

Title           **Eliminating Monitor Overuse (EMO) Hybrid Effectiveness-Deimplementation Trial**

Short Title     EMO Trial

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**ABBREVIATIONS AND DEFINITIONS OF TERMS**

A&F	Audit and feedback
AE	Adverse event
AIM	Acceptability of Implementation Measure
BEEP	Best Evidence for Effective monitoring Practice (guideline)
CDS	Clinical Decision Support
CFIR	Consolidated framework for implementation research
CHOP	Children's Hospital of Philadelphia
CI	Confidence interval
COI	Conflict of interest
CRCU	Clinical Research Computing Unit at the University of Pennsylvania
DCC	Data Coordinating Center
DMS	Data management system
DSMB	Data and safety monitoring board
EHR	Electronic Health Record
EMO	Eliminating Monitor Overuse
FDA	Food and Drug Administration
ICU	Intensive Care Unit
IT	Information technology
LOS	Length of (hospital) stay
MIS-C	Multisystem inflammatory syndrome in children
MOXY	Monitoring OXYgen in Infants Hospitalized With Bronchiolitis (clinical trial)
NHLBI	National Heart, Lung, and Blood Institute
P1,2,3,4	Phase 1, 2, 3, or 4
PASS	Power and Sample Size (software)
PCC	Pediatric Clinical Decision Support Collaborative
Penn	University of Pennsylvania
PHI	Protected Health Information
PRIS	Pediatric Research in Inpatient Settings Network
RDC	Remote data entry module
RTD	Research Technologies Department
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SD	Standard deviation
SpO <sub>2</sub>	Pulse oximetry
UK	United Kingdom
US	United States

## ABSTRACT

### Context:

Bronchiolitis, an infectious lung disease, is the leading cause of infant hospitalization and is responsible for over 100,000 admissions and \$1.7 billion in hospital charges annually. Continuous pulse oximetry monitoring of oxygen saturation (SpO<sub>2</sub>) is a common intervention in bronchiolitis, yet it does not improve outcomes when it is used during periods of the hospitalization when supplemental oxygen is not being administered (i.e. when the patient is “in room air”). The American Academy of Pediatrics, Choosing Wisely, and the Best Evidence for Effective monitoring Practice guidelines all discourage continuous SpO<sub>2</sub> monitoring in children with bronchiolitis who are in room air, making it an opportune target for deimplementation.

### Objectives:

Primary: To test a “usual approach” unlearning deimplementation strategy (educational outreach with audit & feedback) vs. an enhanced unlearning + substitution deimplementation strategy (adding an electronic health record-integrated clinical pathway). The primary outcome is sustainability of guideline-concordant deimplementation in bronchiolitis patients who are in room air.

Secondary: (a) Identify deimplementation strategy mechanisms. (b) Examine the effects of deimplementation on clinical outcomes and unintended consequences.

### Study Design:

Multicenter hybrid type III effectiveness-deimplementation trial with a longitudinal cluster-randomized design.

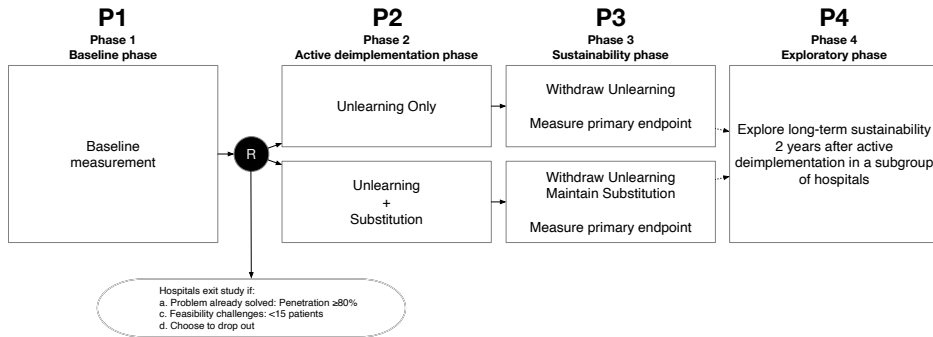
### Setting/Participants:

The trial will be conducted on PRIS Network hospital inpatient units that care for children with bronchiolitis, excluding ICUs, emergency departments, and step-down units. Subject populations include (1) bronchiolitis patients, (2) parents or guardians of bronchiolitis patients who participate in qualitative interviews, (3) hospital staff who care for bronchiolitis patients and participate in questionnaires and interviews, and (4) Clinical Decision Support (CDS) Coaches.

