Trials

STUDY PROTOCOL

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Boosting REsources And caregiver empowerment for Tracheostomy care at HomE (BREATHE) Study: study protocol for a stratified randomization trial

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Abstract

Background Annually, about 4000 US children undergo a tracheostomy procedure to provide a functional, safe airway. In the hospital, qualified staff monitor and address problems, but post-discharge this responsibility shifts entirely to caregivers. The stress and constant demands of caregiving for a child with a tracheostomy with or without ventilator negatively affect caregivers. The aims of the study are to relieve the burden and stress experienced by caregivers at home, improve safety and outcomes for children post-discharge, and identify facilitators and barriers to implementation of comprehensive pediatric discharge programs.

Methods The Boosting REsources and cAregiver empowerment for Tracheostomy care at HomE (BREATHE Study) is a pragmatic two-arm, randomized trial with six sites across the US. Caregivers of a child with a tracheostomy are randomized to comparator ("Trach Me Home") or intervention ("Trach Plus"). The Comparator arm is the current gold standard focusing on caregiver education, technical skill building, and case management. The Intervention arm contains all elements of the Comparator plus educational resources, social support and communication with the outpatient pediatrician. Caregivers will complete three surveys: baseline (pre-discharge), 4-week and 6-month post-discharge. Outpatient pediatricians will complete a survey to assess self-confidence in caring for a child with tracheostomy and satisfaction with discharge communication. Interviews with clinicians and staff will identify facilitators and barriers to implementation. The study will examine whether the Intervention arm leads to lower caregiver burden, lower readmission rates and higher pediatrician satisfaction than Comparator arm.

Discussion The BREATHE Study will advance our understanding of how hospitals can support caregivers with a child with a tracheostomy as they resume life, work, and family activities after discharge.

Trial registration Registered on clinicaltrials.gov (NCT06283953). February 28, 2024.

Keywords Shared decision making, Caregiver, Tracheostomy, Ventilator, Pediatrics, Discharge planning

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Administrative information

Title {1}	PCORI-IHS-2022C1-26100 Boosting resources and caregiver empowerment for tracheostomy care at home (BREATHE Study)
Trial registration {2a and 2b}	ClinicalTrials.gov # NCT06283953
Protocol version {3}	Version 2. Date 3/15/2024
Funding {4}	Funded by the Patient-Centered Outcomes Research Institute (PCORI) IHS-2022C1-26100
Author details {5a}	See title page
Name and contact information for the trial sponsor {5b}	Patient-Centered Outcomes Research Institute Program Officer: Mari Kimura; mkimura@pcori.org
Role of sponsor {5c}	The funding agreement ensured the authors' independence in designing the study, interpreting the data, writing, and publishing

Introduction

Background and rationale {6a}

A tracheostomy (trach) is a procedure where a small plastic tube is placed in the neck of children with compromised airways to provide a functional, safe airway [1]. Approximately 4000 US children undergo a trach each year, with an average age of 5 years old, and a median age of 1 year old. The length of stay after trach is usually 3 weeks or longer. Some children also require a ventilator (vent) in addition to the trach to support breathing if a child cannot breathe on their own. The length of stay is generally longer for these children due to the complexity of their health care needs. Hospital staff monitor the children closely and address any problems, but at discharge, this responsibility shifts almost entirely to the caregiver, and represents a stressful change in their role. Challenges for trach care at home include caregivers having to care for the tube itself, to identify and address incidences of bleeding and infections, and to administer emergency resuscitation in case of mucus plug formation with tube occlusion or accidental decannulation (tube falling out) to prevent life-threatening complications. These life-threatening complications occur in about 5% of cases [2]. Challenges for vent care include drop in oxygen and disengagement from the vent which are life-threatening.

Recent efforts to develop discharge planning programs have focused on management of the medical device to reduce readmissions after the child transitions to home as outcomes often focus exclusively on medical utilization. The discharge planning curricula lack support for decisions that need to be made to return to normal life. There are many practical, under-appreciated challenges that caregivers also experience after discharge to home that severely impact their ability to carry out everyday activities and the outcomes do not capture caregiver burden, distress or experience. Effective discharge communication also varies in practice from the inpatient to the outpatient care team.

Objectives {7}

The purpose of the Boosting REsources and cAregiver empowerment for Tracheostomy care at HomE (BREATHE Study) is to compare two discharge strategies to support caregivers post-discharge with both medical and nonmedical decisions about resuming life, work, and family activities, while safely caring for their child at home. The study aims are:

Aim 1: Reduce the burden on caregivers of children with tracheostomies with or without a ventilator.

- *Hypothesis 1*: Caregivers assigned to the Intervention arm will have lower scores on the Pediatric Tracheostomy Health Status Instrument (PTHSI) burden subscale at 4-week post discharge compared to those in the Comparator arm.

Aim 2: Improve the safety and outcomes for children with tracheostomies, with or without a ventilator, who are living at home by reducing complications, emergency room visits and readmissions in the 6-month following discharge.

- *Hypothesis 2*: Caregivers in the Intervention arm will have fewer trips to the emergency room and lower readmission rates compared to those in the Comparator arm.

Aim 3: Identify facilitators and barriers to implementation of the programs across six sites serving a diverse sample of families. Using mixed methods, we will track adaptations made to program components and examine fidelity to the different elements of the discharge strategies and then explore how child-, caregiver-, clinician-, and site-level factors influence outcomes.

