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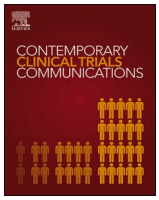

# Tracking activities and adaptations in a multi-site stepped wedge pragmatic trial of a cancer symptom management intervention

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ABSTRACT

*Background:* Pragmatic trials may need to adapt interventions to enhance local fit, and adaptation tracking is critical to evaluation. This study describes the tracking approach for a multisite, stepped-wedge hybrid pragmatic trial testing implementation and effectiveness of a cancer symptom management intervention.
*Methods:* Study activities were documented in a spreadsheet by date and category. Intervention adaptations were tracked across multiple workgroups in a database structured around the Framework for Reporting Adaptations and Modifications-Expanded (FRAME) domains, e.g., reasons for change. Implementation strategies were tracked longitudinally and by cluster in a database using the Longitudinal Implementation Strategy Tracking System (LISTS) method. A logic model was created at the end of the study to describe core intervention components and implementation strategies with dates of adaptations.
*Results:* Between January 2019 and January 2023, 187 study activities were documented. Most intervention activities took place early, but there were important intervention refinements during the course of the trial, including the expansion of interventionist roles to add two new disciplines. Eleven intervention adaptations were documented. Most were unplanned and aimed at improving fit or increasing engagement. Thirty-three implementation strategies were documented, the largest number of which were related to educating stakeholders. Most (but not all) component and strategy additions were consistent with the mechanisms of change as hypothesized at trial launch.
*Conclusions:* A multifaceted approach to adaptation tracking, combined with a logic model, supported identification of meaningful changes for use in evaluation, but further work is needed to minimize burden and ensure robust and practical systems that inform both evaluation and timely decision-making.
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## 1. Background

Implementation science is the study of methods to facilitate the

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uptake of evidence-based practices (EBPs) or interventions, and implementation strategies are things done to support implementation success [1–4]. Hybrid trials are designed to assess both intervention effectiveness and implementation strategies [5,6], where the relative emphasis on effectiveness outcomes takes into consideration whether the intervention needs to be adapted for use in new settings or with new populations [7].

**List of abbreviations**

| | |
|---|---|
| **CFIR** | Consolidated Framework for Implementation Research |
| **E2C2** | Enhanced, EHR-facilitated Cancer symptom Control |
| **EBP** | evidence-based practice |
| **ePROM** | electronic patient-reported outcome measure |
| **FRAME** | Framework for Reporting Adaptations and Modifications-Expanded |
| **FRAME-IS** | Framework for Reporting Adaptations and Modifications to Evidence-based Implementation Strategies |
| **IMPACT** | Improving the Management of symPtoms during And following Cancer Treatment |
| **IRLM** | Implementation Research Logic Model |
| **LISTS** | Longitudinal Implementation Strategy Tracking System |
| **REDCap** | Remote Electronic Data Capture |
| **SCM** | Symptom Care Manager |

In conventional randomized clinical trials, consistent delivery of core intervention components is critical for internal validity and inferring intervention effectiveness [8–10]. If the intervention is not delivered as intended, it is difficult to attribute changes in outcomes to the intervention [11]. Likewise, if core intervention components drift over time, the strength of intervention effects may change. Therefore, intervention adaptations are generally avoided, made only after careful consideration of potential impact, and carefully tracked for use in the evaluation. Logic models are tools for defining an intervention's inputs, activities, and outcomes, as well as the underlying theory of change that connects them. By explicating how a program works, they can be used to identify its core components [12,13]. The Implementation Research Logic Model (IRLM) was developed to similarly guide the logic of implementation strategies and mechanisms of change between strategies and implementation outcomes [14].

In contrast to conventional randomized clinical trials, hybrid pragmatic clinical trials that test the effectiveness of EBPs in real-world settings may need to adapt interventions to enhance their fit within local contexts, either when designing the trial or in response to unanticipated barriers, opportunities, and preferences identified during the trial. When the intervention is deployed across multiple sites over time (e.g., in stepped wedge cluster randomized trials), it becomes especially crucial for study teams to preserve core intervention components and track the type, reach, and timing of adaptations to ensure they are made to enhance intervention or implementation fit and are not the result of intervention drift, random occurrence, or personnel or site idiosyncrasies.