### Study Interventions and Measures:

The study interventions are directed toward hospital staff caring for bronchiolitis patients and include educational outreach, audit & feedback, and an electronic health record-integrated clinical pathway.

Sustainability, the primary outcome, will be assessed as a longitudinal difference in differences comparison of the penetration of guideline-concordant care during at baseline (percentage of bronchiolitis patients in room air who are appropriately not being continuously SpO<sub>2</sub>-monitored at baseline, before any deimplementation strategies are deployed) compared to the penetration 1 year after withdrawal of educational outreach and A&F, and contrasted between study arms (see study diagram). We will also assess other deimplementation outcomes (e.g. fidelity and cost), assess practice routinization and institutionalization as potential mediators, and examine clinical outcomes such as length of hospital stay and unintended monitoring underuse that could result from deimplementation.



#### Gap between Phase 1 and 2: Minimum of 6 months

Can be extended beyond 6 months at discretion of Steering Committee in any of the following conditions:

- $\geq 20\%$  of sites in either arm is unprepared to start active deimplementation
- National RSV percent positivity is  $< 2\%$
- Or for other reasons, with DSMB and NHLBI approval

#### Washout between Phase 2 and 3: Minimum of 6 months

Can be extended beyond 6 months at discretion of Steering Committee in any of the following conditions:

- National RSV percent positivity is  $< 2\%$
- July (new residents) falls within proposed Phase 3
- Or for other reasons, with DSMB and NHLBI approval

**Figure 1. Trial diagram.** The trial includes 3 main phases (baseline, active deimplementation, and sustainability) and an exploratory fourth phase. During the baseline phase (P1), we will measure baseline penetration of guideline-concordant care in approximately 45 hospitals and confirm that sites have adequate bronchiolitis volumes, infrastructure, and capability to complete the trial. Penetration is defined as the percentage of bronchiolitis patients who are in room air (no supplemental oxygen) and are receiving guideline-concordant care (this means they are not being continuously SpO<sub>2</sub>-monitored). Based on the P1 data, we will exclude hospitals with feasibility challenges and those with already high penetration of 80% or higher. We anticipate that this will result in 32-38 randomizable hospitals. If more than 38 hospitals remain after those exclusions, we will then randomize the 38 hospitals with the lowest baseline penetration. Of those that remain, we will randomize no fewer than 32 and no more than 38 hospitals to either: the unlearning only arm (educational outreach with A&F) or the unlearning + substitution arm (adding an EHR-integrated clinical pathway to facilitate the transition from continuous SpO<sub>2</sub> monitoring to intermittent SpO<sub>2</sub> measurement when clinically appropriate). In the active deimplementation phase (P2), these strategies will be deployed in the 32-38 sites. At the end of P2, unlearning (educational outreach with A&F) will be withdrawn from both arms. In the sustainability phase (P3), substitution (EHR-integrated pathway) will be maintained exclusively in the unlearning + substitution arm and the primary outcome (sustainability) will be contrasted between arms as a longitudinal difference in differences comparison of penetration at baseline (P1) versus in the sustainability phase (P3). In the exploratory phase (P4), we will assess longer-term sustainability in a subgroup of up to 16 hospitals, 2 years after withdrawal of education and A&F.