Trial design {8}

A pragmatic two-arm, parallel group randomized trial. The trial is pragmatic in that it is interested in the extent to which these existing (not novel) interventions work in usual care, delivered by clinicians and staff (not research nurses or research coordinators). Figure 1 provides an overview of the study activities.

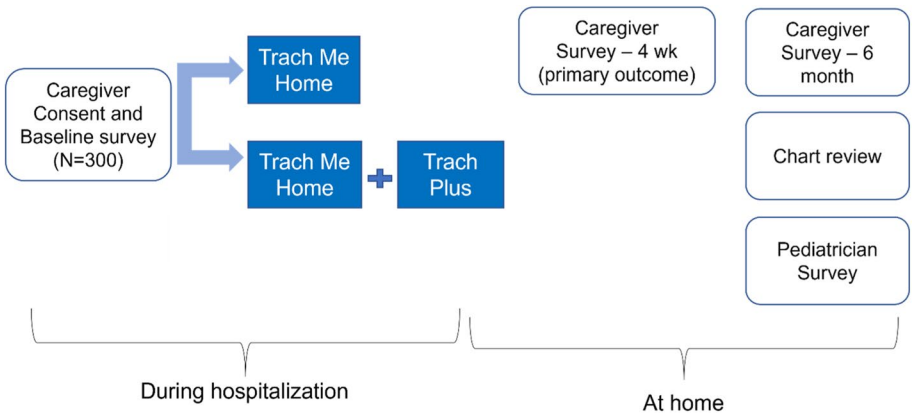

Fig. 1 Study activities and data collection

Methods: participants, interventions and outcomes

This manuscript follows the SPIRIT guidelines [3]. The underlying trial protocol follows the CONSORT guidelines [4, 5]. The trial is registered on clinicaltrials.gov (NCT06283953).

Study setting {9}

The six participating sites perform about 45 (range 32–80) pediatric trachs per year per site. Participating sites include Massachusetts General Hospital (MGH) with Mass Eye and Ear Institute (MEEI) in Boston, MA, Children's Hospital of Philadelphia (CHOP) in Philadelphia, PA, Cincinnati Children's Hospital in Cincinnati, OH, Children's National Hospital in Washington, D.C., Children's Minnesota in Minneapolis, MN and St. Paul, MN, and Rady Children's Hospital in San Diego, CA. The sites care for diverse pediatric patient populations, with estimates of about 51% from racial and/or ethnic minority populations (including about 18% Black, 23% Hispanic, 23% other race or multiracial) and about 20% non-English speaking.

Eligibility criteria {10}

The main participants will be adult primary caregivers of children with a new trach who are being discharged to home. Table 1 details the eligibility criteria for these participants. Primary care pediatricians who care for the children in the study will also be eligible to complete a short survey. Finally, peer mentors who are matched with caregivers in the study will be eligible to complete short surveys and interviews.

Who will take informed consent? {26a}

For caregivers, a member of the clinical team (e.g., physician, nurse, care manager) will introduce the study to gauge interest utilizing a study invitation letter signed by the site PIs. The research coordinator (RC) will schedule a meeting with interested caregivers and provide a study information sheet, and study educational materials created by the caregiver advisors describing the study. The RC will review the study, answer questions and obtain verbal consent.

Consent process for non-English speaking caregivers

All study recruitment materials will be translated into 3 additional languages (Spanish, Simplified Chinese-Mandarin, and Arabic) to support participation from a diverse sample of caregivers. The clinical team approaching caregivers to determine interest in the study and the research team who will obtain consent will be trained to

Table 1 Eligibility for participants

Participant	Eligible	Ineligible
Caregiver	• Lead or primary adult caregiver of infant or child (0–17 years old) with trach or is dependent on a vent • Child plans to discharge to home • Caregiver is able to read or write in English, Spanish, Mandarin, or Arabic	• Child transferred to other hospital or outside facility (and not discharged to home)* • Not planning to reside in the U.S. for at least 12 months post-discharge

*Participating sites that have "in-house" facilities where children are cared for prior to discharge home will be screened and considered for invitation to the study if they are being discharged from that clinic to home

work with Interpreter Services to support full participation of all study participants.

For pediatricians, a notification letter and information sheet will be sent with the survey. Consent will be implied with return of a completed survey.

For peer mentors, an invitation will be sent with an info sheet and a baseline survey to complete. Consent is implied with return of a survey.

For clinician and staff interviews, an invitation will be sent a with cover letter, information sheet and details about how to opt-out of the interviews if they are not interested. The research team will call or email all those who did not opt out, describe the project in detail, answer any questions about the interview, and obtain verbal consent to participate.

Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable {26b}

N/A, this trial does not involve collecting biological specimens for storage.

Interventions

Explanation for the choice of comparator {6b}

The "Trach Me Home" program is an evidence-based program that focuses on building caregiver confidence and competence. Feedback from parents and caregivers and systematic reviews of pediatric discharge programs have identified some gaps, specifically, support in the decisions about managing a child with complex needs, social support and communication between the inpatient and outpatient care teams [6–10].

Intervention description {11a}

Comparator arm

The "Trach Me Home" program is an evidence-based in-hospital program that includes caregiver education, skills training (e.g., how to change their child's trach), and case management (e.g., ordering supplies, equipment and scheduling follow-up visits) [11–13].