There are several approaches for tracking intervention and implementation strategy adaptations, ranging from activity logs to more complex databases for cataloging a number of aspects of the adaptation, including reasons for changes [14–18]. The combination of logic models and adaptation tracking may provide a useful way to capture the core components of the program and implementation plan at various points in time. That documentation may be used in evaluation of intervention effectiveness and implementation outcomes. Description of reasons for adaptations may also inform future scale-up or challenges in transferring a program to new settings.

This paper reports our study team's experience using logic models and adaptation tracking tools while deploying a hybrid pragmatic clinical trial of an EHR-enabled cancer symptom management intervention. The objectives of the different tools used in this study were to: 1) assess the breadth of study activities; 2) evaluate types of adaptations and reasons for them; and 3) document intervention components and implementation strategies to facilitate evaluation.

## 2. Methods

### 2.1. Study setting and intervention

The parent study, the Enhanced, EHR-facilitated Cancer symptom Control trial (E2C2), took place at an academic medical center and affiliated community health system in the Upper Midwest U.S., and was a hybrid type 2 cluster-randomized pragmatic trial of an EHR-enabled cancer symptom management intervention for patients experiencing symptoms across the cancer continuum: sleep interference, pain, physical function loss, anxiety, depression, and energy deficit (fatigue) (SPPADE) [19,20]. The E2C2 trial was conducted as part of a consortium of a coordinating center and three research centers. Each tested the use of EHR-embedded symptom management interventions using electronic patient-reported outcome measures (ePROMs) to assess and address SPPADE symptoms as part of multi-modal, EHR-based systems in ambulatory oncology care settings. The Improving the Management of symPtoms during And following Cancer Treatment (IMPACT) Consortium was funded by the Cancer Moonshot℠.

The intervention was based on a robustly validated collaborative care model and targeted patients and clinical care teams. It included three components, as designed for trial launch: 1) telephonic support by nurse symptom care managers (SCMs) for patients who reported severe symptom intensity on SPPADE ePROMs, using evidence-based algorithms and scripts; 2) patient self-management education materials for each SPPADE symptom delivered electronically (portal or website) or via mail for patients with at least moderate symptom burden (4–6/10); and 3) EHR decision support tools for clinicians whose patients reported severe symptom burden on ePROMs (≥7/10). For patients, mechanisms of change were related to increased knowledge and self-efficacy for symptom self-management, and targeted outcomes included adherence to self-management recommendations and reduced symptom burden. For care teams, patient's symptom reports and corresponding guideline-recommended treatment information in the EHR were expected to increase clinician efficiency of symptom identification and knowledge of evidence-based symptom management approaches.

### 2.2. Study design

The intervention was deployed to clusters representing specialty cancer tumor groups at the high-volume academic medical center and regional community oncology locations in the affiliated health system in five steps, paced every eight months between October 2019 (go live for the first step) and June 2022 (go live for the fifth step), as shown in Fig. 1. Trial oversight and intervention decision-making were conducted by a steering committee and six workgroups, including an implementation workgroup and a data management workgroup. The trial was approved by the Mayo Clinic Institutional Review Board (IRB #18–007779).

### 2.3. Data collection

There were multiple data sources and systems for tracking data, as shown in Fig. 2. While some systems were built de novo for this study, others leveraged existing methods and frameworks from implementation science that have been developed for purposes similar to those in this study: to track intervention changes, to track implementation strategies and changes, and to elaborate program activities and theories of