## 1 BACKGROUND INFORMATION AND RATIONALE

### 1.1 Introduction

Deimplementing overused medical interventions is an essential step to maximize quality and minimize waste in our health care system.<sup>1</sup> Bronchiolitis, an infectious lung disease, is the leading cause of infant hospitalization and is responsible for over 100,000 admissions and \$1.7 billion in hospital charges annually.<sup>2,3</sup> Continuous pulse oximetry monitoring of oxygen saturation (SpO<sub>2</sub>) is a common intervention in bronchiolitis, yet it does not improve outcomes when it is used during periods of the hospitalization when supplemental oxygen is not being administered (i.e. when the patient is “in room air”).<sup>4,5</sup> In addition to being ineffective, its overuse can prolong the hospital stay,<sup>6–8</sup> increase risk of harm,<sup>9</sup> and contribute to alarm fatigue, which threatens patient safety beyond the monitored patient.<sup>10,11</sup> Thus the American Academy of Pediatrics,<sup>12</sup> Choosing Wisely,<sup>13</sup> and the Best Evidence for Effective monitoring Practice (BEEP) guidelines<sup>14</sup> all discourage continuous SpO<sub>2</sub> monitoring in children with bronchiolitis who are in room air, making it an opportune target for deimplementation.<sup>15</sup>

### 1.2 Relevant Literature and Data

**Deimplementing overused health interventions that are not supported by evidence is essential to maximizing quality and value while minimizing harm, waste, and inefficiencies in the health care system.**<sup>1,16</sup> Medical overuse is defined by the Institute of Medicine as care in the absence of a clear medical indication, or when the benefit does not outweigh the risk.<sup>17</sup> Overuse can be measured directly when evidence-based guidelines (a) specify conditions in which a practice is appropriate and (b) also consider the balance between benefits and harms.<sup>18</sup> Deimplementation is the systematic divestment of overused practices that do not improve outcomes.<sup>19,20</sup> Recently, experts have called for deimplementation research to identify the best strategies for minimizing low-value care delivery to children, the focus of this proposal.<sup>21</sup>

**Medical overuse is a documented problem during inpatient treatment of acute viral bronchiolitis (“bronchiolitis”), a common acute lung disease caused by respiratory viral infection in children under 2 years old.**<sup>2,3,12</sup> In the US, bronchiolitis leads to over 100,000 hospitalizations annually<sup>22</sup> in a seasonal pattern, with most cases occurring between December and March.<sup>23</sup> Treatment often includes feeding support, nasal suctioning, and supplemental oxygen.<sup>12</sup> Bronchiolitis patients are often continuously SpO<sub>2</sub>-monitored despite evidence that it does not improve outcomes when it is used during periods of the hospitalization when supplemental oxygen is not being administered (i.e. patient is “in room air”).<sup>24</sup> Rather, in those patients continuous SpO<sub>2</sub> monitoring may overidentify brief, self-limited desaturations that do not impact patient outcomes.<sup>25</sup> As a result, three sets of national guidelines now discourage the use of continuous SpO<sub>2</sub> monitoring in hospitalized children with bronchiolitis who are in room air.<sup>12–14</sup>

**Overuse of continuous SpO<sub>2</sub> monitoring is associated with increased oxygen administration, prolonged length of stay, and increased costs in retrospective studies.**<sup>7,8</sup> In addition, in a clinical trial, infants with bronchiolitis randomized to oximeters that inflated SpO<sub>2</sub> readings to appear slightly better than the actual values were discharged 10 hours sooner than a control group, with no differences in clinical outcomes and lower hospital costs.<sup>6,26</sup> This finding suggests that the SpO<sub>2</sub> value may be over-weighted in clinician decision making. Unfortunately, longer hospital stays translate into increased risk of injury: one study reported 12 unnecessary harms inflicted per 100 bronchiolitis admissions (e.g. falls from cribs, medication errors).<sup>9</sup> In addition, longer hospitalizations prolong the stress and anxiety experienced by parents,<sup>27</sup> who also suffer financial impacts.<sup>28</sup> Given that nearly all children hospitalized with bronchiolitis recover fully,<sup>22</sup> and deteriorating after showing clinical improvement occurs in just 4% of cases,<sup>29</sup> excess monitoring causes unnecessary burden in a high prevalence disease for which experts have called on clinicians to “safely do less.”<sup>30</sup>

**Overmonitoring also contributes to alarm fatigue, which threatens patient safety beyond the monitored patient.** Alarm fatigue is a well-described result of exposure to non-actionable alarms, leading to desensitization.<sup>31,32</sup> In children’s hospital wards, monitors alarm 42–155 times per patient day.<sup>33</sup> SpO<sub>2</sub> alarms are the most frequent but 99% are non-actionable; this “crying wolf” effect leads

clinicians to distrust alarms and slows their response times to all alarm types, including those that are potentially critical. Response delays averaged 7 minutes in a study we conducted using video.<sup>10,11,34</sup> One way to reduce alarm fatigue is to reduce monitoring in populations in which it has no benefit,<sup>35</sup> including bronchiolitis patients in room air.