Intervention arm

The "Trach Plus" arm will receive the "Trach Me Home" program plus additional features: (1) caregiver education with topics such as home nursing and supply management, (2) social support via a connection with a peer mentor, and (3) individualized communication from the inpatient hospital team to the outpatient pediatrician.

Criteria for discontinuing or modifying allocated interventions {11b}

N/A, there will be no special criteria for discontinuing or modifying allocated interventions.

Strategies to improve adherence to interventions {11c}

Prior to the study launch, each site will complete a workflow template to outline how the components of the discharge programs will be implemented, by whom and how they will be documented. RCs at each site will connect with the nurse, care manager, or care team to provide a fidelity checklist that will facilitate the delivery of appropriate interventions depending on study assignment. Caregivers will self-report use of the educational components and interactions with peer mentor (as appropriate). Pediatricians will self-report receipt of discharge communication.

Relevant concomitant care and interventions that are permitted or prohibited during the trial {11d}

The trial is enrolling caregivers of children with tracheostomies. The medical care and interventions for the children will not be impacted or in any way restricted by the participation or not of their caregiver in the study. Access to the caregiver video education developed as part of the study will be restricted to those in the assigned study arm. The peer mentor intervention will be available to all in the assigned arm and to those in the other arm only upon request. For example, if a parent asks to be connected to another parent, the site will be able to connect them regardless of study assignment.

Provisions for post-trial care {30}

Not applicable. There is no anticipated harm and compensation for trial participation.

Outcomes {12}

The caregiver partners collaborating on this study were involved in the study design and identified important outcomes to assess. The primary outcome is caregiver burden self-reported by caregiver participants. Table 2 includes details on the measures used to assess primary and secondary outcomes.

The caregiver surveys includes the caregiver burden subscale of the Pediatric Tracheostomy Health Status Instrument (PTHSI) survey [14, 15], adapted Medical Complications Associated with Tracheostomy (MCATs), psychosocial measures PROMIS Anxiety [16–18], self-efficacy [19], social support [20, 21], post traumatic growth [22], financial toxicity [23]), decision making (shared decision making, decisional conflict and decision regret), use of interventions, and caregiver and child demographics and characteristics.

The pediatrician survey includes items adapted from prior studies that assess timeliness, relevance, and completeness of communication as well as their ability to ask questions or get support as needed and satisfaction with discharge communication. The survey was pretested in

Table 2 Description, source, and timing of the primary and secondary study outcomes

Primary or secondary	Name of outcome	Specific measure to be used	Survey timepoints
Primary	Caregiver burden subscale	Subscale of the Caregiver-reported Pediatric Tracheostomy Health Status Instrument (PTHSI) survey [14, 15]	4-week
Secondary	Caregiver burden subscale	Subscale of the Caregiver-reported PTHSI	6-month
Secondary	Medical utilization	Modified subset of the Medical Complications Associated with pediatric Tracheostomy scale (MCAT)	6-month
Secondary	Medical utilization	Modified subset of the Medical Complications Associated with pediatric Tracheostomy scale (MCAT)	4-week
Secondary	Readmission rates	Chart review will calculate the rate of ED visits and readmissions	6-month
Exploratory	Number of Readmissions	Chart review will calculate the number of readmissions and ED visits	6-month
Secondary	Frequency of pediatrician communication	EMR and pediatrician reported communication with pediatrician prior to and shortly after discharge	6-month
Secondary	Pediatrician satisfaction	Pediatrician reported Satisfaction with discharge communication items	6-month

cognitive interviews with four pediatricians and was pilot tested with 30 pediatricians prior to study launch [24–27]. Figure 2 provides details of when other assessments will be collected.

Figure 3 illustrates the conceptual framework that links the interventions to the outcomes, and provides rationale for the inclusion of different measures, such as caregiver social support and anxiety.

Participant timeline {13}

We plan to enroll caregivers over 30 months, from April 2024 to October 2026.

Sample size {14}

Our target enrollment is 300 caregivers over 30 months, so 300 completed baseline surveys (T0). We estimate a survey completion rate of 85% at the 4-week (T1) and 80% at the 6-month timepoints, for a sample size of 256 (T1) and 240 (T2). The CONSORT diagram has estimates for enrollment (see Fig. 4).

For the primary outcome, caregiver burden as measured by the PTHSI, the study will have 80% power to detect a small, standardized effect size (Cohen's *d*) of 0.35 at T1 and 0.36 at T2 with a two-sided significance level of 0.05. Our preliminary data show that the standard deviation is 5.8 for PTHSI. Thus, the study will have 80% power to detect a mean difference of 2.0 in PTHSI at T1 (clinically meaningful difference in the caregiver burden domain of the PTHSI scale is about 8).

For the secondary outcome, 6-month readmission rates, the study will have 80% power to detect a 12% reduction (20% vs. 8%) with a sample size of 300. National studies suggest that 30-day unplanned all cause readmission rates for high severity diagnoses (like trachs) are 20% in high rate hospitals and 12.7% in low rate hospitals [28].

For the pediatrician 6-month survey, we expect a 60% response rate for a total of 180 surveys. We will have 80% power to detect a standardized effect size of 0.42 with two-sided significance level of 0.05. The HTE analyses will be exploratory in nature; therefore, we did not factor the subgroups in the sample size consideration.