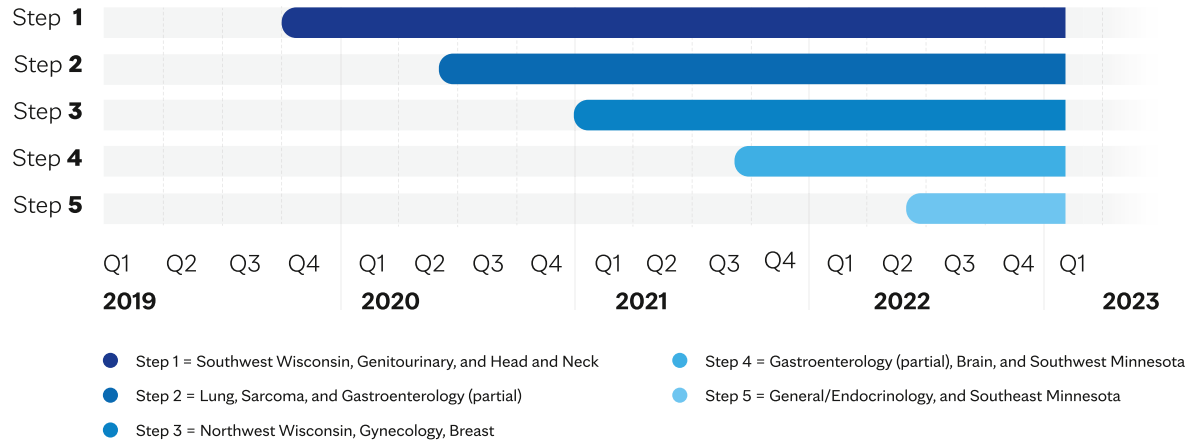


**Fig. 1.** Timeline for cluster-randomized stepped-wedge design: Clusters were randomized to intervention start in five steps. Gray indicates the pre-implementation and usual care periods when patient-reported outcome measures were being administered but there was no patient intervention based on reported symptom scores. Blue indicates the intervention period when symptom support and self-management education was offered to patients based on symptom scores, and providers received notifications of patients reporting high symptom burden. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

change to identify core intervention components and strategies.

First, the project manager and coordinator team collected a list of study-related activities from workgroup documents and meetings weekly, and the implementation workgroup categorized and tracked them in an Excel spreadsheet by date. Categories were first developed to distinguish operational activities, engagement activities, and research and evaluation activities, based on the expectation that research and evaluation activities would be most useful for evaluating outcomes at the end of the trial. As more activities were collected, the system was refined (e.g., disaggregating patient engagement and practice engagement), and previous activities were reclassified as needed. Subcategories were also added. The last subcategory to be added was for operational activities related to the COVID-19 pandemic. There were eight final categories: EHR Build and Implementation, Intervention, Operations, Patient Education Materials, Implementation and Process Evaluation, Trial Design and Evaluation, Patient Engagement, and Practice Engagement.

Second, the implementation workgroup developed a system for discussions about proposed adaptations, which were approved by the steering committee and subsequently tracked in a secure, web-based software platform (i.e., a Research Electronic Data Capture [REDCap] database) [21,22], structured around the Framework for Reporting Adaptations and Modifications-Expanded (FRAME) domains, e.g., reasons for change [18]. The study team augmented the eight existing FRAME goals of modifications (e.g., to increase reach or engagement, to improve feasibility, to reduce cost) with the addition of the "improve fit with clinical process/stakeholders" goal.

Third, the implementation workgroup tracked implementation strategies and strategy changes longitudinally and by cluster in a separate REDCap database using the Longitudinal Implementation Strategy Tracking System (LISTS) method [23,24]. LISTS names and describes strategies using the Expert Recommendations for Implementing Change (ERIC) taxonomy [1] and defines key aspects of them using the framework by Proctor and colleagues [25] and the Consolidated Framework for Implementation Research (CFIR) [26]. Elements of the Framework for Reporting Adaptations and Modifications expanded to Evidence-based Implementation Strategies (FRAME-IS) [16] are used to capture modifications to implementation strategies, including: 1) when they took place, 2) who requested them, 3) the reason for them, and 4) whether they were planned or unplanned. The LISTS method was developed by members of the IMPACT consortium—including members of the E2C2 study team—and was used by all three research centers in their individual research studies.