**Two clinical trials randomized at the patient level demonstrated that intermittent SpO<sub>2</sub> measurement is an equally safe alternative to continuous SpO<sub>2</sub> monitoring for children in room air.** A 4-hospital trial found no significant difference in safety,<sup>4</sup> and the 6-hospital Monitoring OXYgen in Infants Hospitalized With Bronchiolitis (MOXY) trial also showed no significant differences in adverse safety outcomes, with nursing satisfaction higher in the intermittent monitoring group.<sup>5</sup>

**Specific attention to sustainability is needed, as sustaining guideline-concordant care over time is challenging, important, and understudied.**<sup>36</sup> Across a broad range of clinical specialties, fewer than half of studies measuring clinicians' guideline-concordant care over time report successful sustainment >1 year after implementation.<sup>37</sup> For example, in a cluster-randomized trial of educational outreach with A&F to deimplement inappropriate antibiotic prescribing to children with acute respiratory tract infections, the immediate post-implementation results showed a nearly 50% reduction in inappropriate prescribing.<sup>38</sup> However, 18 months after withdrawal of A&F, inappropriate prescribing practices had returned to baseline. No studies have rigorously evaluated sustainability of deimplementation in pediatric hospital settings.

**When aiming to align clinical practice with guidelines in pediatric hospital medicine, the usual approach involves unlearning-based strategies.**<sup>39–41</sup> Enhancing unlearning with electronic health record (EHR)-based substitution may boost sustainability of deimplementation. In a special report, the NHLBI Implementation Science Work Group concluded that A&F and educational outreach are generally effective in improving outcomes.<sup>42</sup> A&F in particular is so widely accepted that experts consider studies of A&F vs. no A&F controls "unlikely to provide valuable insights" and "research waste," instead calling for trials of A&F alone vs. A&F + co-interventions as we propose in this application.<sup>43,44</sup> Helfrich's Dual Process Theory-based deimplementation framework<sup>45</sup> offers a useful basis for experimentally testing A&F co-interventions, separating strategies into two categories targeting: (1) unlearning the ineffective practice using knowledge-based methods (e.g., presenting clinicians with evidence and guidelines, conducting A&F) and (2) substituting the ineffective practice with an alternative practice that becomes integrated into everyday work (e.g., using EHR-integrated clinical pathways to support intermittent SpO<sub>2</sub> measurement). This is consistent with evidence that, when aiming to reduce low-value care, (a) multicomponent interventions have the greatest potential for success, (b) education is necessary but rarely sufficient, and (c) A&F and EHR-based "clinical decision support" (CDS) are the most promising strategies to address overuse.<sup>46–48</sup> Two small-scale continuous SpO<sub>2</sub> monitoring deimplementation efforts in bronchiolitis that used enhanced approaches showed short-term success. Schondelmeyer et al. used educational outreach, audit & feedback (A&F), and EHR guidance and found a significant reduction in continuous SpO<sub>2</sub> monitoring duration.<sup>49</sup> Mittal et al. used a clinical pathway that guided staff to limit continuous SpO<sub>2</sub> monitoring to only patients with severe bronchiolitis, resulting in length of stay reduction from 53 to 33 hours.<sup>50</sup> EHR-based strategies also offer promise of sustainability. In a 60-hospital collaborative focused on infant sepsis guideline adherence, unlearning strategies were not sustained due to time constraints and competing priorities.<sup>39,51</sup> However, EHR-based strategies were not only sustained but increased in use 11 months after the active intervention period.<sup>51</sup> The authors concluded that EHR-based strategies as well as clinical pathways and policies were the most feasible for sustaining guideline-concordant care.<sup>51</sup> Randomized trials are needed to evaluate this conclusion.