Recruitment {15}

The clinical team will be screening all tracheostomy procedures to identify eligible participants for the study. When an eligible caregiver is identified, the clinic team will briefly introduce the study utilizing the invitation letter signed by the site PIs and if the caregiver is interested, will notify the study staff who will set up a time to meet with the caregiver to discuss in more detail. The research coordinator will meet with the eligible caregiver in the hospital and provide a study information sheet, and study educational materials created by the caregiver advisors describing the study. The RC will review the study, answer questions, and obtain verbal consent. During the consent process, the caregivers will be told that the study is comparing different approaches to support caregivers of children with tracheostomy after discharge, but they will not be given details about the components in each arm. If they are not sure about participating, caregivers will be given a copy of the all the study information materials to take home along with a business card of the research coordinator to call if they have any additional questions. If the caregiver declines to join the study, the research coordinator will be trained to ask for a reason and document it in the study database.

Methods to enhance enrollment of diverse populations

Caregiver advisors who have experience with trachs are serving as advisors for the study and have reviewed and participated in the design of the study, development of

	Study Period				
	Enrollment	Allocation	Post-Allocation		
TIMEPOINT	Pre-randomization	Pre-discharge	Baseline (pre-discharge)	4-week (post-discharge)	6-month (post-discharge)
ENROLLMENT					
Eligibility screen	x				
Consent	x				
RANDOMIZATION:					
Randomization to study arm		x			
INTERVENTIONS:					
'Trach Me Home'			x		
'Trach Me Home' and 'Trach Plus'			x	x	x
ASSESSMENTS (CAREGIVER):					
Child and caregiver demographics			x		x
Child medical history and co-morbidities			x		
Caregiver burden				x	x
Medical utilization				x	x
PROMIS anxiety			x	x	x
Self-efficacy			x	x	x
Social support			x		x
Post-traumatic growth				x	x
Financial toxicity					x
Shared decision making			x		
Decisional conflict			x		
Decision regret					x
Use of interventions				x	x
ASSESSMENTS (PEDIATRICIAN):					
Pediatrician demographics					x
Frequency of pediatrician communication					x
Pediatrician satisfaction					x
ASSESSMENTS (EMR):					
Child and caregiver demographics	x				
Child medical history and co-morbidities	x				
Intervention Fidelity Checklist				x	x
Readmission rates					x
Number of readmissions					x

Fig. 2 SPIRIT figure for study assessments

the recruitment materials, and selection of study outcomes. We have a diverse group of caregiver advisors including two whose primary language in not English. This will be particularly helpful for participants who speak languages other than English.

Assignment of interventions: Allocation

Sequence generation {16a}

Study statistician will create computer-generated randomization sequences using block randomization with varying block sizes, stratified by site and complexity level. Complexity level is defined as (1) low complexity (all ages), (2) high complexity and age < 1, and (3) high complexity and age ≥ 1. After caregivers give consent to the study, the RC will enter the information into the study database and will obtain the random assignment from REDCap. Analyses will account for all stratifying factors.

Concealment mechanism {16b}

The sequences will be created centrally by the study statistician and embedded into a REDCap database. RCs will learn of the assignment only after a caregiver has agreed to enroll into the study, to provide allocation concealment.

Implementation {16c}

Once assigned to an arm, the RC will connect with the nurse, case manager, and/or care team to confirm

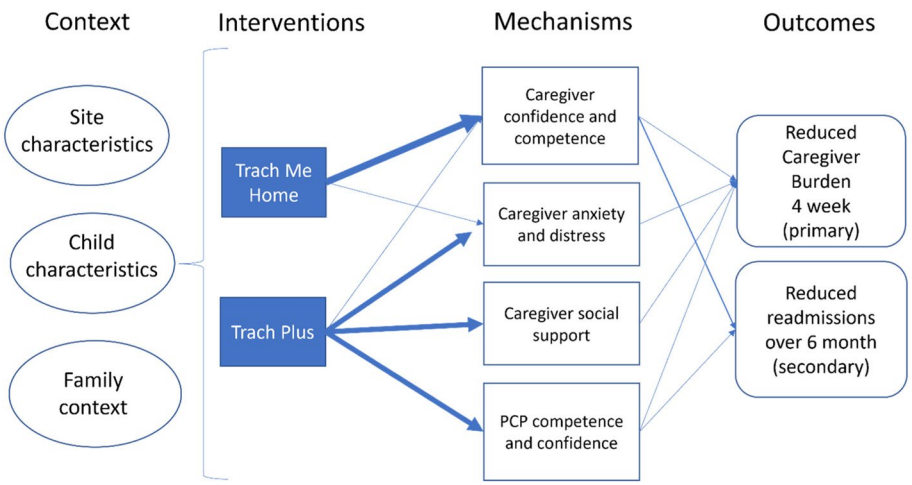

Fig. 3 Conceptual framework for proposed study

participants' study assignment and facilitate delivery of appropriate interventions.

Changes to intervention allocation

There are no established criteria for discontinuing or modifying the allocated intervention for study participants due to the low-risk nature of the study. Subjects are free to withdraw from the study at any time for any reason.

Assignment of interventions: Blinding

Who will be blinded {17a}

Blinding of clinical team delivering the interventions and of caregiver participants receiving the interventions is not possible for this pragmatic study. However, caregivers will not be given details about what is included in the other study arm. Further, we will minimize evaluator bias in outcome assessment by encouraging participants complete surveys electronically and by centralizing data entry of paper surveys at the coordinating center where staff entering surveys will be blinded to assignment. Finally, outcome assessors collecting data on readmissions rates and ED visits will be blinded to study assignment.