### 2.4. Data analysis

First, study activities in the Excel tracking log were summarized in six time periods to signify the period before the first step was randomized ("pre-implementation") and periods marking the duration between when each step entered the intervention. Second, intervention adaptations recorded in REDCap were summarized by study period and FRAME domain. Third, implementation strategy adaptations were similarly reviewed and summarized by FRAME-IS domains. Finally, the implementation team used the results of these analyses to create a logic model that described the core components of the intervention at the end of the study and highlighted changes in elements, including dates of changes. The model was reviewed by members of other workgroups for accuracy. The objective of this deliverable was to provide a way for workgroups evaluating intervention and implementation outcomes to consider which components were active during study phases, as well as whether adaptations may have impacted mechanisms of change. The logic model also served as a tool for considering whether an activity or an adaptation was related to the intervention or the implementation strategies, based on their target and the mechanisms of change. For example, ePROM reporting addresses a clinical/patient outcome and is part of the intervention, but efforts to make reporting more accessible are implementation strategies aimed at improving an implementation outcome like patient reach.

## 3. Results

### 3.1. Activity tracking across workgroups

Between January 2019 and January 2023, 187 study activities were documented (Table 1). More than one-third of activities (n = 72, 38.5%) took place during pre-implementation, including most "practice engagement" (n = 23 of 43, 53.5%) and "EHR build and implementation" activities (n = 14, 56%). Similarly, while "Intervention" activities were spread across years, most took place in earlier periods. In the pre-implementation phase, they included development of evidence-based care algorithms for SCM intervention delivery and twice-weekly interdisciplinary care conferences for initial presentation of most new patients. In the first two steps, intervention activities included refinements in components and their delivery, e.g., addition of an optional health coach for patients interested in behavioral symptom management approaches, as well as the addition of a clinician-facing dashboard to view ePROM responses. A major change in the third step included addition of


**Fig. 2.** Descriptions of study tracking approaches: Three approaches were used to track activities, intervention adaptations, and implementation strategies and strategy adaptations. Processes leveraged existing implementation frameworks and methods, including the FRAME and the LISTS method, which includes elements of the ERIC taxonomy, the CFIR, and FRAME-IS. At the end of the study, a logic model was created to capture key intervention components and strategies.

a physical therapist (PT) and social worker (SW) to the interventionist team to serve as the SCM for patients reporting severe loss of function or anxiety/depression, respectively. This change was prompted by the observation that RNs were generally referring patients to PTs and SWs for these symptoms. Routing patients directly to these disciplines, therefore, was expected to be more cost effective and responsive to patient need.

Almost one-third of operations activities (n = 12, 32.4%), i.e., activities related to workflows and development of standard operating procedures, were in response to the COVID-19 pandemic. Examples include institution-wide deferrals of elective visits, pause on the use of kiosks and tablets at clinic visit check-in, and development of workflows for assigning ePROMs to telehealth encounters. EHR, intervention, and practice engagement activities in the last step included efforts to understand intervention sustainability and transition intervention components to the clinical practice.

### 3.2. Intervention adaptation tracking

There were 11 intervention adaptations tracked in the REDCap database, most of which occurred in the six months around the trial midpoint. The majority of adaptations (n = 9, 69.2%) were suggested by the SCMs, followed by other members of the study team (n = 5, 45.5%). Most (n = 8, 72.7%) were unplanned and in response to an identified need or concern. The most common goals of adaptations were to improve fit with recipients (n = 8, 72.7%) and increase reach or engagement (n = 6, 54.5%), as shown in Fig. 3.

