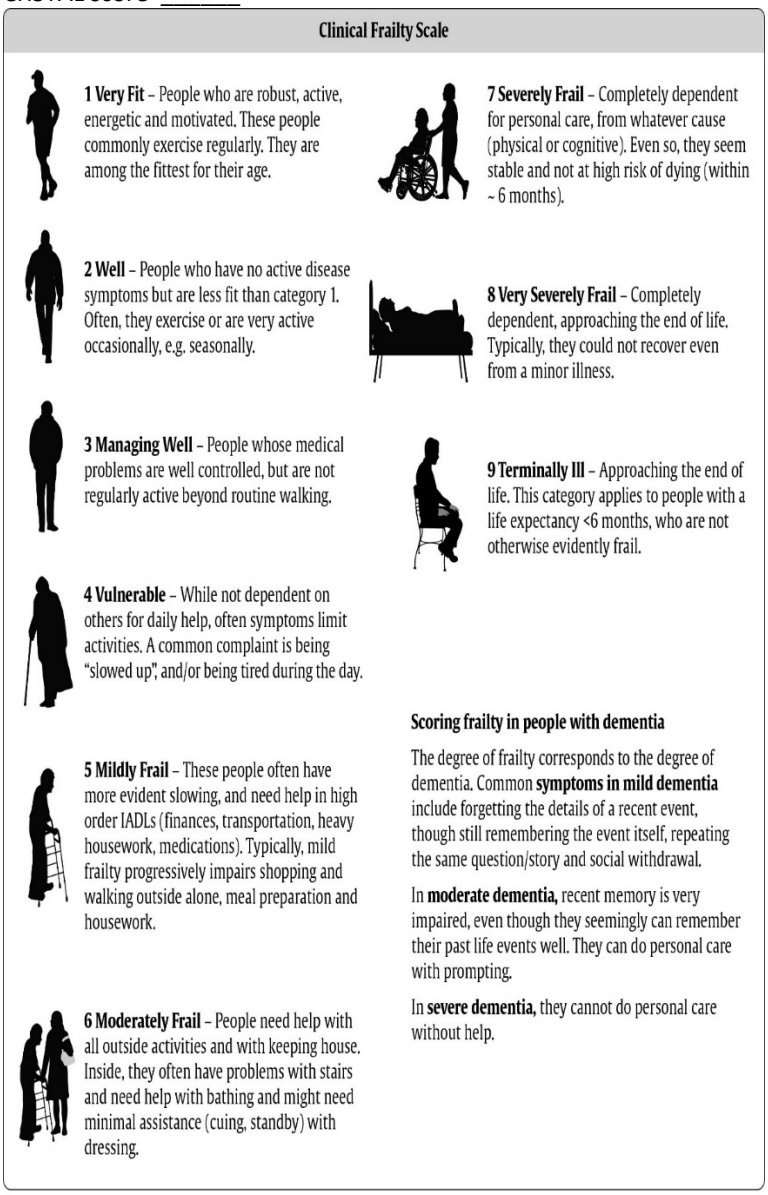
CriSTAL Tool

Date: ___/___ /_____	**Consultancy team:**	
☐	**Age ≥75** *(1 point)*	
☐	Admitted via Emergency Department *(1 point)*	
☐	Nursing home resident /in supported accommodation *(either: 1 point)*	
☐	Meets ≥= selected deterioration criteria on admission *(max 1 point if it meets ≥2 RRT criteria)*	
	☐	1 - Decreased LOC: Glasgow Coma Score change >2 or AVPU =P or U
	☐	2 - Systolic blood pressure <90 mmHg
	☐	3 - Respiratory rate <5 or >30 per minute
	☐	4 - Pulse rate <40 or >140 per minute
	☐	5 - Need for oxygen therapy or known oxygen saturation <90%
	☐	6 - Hypoglycaemia: BGL 1.0 - 4.0 mmol/L
	☐	7 - Repeat or prolonged seizures (> once in 24 hours or >5 minutes duration)
	☐	8 - Low urinary output (<15 ml/hour or <0.5 ml/kg/hour)
AND	**OTHER RISK FACTORS /PREDICTORS** (*tick as many as relevant- max 7 points*)	
	Personal history of active disease:	
☐	1 - Advanced malignancy	
☐	2 - Chronic kidney disease	
☐	3 - Chronic heart failure	
☐	4 - Chronic obstructive pulmonary disease	
☐	5 - New cerebrovascular disease	
☐	6 - Myocardial infarction (new or pre-existing history)	
☐	7 - Moderate/severe liver disease	
☐	Evidence of cognitive impairment *(tick as many as relevant – only 1 point if ≥1 mental condition)* ☐ Long term mental disorder ☐ Dementia ☐ Behavioural alterations ☐ Mental disability from stroke	
☐	Proteinuria on a spot urine sample: ++ or >30 mg albumin/g creatinine ☐ Yes *(1 point)* ☐ No ☐ Don't know	

☐	Abnormal ECG (atrial fibrillation, ventricular tachycardia, other abnormal rhythm or >5 ectopics/min, changes to Q or ST waves) *(tick as many as relevant – only 1 point if ≥1 abnormality)* ☐ Acute abnormality ☐ Chronic abnormality ☐ Both chronic and acute this assessment ☐ No abnormality ☐ Don't know
☐	**Previous hospitalisation for at least one night in past year** *(only 1 point if ≥1 hospital admission)* ☐ Yes ☐ No ☐ Not documented Total No. of hospitalisations in the past year _____
☐	**Repeat ICU admission at previous hospitalisation** *(only 1 point if ≥1 ICU admission)* ☐ Yes ☐ No ICU admission at all ☐ Unknown
AND	**Evidence of frailty (Clinical Frailty score)**
☐	Rockwood >= 5 ☐ Yes *(1 point if Yes)* ☐ No Actual CFS score _____

CriSTAL score _____



Clinical Frailty Scale

1 Very Fit – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 Well – People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g. seasonally.