Procedure for unblinding if needed {17b}

N/A, unblinding will not occur as the clinical team and participants are aware of the interventions.

Data collection and management

Plans for assessment and collection of outcomes {18a}

Caregiver data collection

The main data sources are caregiver and pediatrician surveys, and the EHR. Caregivers will complete three surveys as part of the study. Caregivers will be asked to complete a baseline survey (T0) prior to discharge. For the baseline survey, the RC will provide a link to the baseline survey along with $10 (Clincard or gift card depending on the site policy). The RC will be available to support the caregiver to complete the survey on an iPad in clinic if needed. For the 4-week and 6-month surveys, the RC will send the survey link to the enrolled caregivers along with $10 (Clincard, or gift card) using their preferred method of contact. The RC will make up to three reminder calls and send three reminder texts or emails. The online survey will follow best practices for web survey design to minimize measurement error and promote high response rates.

Pediatrician data collection

About 6 months post-discharge the MGH research team will survey the pediatricians for each caregiver participant. The pediatricians will be sent an invitation letter, survey, and a $20 gift card. The study staff will attempt up to three reminder calls and will send up to four reminder emails or one reminder mailing.

Peer mentor data collection

Peer mentors will complete a survey after initial training. The survey collects demographic data as well as their experience and skills to be a peer mentor. The peer mentors will be emailed a cover letter, information sheet, and survey. Research staff will follow up with three emails and a phone call reminder. Annually, we will send a survey to ask peer mentors to reflect on their experience in the past year to assess successes and challenges to continue to support their efforts. A survey link will be emailed to them to complete with up to 3 email reminders. They will be provided $20 for completion of the annual survey.

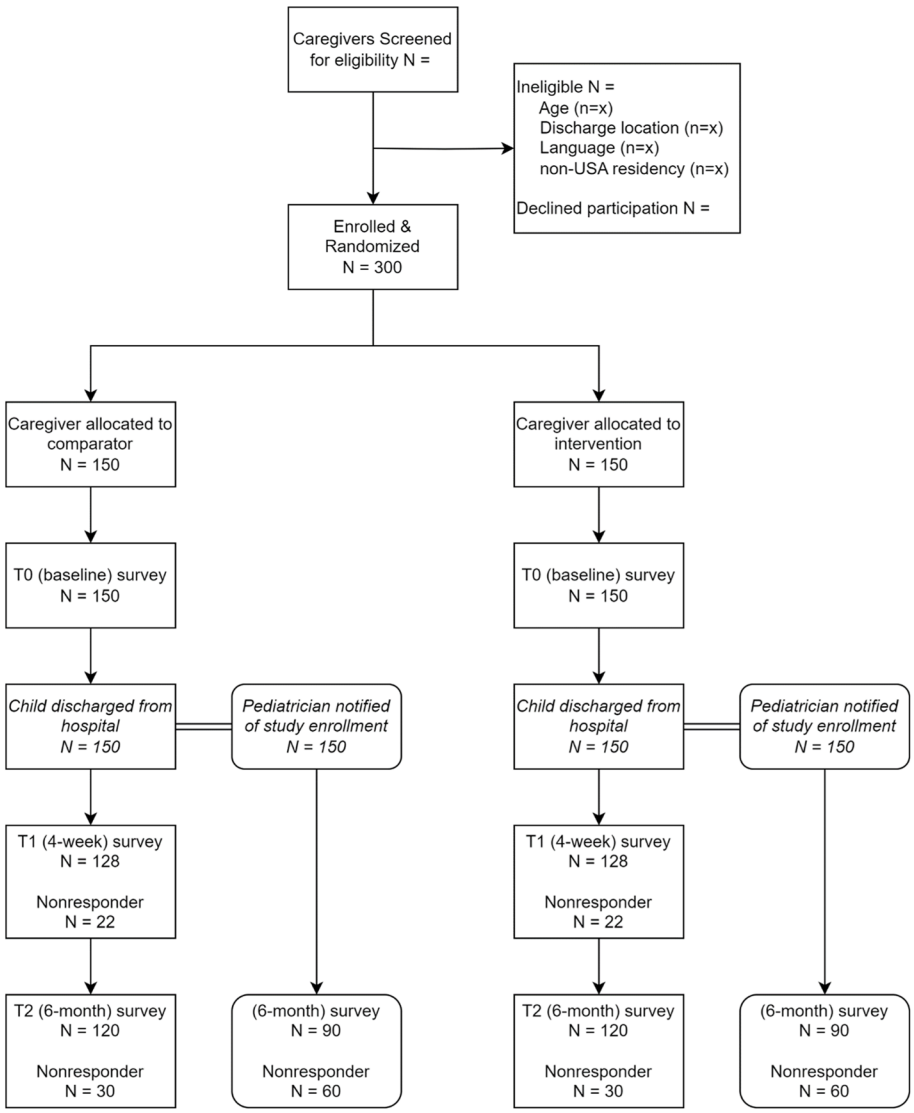

Fig. 4 CONSORT diagram with estimates for enrollment and completion

Other data collection

Chart review

Study staff will conduct chart review at 6 months to assess medical complications, unplanned visits to specialists, emergency room visits, and readmissions in the 6 months following discharge. Research coordinators will be trained to abstract data consistently across sites using standardized definitions. The data will be abstracted into a REDCap database that does not include information about study assignment.