### 3.3. Implementation strategy and adaptation tracking

Between September 2018 and February 2021, the study team deployed 33 implementation strategies. Strategies were most frequently aimed at addressing intervention reach (n = 69, 78.4%), fidelity (n = 62,

**Table 1**
Study activities by category and phase.

| Category | Phase[a] | | | | | | Total *n* (%) | Example |
|---|---|---|---|---|---|---|---|---|
| | Pre-implementation | Step 1 | Step 2 | Step 3 | Step 4 | Step 5 | | |
| EHR build and implementation | 14 | 4 | 1 | 0 | 0 | 6 | 25 (13.4%) | Addition of an Epic Synopsis view symptom report for all clinicians (Step 5) |
| Intervention | 5 | 8 | 8 | 1 | 3 | 4 | 29 (15.5%) | Addition of optional health coach to SCM interventionist team (Step 1) |
| Operations | 10 | 12 | 6 | 3 | 5 | 1 | 37 (19.8%) | Development of ePROM workflows for telehealth (Step 1) |
| Patient education material | 9 | 7 | 2 | 0 | 4 | 1 | 23 (12.3%) | Audio recording of *My Guide to Cancer Symptoms* for web (Step 1) |
| Implementation and process evaluation | 4 | 7 | 3 | 0 | 1 | 0 | 15 (8%) | Development of fidelity monitoring plan (Step 2) |
| Trial design and evaluation | 3 | 1 | 0 | 0 | 1 | 0 | 5 (2.7%) | Approval of cluster randomization plan (Pre-implementation) |
| Patient engagement | 4 | 2 | 2 | 1 | 1 | 0 | 10 (5.3%) | Development of *Introduction to the SCM* video for web (Step 1) |
| Practice engagement | 23 | 8 | 4 | 1 | 2 | 5 | 43 (23%) | Kick-off presentations delivered to tumor groups (all phases) |
| **Total, *n* (%)** | 72 (38.5%) | 49 (26.2%) | 26 (13.9%) | 6 (3.2%) | 17 (9.1%) | 17 (9.1%) | 187 | |

Abbrev: ePROMs = electronic patient-reported outcome measures.
[a] Pre-implementation = January 2019 to September 2019; Step 1 = October 2019 to May 2020; Step 2 = June 2020 to January 2021; Step 3 = February 2021 to September 2021; Step 4 = October 2021 to May 2022; Step 5 = June 2022 to January 2023 (end of study period).

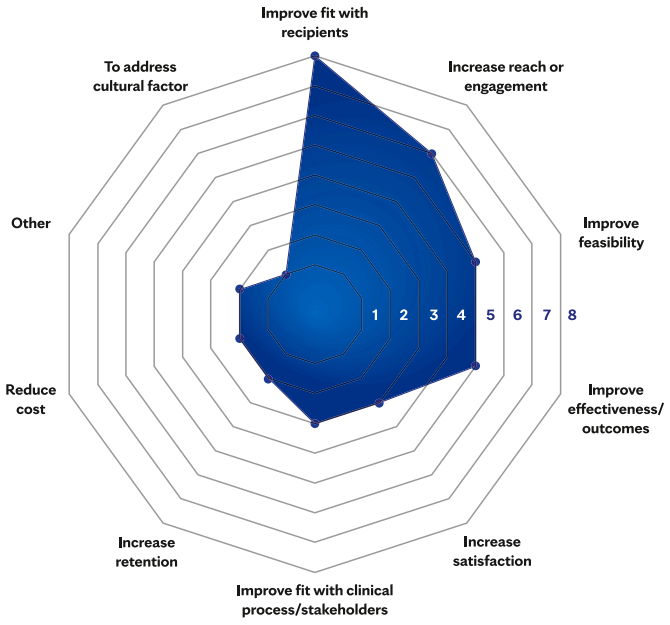


**Fig. 3.** Goals of intervention adaptations: Each intervention adaptation was documented using constructs from the FRAME taxonomy [18]. This figure shows the number of goals identified as the intent of documented adaptations. Eight adaptations, for example, were intended to improve fit with recipients. Tracking the goals of intervention adaptations is critical to understanding how adaptations may impact implementation or patient outcomes.

70.5%), adoption (n = 40, 45.5%), sustainability (n = 38, 43.2%), acceptability (n = 24, 27.3%), and feasibility (n = 22, 25%). The largest number of strategies were related to training and educating stakeholders (n = 13, 39.4%), e.g., development of toolkits and presentations of educational content. Targeted determinants from the CFIR inner setting domain included the implementation climate (e.g., whether the intervention is compatible with workflow and a priority for users), while outer setting determinants were related to perceptions of patient needs.