Table 1. 6-hospital pilot trial results.			
Penetration of guideline-concordant care			
Hospital	Baseline % (95% CI)	Intervention % (95% CI)	P
1	22% (13-30%)	57% (50-64%)	<.001
2	31% (17-44%)	91% (84-99%)	<.001
3	34% (26-42%)	73% (65-81%)	<.001
4	35% (24-46%)	70% (61-79%)	<.001
5	37% (27-46%)	80% (75-86%)	<.001
6	78% (72-84%)	90% (87-93%)	.001
Overall	47% (43-51%)	77% (75-80%)	<.001

**NHLBI U01-Funded Preliminary Studies.** First, our team led a 56-hospital, 3,612-patient observational study of SpO<sub>2</sub> monitor overuse.<sup>24</sup> Across all hospitals, 46% of bronchiolitis patients in room air were continuously SpO<sub>2</sub>-monitored, discordant with guidelines. The remaining 54% were appropriately unmonitored. In other words, at baseline, the penetration of guideline-concordant care was just 54%, with strikingly wide variation in penetration ranging from 8% to 98% between hospitals, not attributable to differences in patient populations. This variation suggests that achieving high penetration is feasible. Second, we conducted qualitative interviews with clinicians and administrators from 12 hospitals to

understand barriers to deimplementation, guided by the Consolidated Framework for Implementation Research (CFIR).<sup>52,53</sup> Key barriers included educational gaps, lack of clear instructions of when to monitor, and normative culture of monitoring. Third, we convened 39 stakeholders from 15 hospitals to develop deimplementation strategies using implementation mapping.<sup>54</sup> Applying a deimplementation framework,<sup>45</sup> we categorized strategies into: (1) unlearning (educational outreach with A&F) and (2) substitution (replacing continuous monitoring with intermittent measurement, supported by an EHR-integrated clinical pathway). Fourth, we performed a 6-hospital, single arm trial of educational outreach with A&F, using historical controls.<sup>55</sup> Each hospital increased penetration compared to baseline (Table 1, manuscript forthcoming). In a survey, 1,193 nurses and physicians considered education and A&F to be feasible and acceptable.<sup>56</sup>

**Building on this body of evidence and our previous NHLBI-funded preparatory work, we propose to conduct the Eliminating Monitor Overuse (EMO) SpO<sub>2</sub> hybrid type III clinical trial.**

Despite the evidence and guidelines, continuous SpO<sub>2</sub> monitoring continues to be overused in hospitalized children with bronchiolitis, making it a prime target for deimplementation efforts. In the 56-hospital observational study we conducted, 46% of bronchiolitis patients who were in room air were continuously SpO<sub>2</sub>-monitored, discordant with guidelines.<sup>24</sup> In the EMO SpO<sub>2</sub> trial, we will test the effects of a “usual approach” unlearning strategy (educational outreach with A&F) vs. an enhanced unlearning + substitution strategy (adding an EHR-integrated clinical pathway) on the sustainability of guideline-concordant deimplementation in children with bronchiolitis who are in room air. The trial will allow us to determine if the EHR-integrated clinical pathway enhances sustainability, with a focus on its effects 1 year after withdrawal of educational outreach and A&F, an outcome highly relevant to clinical practice and implementation science.

### 1.3 Compliance Statement

This study will be conducted in full accordance all applicable Children’s Hospital of Philadelphia Research Policies and Procedures and all applicable Federal and state laws and regulations. All episodes of noncompliance will be documented.

The investigators will perform the study in accordance with this protocol, will obtain consent as detailed herein, and will report unanticipated problems involving risks to subjects or others in accordance with Children’s Hospital of Philadelphia IRB Policies and Procedures and all federal requirements. Collection, recording, and reporting of data will be accurate and will ensure the privacy, health, and welfare of research subjects during and after the study.