Qualitative interviews

We will conduct 30-min qualitative interviews via phone or Zoom. We will invite key informants at each site to explore barriers and resources required for successful implementation of the program by health systems. The interviews will follow a semi-structured interview guide and will be audio-recorded and professionally transcribed for analysis. We will enroll a selected subset of caregiver participants who have completed the 6-month follow-up activities ($n=5$ per site) and who indicated that they would be interested in sharing experiences. They will be provided $20 incentive for completion of the interview. A subset of clinicians, peer mentors, core staff from each site ($n=5$ per site), and pediatricians ($n=5$ per site) will also be selected to explore experiences, barriers, and resources required for successful implementation of the programs by health systems. Clinicians and staff

will receive a $50 incentive for completing the interview. Pediatricians and peer mentors will receive $30 incentive for completing the interview.

Plans to promote participant retention and complete follow-up {18b}

A communications workgroup (comprised of study co-investigators, staff, and caregiver study advisors) will be responsible for organizing and creating content for the participant communication. We plan to send a study newsletter to participating caregivers every 6 months to provide updates, share news and insights, and highlight stories from our caregiver and stakeholder partners. While enrollment is ongoing, the newsletter will not include any details on interventions or findings, rather, will focus on enrollment targets and stories from sites to maintain and build connection with participants. In addition to providing a mechanism to share results with participants, the newsletters will also help to increase retention and completion of the follow-up surveys. The final newsletter will include results from the study as well as plans for dissemination and wider implementation.

We will ask study participants, upon consent into the study, whether they would like to be put on the distribution list for the study newsletters. We will also ask them to indicate their preferred method of contact (text, email, or mail). Finally, all newsletters and study results will be posted to the study webpage within the Health Decision Sciences Center (HDSC) website as soon as they are available. Members of our team will work closely with our caregiver partners and external experts (graphic and web designers) to create the content and make sure that it is engaging.

Data management {19}

The data sources are surveys (caregiver, pediatrician, and peer mentor), interviews (audio files and transcripts), and EHR data extraction and chart review during enrollment and up to 6 months post-charge. The MGH research team will create REDCap projects to manage screening, randomization, enrollment, survey tracking, and chart review across the 6 sites. Data dictionaries, variable naming, and coding conventions will be shared to ensure consistency of data collection. Codebooks will be created for each survey with consistent labeling of variables. The data from surveys and chart review will be entered into REDCap (web-based, HIPAA compliant system) [29].

For any surveys that are not completed online, sites will send scanned copies of the survey to MGH coordinating center. MGH study staff will be trained and double code 10 of each of the surveys to identify any issues or potential errors in coding. Periodically, 10% of the data will be double coded to ensure high-quality data entry. In addition, staff will check range of data values and missing data. Paper surveys will be scanned and stored electronically. Databases will be backed up weekly during the data collection phase.

Confidentiality {27}

To address privacy and confidentiality issues, the surveys will be identified by code number only. Study papers (screeners, notes, surveys) that have been scanned or entered into the REDCap database will be disposed of in the confidential shredder. All caregiver (and child) identifiers will be kept in password-protected files on password-protected MGB servers for the MGH team and the other participating sites. The analytic database with outcomes data will not contain any identifying information and will be coded by unique study ID number only.

Biological specimens {33}

N/A, see above 26b, there will be no biological specimens collected.

Statistical methods

Statistical methods for primary and secondary outcomes {20a}

The hypotheses will be evaluated using an intention-to-treat approach, with no special allowance for non-compliance or nonadherence. A two-sample *t*-test or a Wilcoxon rank sum test (whichever is more appropriate) will be used to compare the PTHSI score at 4-week and Medical Complications score at 6 months between study arms. The primary analysis (Aim 1) will be limited to subjects who completed surveys. To assess the potential selection bias, responders and non-responders will be compared between study arms. As a sensitivity analysis, we will use the multiple imputation approach to assess the impact from missing data. A chi-square test will be used to compare the readmission rate at 6 months (Aim 3). Readmission in following discharge will be assessed through chart review and, therefore, is not subject to missing data.

For outcomes assessed from multiple time points (e.g., PROMIS anxiety), repeated measures analysis with the generalized estimating equations (GEE) approach will be used to compare between study arms accounting for the correlated data structure over time. The models will include time, time and group interaction, randomization stratifying factors (child age, medical complexity, site), and other known predictors of outcomes including both child characteristics (gender, race/ethnicity, length of stay, insurance type and medical conditions/comorbidities) and caregiver characteristics (age, gender, race/ethnicity, primary language).

With only three time points, we will model time as a categorical variable (baseline, 4-week, 6-month post discharge) and use an unstructured correlation matrix to allow for flexibility.

For Aim 3, we will collect and analyze quantitative and qualitative data to help interpret the quantitative findings from Aims 1 and 2 (Fig. 1). The explanatory analyses will use an iterative process analyzing both the quantitative data and the qualitative data parallelly. Using the conceptual framework listed in Fig. 3, we will examine the relationship (1) between intervention and outcomes, (2) between intervention and mechanism variables, and (3) between mechanism variables and outcomes. We will decompose the total effect into indirect and direct effects to quantify the proportion of intervention effects that is facilitated through the mechanism variables. We will start with the three-step approach described by Baron and Kenny [30] and incorporate the new advances in mediation analysis [31] to allow for more flexible models such as including interactions and nonlinearities. Using the qualitative data from interviews with clinicians, caregiver participants, and pediatricians, we will identify key themes including resources, barriers, and strategies. The mixing will take place at the interpretation stage where we will seek to use the qualitative results to shed light on surprising or counterintuitive findings, help generate hypotheses for mechanisms by which some sites or some populations may have more successful outcomes than others, and to explore opportunities for strategies to promote widespread adoption.