3 Managing Well – People whose medical problems are well controlled, but are not regularly active beyond routine walking.

4 Vulnerable – While not dependent on others for daily help, often symptoms limit activities. A common complaint is being "slowed up", and/or being tired during the day.

5 Mildly Frail – These people often have more evident slowing, and need help in high order IADLs (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 Moderately Frail – People need help with all outside activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (cuing, standby) with dressing.

7 Severely Frail – Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 Very Severely Frail – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9 Terminally Ill – Approaching the end of life. This category applies to people with a life expectancy <6 months, who are not otherwise evidently frail.

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia,** recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia,** they cannot do personal care without help.

Appendix 2

REF: Highet G, Crawford D, Murray SA, Boyd K. Development and evaluation of the Supportive and Palliative Care Indicators Tool (SPICT): a mixed-methods study. BMJ Supportive & Palliative Care. 2014;4(3):285-90. doi: 10.1136/bmjspcare-2013-000488.

Supportive and Palliative Care Indicators Tool (SPICT™)

The SPICT™ is used to help identify people whose health is deteriorating. Assess them for unmet supportive and palliative care needs. Plan care.	
Date: ___/___ /_____	**Consultancy team:**
Look for any general indicators of poor or deteriorating health.	
☐	Unplanned hospital admission(s)
☐	Performance status is poor or deteriorating, with limited reversibility. (e.g. The person stays in bed or in a chair for more than half the day
☐	Depends on others for care due to increasing physical and/or mental health problems. ☐ The person's carer needs more help and support.
☐	The person has had significant weight loss over the last few months, or remains underweight
☐	Persistent symptoms despite optimal treatment of underlying condition(s)
☐	The person (or family) asks for palliative care; chooses to reduce, stop or not have treatment; or wishes to focus on quality of life
Look for clinical indicators of one or multiple life-limiting conditions	
Cancer	
☐	Functional ability deteriorating a due to progressive cancer.
☐	Too frail for cancer treatment or treatment is for symptom control.
Dementia/frailty	
☐	Unable to dress, walk or eat without help.
☐	Eating and drinking less; difficulty with swallowing.
☐	Urinary and faecal incontinence.
☐	Not able to communicate by speaking; little social interaction.
☐	Frequent falls; fractured femur.
☐	Recurrent febrile episodes or infections; aspiration pneumonia.
Neurological disease	
☐	Progressive deterioration in physical and/or cognitive function despite optimal therapy.
☐	Speech problems with increasing difficulty communicating and/or progressive difficulty with swallowing.
☐	Recurrent aspiration pneumonia; breathless or respiratory failure.
☐	Persistent paralysis after stroke with significant loss of function and ongoing disability.

Heart/ vascular disease	
☐	Heart failure or extensive, untreatable coronary artery disease; with breathlessness or chest pain at rest or on minimal effort.
☐	Severe, inoperable peripheral vascular disease.
Respiratory disease	
☐	Severe, chronic lung disease; with breathlessness at rest or on minimal effort between exacerbations.
☐	Persistent hypoxia needing long term oxygen therapy.
☐	Has needed ventilation for respiratory failure or ventilation is contraindicated.
Kidney disease	
☐	Stage 4 or 5 chronic kidney disease (eGFR <30ml/min) with deteriorating health.
☐	Kidney failure complicating other life limiting conditions or treatments.
☐	Stopping or not starting dialysis.
Liver disease	
☐	Cirrhosis with one or more complications in the past year: • Diuretic resistant ascites • Hepatic encephalopathy • Hepatorenal syndrome • Bacterial peritonitis • Recurrent variceal bleeds
☐	Liver transplant is not possible
Other conditions	
☐	Deteriorating and at risk of dying with other conditions or complications that are not reversible; any treatment available will have a poor outcome.

Appendix 3

REF: https://www.spirit-statement.org/interventions/

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin JA, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. BMJ : British Medical Journal. 2013;346:e7586. doi: 10.1136/bmj.e7586.

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Page
Administrative information			
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	1
	2b	All items from the World Health Organization Trial Registration Data Set	1, Synopsis
Protocol version	3	Date and version identifier	1
Funding	4	Sources and types of financial, material, and other support	1-2
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	2-3
	5b	Name and contact information for the trial sponsor	Pre-amble
	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	1-3
	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)	2-3
Introduction			
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	5-6
	6b	Explanation for choice of comparators	6
Objectives	7	Specific objectives or hypotheses	6

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, noninferiority, exploratory)	6-7

Methods: Participants, interventions, and outcomes

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	8
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)	9-10
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	10-11
	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)	15
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	24-25
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	9
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, 19-23
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)	17-18
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	25
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	13

Methods: Assignment of interventions (for controlled trials)

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	15-16
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	15-16
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	15-16
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	16
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
Methods: Data collection, management, and analysis			
Data collection methods	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	16, 19-23
	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	15
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	16, 24-25
Statistical methods	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	25-30
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	29-30
	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)	29
Methods: Monitoring			
Data monitoring	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	25

	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	N/A
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	24
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	27
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)	30
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	13-14
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
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	31-32
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	N/A
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	24
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	N/A
Dissemination policy	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	32
	31b	Authorship eligibility guidelines and any intended use of professional writers	32
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	32
Appendices			
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

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.