## 2 STUDY OBJECTIVES

### 2.1 Specific Aim 1

To compare the effects of an unlearning-based deimplementation strategy alone versus a deimplementation strategy that combines unlearning and substitution-based approaches on deimplementation outcomes.

The objective of this aim is to test the effects of unlearning only (educational outreach with A&F) vs. unlearning + substitution (educational outreach with A&F plus an EHR-integrated clinical pathway) on the primary trial outcome: sustainability of guideline-concordant deimplementation.

**Hypothesis.** Compared to the unlearning only strategy, the unlearning + substitution strategy will result in better sustainability of guideline-concordant deimplementation 1 year after withdrawal of educational outreach and A&F.

### 2.2 Specific Aim 2

To identify deimplementation strategy mechanisms linked to penetration and sustainability using mixed methods.

The objective of this aim is to identify, test, and deeply explore mediators and moderators of the relationship between strategies and outcomes. We will also use qualitative inquiry of clinicians to explore mechanisms, and qualitative inquiry of parents to understand perceptions of deimplementation.

**Hypothesis.** Primary. The unlearning + substitution strategy will result in better penetration and sustainability than the unlearning only strategy because the EHR-integrated pathway will produce better routinization<sup>57</sup> and institutionalization<sup>57</sup> of the change in practice (mediators). Secondary. Strategies in both study arms will be more effective in settings with more positive implementation climate<sup>58</sup> and leadership,<sup>59</sup> and where clinicians respond to deimplementation messaging with less psychological reactance (moderators).<sup>60</sup>

### 2.3 Specific Aim 3

To examine the effects of deimplementation on clinical outcomes and unintended consequences.

The objective of this aim is to examine clinical outcomes and unintended adverse consequences for patients associated with the deimplementation strategies themselves and/or from the resulting increases in penetration.

**Hypothesis.** Primary. Increased penetration of guideline-concordant care will be associated with decreased hospital length of stay (LOS) in bronchiolitis patients. Secondary. Increased penetration will also be associated with decreased duration of oxygen supplementation in bronchiolitis patients.

## 3 INVESTIGATIONAL PLAN

### 3.1 General Schema of Study Design

We will conduct a hybrid type III effectiveness-deimplementation trial<sup>61</sup> with a longitudinal cluster-randomized design within the Pediatric Research in Inpatient Settings (PRIS) Network.<sup>62</sup> The trial includes 3 main phases (baseline, active deimplementation, and sustainability) and an exploratory fourth phase. Given the seasonal pattern of bronchiolitis, each phase was originally designed to take place during a 4-month winter period (December-March) spanning across 4 years. Due to the changes in bronchiolitis seasonality post-Covid, we uncoupled the study phases from winters. Each phase is still intended to be 4 months, however each phase may be extended beyond 4 months at

the discretion of the Principal Investigators if challenging circumstances arise that limit sites' abilities to collect sufficient data (e.g. staffing challenges or differences in seasonal bronchiolitis patterns due to the Covid pandemic). We also set parameters around the required gaps that must occur between each phase. See Figure 1 for those details.

### 3.1.1 Baseline Phase

During the **baseline phase (P1)**, we will measure baseline penetration of guideline-concordant care in **approximately 45 hospitals** and confirm that sites have adequate bronchiolitis volumes, infrastructure, and capability to complete the trial. Penetration is defined as the percentage of bronchiolitis patients who are in room air (no supplemental oxygen) and are receiving guideline-concordant care (this means they are not being continuously SpO<sub>2</sub>-monitored). Based on the P1 data, we will exclude hospitals with inadequate patient volumes or data collection challenges. We will then cluster-randomize the **32-38 hospitals** with the lowest baseline penetration to either: the unlearning only arm (educational outreach with A&F) or the unlearning + substitution arm (adding an EHR-integrated clinical pathway to facilitate the transition from continuous SpO<sub>2</sub> monitoring to intermittent SpO<sub>2</sub> measurement when clinically appropriate).

### 3.1.2 Active Deimplementation Phase

In the **active deimplementation phase (P2)**, the above strategies are deployed in the 32-38 sites. At the end of P2, unlearning (educational outreach with A&F) is withdrawn from both arms.