Interim analyses {21b}

N/A, there are no stopping rules or interim analyses for this study.

Methods for additional analyses (e.g., subgroup analyses) {20b}

Heterogeneity analyses

As an exploratory analysis, we will examine the heterogeneity of treatment effect (HTE) among different subgroups. Studies show that social context, transitional care, caregiver education, and other elements delivered post discharge will impact readmission rates [32]. Other factors that might potentially impact the treatment effect include child age, length of stay, insurance type, number of chronic conditions (use pediatric complex chronic condition classification system v2) [33], and study site. We will conduct these pre-specified HTE analyses by testing the interaction between study arm and subgroups and report the effect estimates with 95% confidence level within each subgroup.

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}

Non-adherence

The hypotheses will be evaluated using an intention-to-treat approach, with no special allowance for noncompliance or nonadherence.

Missing data

The primary outcome relies on participant survey responses and several steps have been included to ensure the quality of data and to prevent missing data. First, surveys will be pre-tested with our caregiver and stakeholder partners prior to launching the study. The pre-test will identify any issues with instructions, wording of items, layout of items and responses, instructions, and delivery mechanism. In addition, we will use this pretest as an opportunity to train research coordinators and confirm accuracy and completeness of codebooks, and data entry protocol. Second, we have a structured protocol that follows a modified Dillman approach, with incentives and multiple reminders to minimize missing data for survey outcomes [34, 35]. Third, caregiver participation does not require in-person study visits which may be very difficult for caregivers to manage; rather, we will enable participants to complete surveys electronically (via computer or smartphone) or to have it administered by the research coordinator over the phone (with interpreter support as needed). Finally, we will put the primary and key secondary outcomes first in the survey in order to further promote completion. While we expect these strategies to ensure high-quality data collection, we also recognize that with the severity of the situation, burden on the caregivers and vulnerability of the sample, will likely result in some missing data. Our estimates are 15% for the 4-week survey and 20% for the 6-month surveys and we will handle this in the analytic plan. Of note, we will survey all enrolled participants at 6 months, regardless of completion status of 4-week survey.

As a sensitivity analysis, we will use the multiple imputation approach to assess the impact from missing data.

Plans to give access to the full protocol, participant-level data and statistical code {31c}

The full protocol, de-identified data (where possible), and statistical code will be included in a public registry within 12 months of completion of the project.

Oversight and monitoring

Composition of the coordinating center and trial steering committee {5d}

The coordinating center study team is made up of the co-PIs as well as the nurse co-investigator, project manager, data manager, and statistician from MGH. The team

is responsible for the overall organization, data management, and implementation of the minimal risk trial across sites. There is not an independent trial steering committee. The responsibility for the supervision, adherence to the protocol and safety, and rests with the co-PIs. The study has an external stakeholder advisory group that includes parent partners, pediatricians, quality and safety experts, hospital and health system leadership, and representatives from professional societies and consumer organizations. The advisory group meets quarterly and provides advice and direction to the study team.

Composition of the data monitoring committee, its role and reporting structure {21a}

The trial is minimal risk and the data and safety monitoring plan (DSMP) is commensurate with the potential risk level. There is not an outside DSM committee, the two co-PIs and the statistician are responsible for implementing the DSMP.

Adverse event reporting and harms {22}

The RCs and project manager will notify the PI about any serious or moderate potential adverse events (AEs) immediately and any minor or potential ones at regular meetings. The Co-PIs will review AEs individually real-time and in aggregate on a regular basis at team meetings. The Co-PIs and co-investigators will review potentially serious adverse events (SAEs) as soon as they are discovered. The Co-PIs will ensure all protocol deviations, AEs, and SAEs are reported to the IRB according to the standard requirements.

Frequency and plans for auditing trial conduct {23}

The coordinating center will review site-level data monthly in order to confirm study activities are proceeding according to the protocol and to generate monthly CONSORT reports once enrollment begins. The coordinating center will work with sites to identify any protocol deviations and will develop a remediation plan to prevent deviations in the future.

Plans for communicating important protocol amendments to relevant parties (e.g., trial participants, ethical committees) {25}

Drs. Hartnick and Sepucha are responsible for assuring that caregiver, peer mentor, and pediatrician participants are adequately informed prior to engaging in any research procedures, that all participants meet eligibility criteria, and that the study is conducted according to the IRB-approved research plan. Study data will be accessible at all times for the Co-PIs to review. The Co-PIs will examine study conduct including enrollment, accrual, drop-outs, and protocol deviations monthly with the staff at each site. The MGH project team will meet monthly with research staff across the sites and will review administration of the protocol and documentation in REDCap, including reminder phone calls to participants, and participant survey administration and completion rates.