Most strategies were prospectively planned and deployed across all clusters in a similar fashion. However, a few key strategy changes related to intervention delivery were not planned at study conception. They include a change from a patient opt-in approach to SCM contact when high symptom burden was reported to an automatic (i.e., opt-out) approach to SCM contact (May 2020), and a subsequent return to an opt-in approach (November 2020) [27]. Another key strategy change was the addition of an Interactive Voice Response (IVR) option for ePROM reporting among patients who did not use the patient portal. This change in ePROM completion mode started January 2021. There were also adjustments made to the format and frequency of support for the internal implementation facilitators (referred to as "symptom sages"), whose role was to provide cluster-level support to care teams and foster communication between the study team and care teams.

### 3.4. Logic model

The implementation team adapted the original logic model for the intervention to include changes in intervention components as well as the addition of implementation strategies used during the trial, as shown in Fig. 4 adapted from Smith, Li, and Rafferty [14]. Most component and strategy additions were consistent with the mechanisms of change as hypothesized at trial launch. For example, the addition of a social worker and physical therapist were in support of patient knowledge about options for specific types of symptom management. One hypothesized mechanism that did emerge during the trial was related to the changes between patient opt-in and opt-out approaches for SCM support among patients reporting high symptom burden. While an opt-out approach was meant to increase the likelihood that patients would access SCM support, it was ultimately discarded because it required the SCMs to contact patients who might not be interested in symptom management—time which could have been better utilized delivering care—and because the opt-out approach did not increase the number of participants willing to work with SCMs. Likewise, the development of action plans was aimed at engaging patients with symptom self-management tools and promoting self-efficacy.

## 4. Discussion

Our team's approach highlights the breadth of activities that took place throughout the trial period. In the pre-implementation phase, activities were focused on the EHR build and development of patient education materials and symptom management algorithms, as well as engagement activities with care teams and patients. These types of


**Fig. 4.** Revised E2C2 logic model with implementation strategies: The logic model created at the end of the study provides a reference for the final intervention components and implementation strategies, along with adaptations. Adaptations that happened during the trial are highlighted and include the month and year of the change.

activities did not end with the start of intervention activities, though; considerable numbers of activities in these categories persisted through the first and second steps of trial randomization, when additional unanticipated implementation determinants, such as practice-specific workflows, were identified. The activity tracking log included brief descriptions of each activity, yet these sufficed for classification. Tracking logs have been shown to be feasible and acceptable approaches to tracking intervention and implementation strategy adaptations, although more detailed logs may still be challenging to implement [17]. In this study, documentation of activities by a project manager, who attended all workgroup meetings and completed meeting minutes, and categorization of activities by the implementation workgroup were critical for minimizing burden on most workgroups while leveraging the expertise of the implementation workgroup. The classification process, which involved consensus-focused discussion during implementation workgroup meetings, also highlighted the importance of tracking and reviewing a range of activities; although there were tracking categories specific to the intervention, the relevance of activities in other categories, e.g., operational activities, to the intervention and its delivery may not have been immediately apparent in some workgroups.

The detailed approach to database tracking of intervention and implementation adaptations in this study provided important information about the changes—including why they were made—which can inform conversations around intervention specification and sustainability. These data may also inform scale-up to new settings or populations [28,29]. The use of existing robust implementation science methods and frameworks (e.g., FRAME, LISTS, CFIR) may also enable comparison with other studies of remote symptom management interventions. The retrospective assessment reported here identified activities that were missed by one system but captured in another, including adaptations that were captured in the tracking log but not picked up by the implementation workgroup at the time of the change. This suggests that some redundancy of systems may benefit later data triangulation.