Dissemination plans {31a}

In addition to tradition dissemination of results via peer review manuscripts and national meetings, we will also make the intervention components available through our MGH Health Decision Sciences website and the Careways website. We will include a guide to support implementation with sample workflows from our participating sites. A communications workgroup will organize and create content (e.g., newsletter) for the participant communication throughout the study duration. All newsletters and study results will be posted to the study webpage within the HDSC website. Once the results are available, we will engage our parent partners to hold a free webinar, targeted to parent/caregiver participants, to present the results, highlight key findings, and allow participants to ask questions and provide feedback. To support the communication of results to caregiver community, we will work with a graphic designer to create infographics and messaging strategies.

Discussion

The results of the BREATHE study will have immediate implications for management of children with trachs as these children (and their parents and caregivers) transition from the intensive care units to hospital wards and then, to home. The study will evaluate effectiveness of communication and educational support systems between parents, specialists, and primary care clinicians. Guided by a diverse advisory group (particularly parent/caregivers and those with quality improvement and health care system innovation experience), we designed the intervention components to be scalable and accessible to sites and caregiver populations. For example, we have training materials and protocols for the peer mentors and education videos and programming available via web links and QR codes. Further, a deliverable from the work in Aim 3 will be a training guide that will highlight key resources needed for successful implementation, common barriers that sites may face and proven strategies to overcome those barriers that will greatly facilitate adoption into clinical practice.

Limitations

There are several potential limitations of this study. First, the clinical team delivering the intervention and caregiver participants receiving the interventions are not blinded. Second, despite the stratified randomization, there may

be an imbalance in child characteristics across arms. However, it is not clear whether or how that may impact the results, and if necessary, we will be able to examine child and caregiver characteristics and adjust for them in the statistical analysis. Third, contamination is possible as study interventions may influence "usual care", e.g., the in-patient care team starts to engage outpatient pediatricians more regularly for all patients, which may diminish the magnitude of the treatment effect in the intervention arm. We will track fidelity to the components for each arm and will document if caregivers in the Comparator arm received study interventions.

Trial status

Study is enrolling participants. Fifteen participants have enrolled to date. Protocol version 2. 03/19/2024. Target enrollment to run through October 2026.

Abbreviations

Trach	Tracheostomy
RC	Research coordinator
Vent	Ventilator
MCAT	Medical Complications Associated with Tracheostomy
PTHSI	Pediatric Tracheostomy Health Status Instrument
HTE	Heterogeneity of the treatment
EMR	Electronic medical record

Acknowledgements
N/a.

Authors' contributions {31b}
All authors read and approved the final manuscript. KS: conceptualization, methodology, investigation, resources, writing-original draft, writing-reviewing and editing, visualization, supervision, project administration, funding acquisition. KC: conceptualization, methodology, investigation, writing-original draft, writing-reviewing and editing, visualization, supervision project administration, funding acquisition. LL: investigation, resources, writing-reviewing and editing, supervision, project administration. YC: investigation, resources, writing-reviewing and editing, project administration. HV: resources, writing-reviewing and editing, supervision, project administration. MB: investigation, resources, writing-reviewing and editing, supervision, project administration. SB: investigation, resources, writing-reviewing and editing, supervision, project administration. JC: investigation, resources, writing-reviewing and editing, supervision, project administration. SC: investigation, resources, writing-reviewing and editing, supervision, project administration. JG: investigation, resources, writing-reviewing and editing, supervision, project administration. TG: investigation, resources, writing-reviewing and editing, supervision, project administration. HGM: investigation, resources, writing-reviewing and editing, supervision, project administration. LJ: investigation, resources, writing-reviewing and editing, supervision, project administration. ADLJ: investigation, resources, writing-reviewing and editing, supervision, project administration. JO: investigation, resources, writing-reviewing and editing, supervision, project administration. RCP: investigation, resources, writing-reviewing and editing, supervision, project administration. AR: investigation, resources, writing-reviewing and editing, supervision, project administration. SR: investigation, resources, writing-reviewing and editing, supervision, project administration. LS: conceptualization, methodology, investigation, writing-original draft, writing-reviewing and editing, project administration, funding acquisition. MS: investigation, resources, writing-reviewing and editing, supervision, project administration. MT: investigation, resources, writing-reviewing and editing, supervision, project administration. MW: investigation, resources, writing-reviewing and editing, supervision, project administration. KW: investigation, resources, writing-reviewing and editing, supervision, project administration. PY: investigation, resources, writing-reviewing and editing, supervision, project administration. HZ: investigation, resources, writing-reviewing and editing, supervision, project administration.CH: conceptualization, methodology, investigation, resources, writing-original draft, writing-reviewing and editing, visualization, supervision, funding acquisition.

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Data availability {29}
The full protocol, de-identified data (where possible), and statistical code will be included in a public registry within 12 months of completion of the project.

Declarations

Ethics approval and consent to participate {24}
Ethical approval for the study was given by the Mass General Brigham (MGB) Institutional Review Board (IRB). The external sites are approved to rely on the review and approval of the MGB IRB. Participants will give verbal consent to the study.

Consent for publication {32}
Not applicable, no identifying images or other personal or clinical details of participants are presented here or will be presented in reports of the trial results. The participant information materials are available from the corresponding author on request.

Competing interests {28}
KS reports grants from Patient Centered Outcomes Research Institute (PCORI), during the conduct of the study and KS developed the Shared Decision Making Process scale (copyright Massachusetts General Hospital) that is being used as an outcome measure in the study. LS has received payment for expert witness consultation from the US Department of Justice on medical malpractice cases. LS receives research funding from PCORI to conduct studies on shared decision making between patients and clinicians.

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