These findings suggest several key recommendations for researchers conducting pragmatic trials wherein the intervention, or the manner in which it is implemented, may require adaptation during the course of the trial to be responsive to local barriers, opportunities, or the needs and preferences of patients, care teams, or others. First, maintaining the fidelity of key intervention components is critical to the evaluation, and identifying program theory is one way to identify key intervention components. We recommend the use of tools like logic models, which can engage teams in conversations about the intervention, how it is intended to achieve outcomes, and what factors may impact success. In

doing so, they may help study teams come to agreement on core components and causal mechanisms and help them recognize when an adaptation decision may inadvertently change aspects of intervention effectiveness.

Second, study teams should balance more- and less-accessible methods and expertise. They may benefit from the growing number of frameworks and methods from implementation science and related fields that support adaptation tracking. However, tools like FRAME and the LIST method may be most feasibly used by individuals or teams with expertise in implementation science. Various research and operational workgroups are regularly making decisions that could impact intervention or implementation, though, and meeting minutes, emails, and other documents are routinely created and capture many of them. Project managers and coordinators play a key role in documentation. Study teams should consider the range of information being tracked as a part of study execution and ways that it can be used in analysis. They should also consider ways to balance the need for timely information for decision-makers as the trial is progressing against the need for more comprehensive analysis for effectiveness and implementation evaluations at the end of the trial. Key prompts from FRAME that ask operational leaders to consider the intent and implications of an intervention adaptation may help guide timely decisions while populating tracking databases for later analysis by the implementation team.

Third, our team took a broad approach to capturing as many activities as possible, followed by review from a smaller implementation workgroup. While this leveraged a range of available information, as noted above, and increased chances that important activities and adaptations were captured, this redundancy and review process involved considerable effort for the implementation workgroup and the steering committee, which reviewed proposed adaptations. Therefore, study planning should include designation of personnel and effort for tracking tasks, aligning as much as possible with routine tasks. Our team reserved the final 10–15 min of biweekly implementation workgroup meetings to review the list of activities assembled by the project manager and coordinator team. Effort to collate activities for review will vary by the size, scope, and phase of the study, but in this large multi-site trial, we estimate approximately 1 h per week was required. Likewise, investigators submitting funding proposals for pragmatic hybrid trials should include descriptions of robust systems for tracking implementation and adaptations and include sufficient planned effort for project management or other coordinating roles, as well as implementation scientists.

There are limitations to this work, including changes to how the study team defined which components were related to the intervention (e.g., ePROMs and SCM telephonic support) and which were related to its implementation (e.g., mode of ePROM reporting, videos to increase uptake of nurse support). Likewise, tracking systems themselves were developed and refined over time, and workgroups each made decisions about the level of detail to be documented. The implementation workgroup also refined activity classifications over time, including responses to unanticipated events like the COVID-19 pandemic, and ensured activities were reclassified as needed. The development of a logic model, which was reviewed by members from several workgroups, minimizes the chances that critical aspects of the intervention or implementation strategies were omitted, given the large number of parallel workstreams across the workgroups. Finally, specific adaptations made in this trial may have limited generalizability to comparable trials of ePROM-based interventions, but the process described here may be transferrable to other settings and types of trials.

## 5. Conclusion

The pragmatic nature and diverse range of activities required by hybrid trials create challenges for tracking adaptations. While a growing number of tools are available to support this work, ways to feasibly and practically integrate them in trials is critical for robust evaluations. Replication of tracking approaches that leverage the methods and frameworks of implementation science but integrate them into the routine work of diverse study teams is one way to build the evidence base on adaptation tracking. Further work is needed to minimize burden and ensure robust and practical systems that inform both evaluation and timely decision-making.

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## Author contributions and consent for publication

JLR, JMG, and DRP conceived the study. JLR, KJF, NKT and JMG did the data collection and analysis. JLR and JMG drafted the manuscript, and KJF, NKT, JDA, SAM, DRP, LLC, KJR and AC edited and reviewed various versions of the manuscript. The authors read and approved the final manuscript.

## Ethics approval and consent to participate

This study was approved by the Mayo Clinic Institutional Review Board (IRB#18–007779).

## Consent for publication

Not applicable.

## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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