### 3.1.3 Sustainability Phase

In the **sustainability phase (P3)**, substitution (EHR-integrated pathway) is maintained exclusively in the unlearning + substitution arm and the primary outcome (sustainability) is contrasted between arms as a longitudinal difference in differences comparison of penetration at baseline (P1) versus in the sustainability phase (P3).

### 3.1.4 Exploratory Phase

In the **exploratory phase (P4)**, we assess longer-term sustainability in a subgroup of up to 16 hospitals, 2 years after withdrawal of education and A&F.

## 3.2 Allocation to Treatment Groups (Randomization) and Blinding

This cluster-randomized trial uses covariate-constrained randomization<sup>63-65</sup> to randomize at the hospital level, accounting for important hospital-level covariates and minimizing differences in these covariates between study arms. Following the baseline measurement phase in approximately 45 hospitals during P1 (described above), we will exclude hospitals with inadequate patient volumes or data collection challenges from further trial participation and then cluster-randomize the 32-38 hospitals with the lowest baseline penetration to the study arms (unlearning only [n=16] or unlearning + substitution [n=16]). Cluster randomization is well-suited to strategies applied to groups, as it avoids the potential for contamination that would occur with randomization at the unit or clinician level.<sup>66</sup> We will use covariate-constrained randomization<sup>63</sup> methods to achieve optimal balance between arms for 3 important hospital characteristics: hospital type (2 groups: freestanding children's hospitals vs. general or community hospitals), presence of pre-existing EHR CDS for bronchiolitis that promotes use of intermittent "spot checks" instead of continuous pulse oximetry in patients not requiring supplemental oxygen, and baseline penetration in P1. Assessment of pre-existing EHR CDS will be conducted in P1 and assessed using screenshots of the CDS from each institution and brief descriptions of the functionality from the site teams. Randomization will not be blinded, and will be performed by the Analytic Core. The combination of balanced allocation of hospitals in covariate-constrained randomization and additional patient-level covariate adjustment in the analysis (see below) will limit bias and increase statistical power. There is no blinding in the trial.

### 3.3 Study Duration, Enrollment and Number of Sites

#### 3.3.1 Duration of Subject Study Participation

This is a cluster-randomized clinical trial with interventions assigned at the hospital level. There are several categories of subjects:

- Hospital staff who are exposed to the interventions, complete study questionnaires, and/or participate in qualitative interviews
  - Maximum anticipated duration: Trial duration (4 years)
- Bronchiolitis patients who are directly observed
  - Maximum anticipated duration: their length of hospital stay
- Parents or guardians of bronchiolitis patients who participate in qualitative interviews
  - Maximum anticipated duration: 1 day
- Clinical Decision Support Coaches who participate in qualitative interviews
  - Maximum anticipated duration: 1 day

#### 3.3.2 Total Number of Study Sites/Total Number of Subjects Projected

The study will be conducted at approximately 45 investigative sites in the United States and Canada. We will initially seek IRB approval to enroll up to 55 sites in order to allow for attrition during the IRB reliance, data use agreement, and study startup processes based on our prior experience with these processes with smaller hospitals in the PRIS Network.

Total number of subjects are provided in Section 3.4 broken down by specific subpopulations.

### 3.4 Study Populations with Inclusion and Exclusion Criteria

#### 3.4.1 Population 1: Hospital Staff

Population 1 encompasses all hospital staff who are exposed to the interventions by being present on participating hospital units or overseeing bronchiolitis care during active deimplementation, sustainability, and exploratory phases. These hospital staff members are considered third parties to the research. They are not considered research subjects unless they participate in study questionnaires or qualitative interviews (and thereby fall into hospital staff research subject subpopulations 1a or 1b, outlined below).

##### 3.4.1.1 Population 1a

*Hospital staff who complete study questionnaires.* We will administer questionnaires to hospital staff in approximately 32-38 hospitals at 3 different time points (post-randomization, during P2, and during P3) to measure acceptability, potential mediators, and potential moderators. We estimate based on our pilot study distributing the questionnaires to 200 staff per hospital at each time point and achieving a maximum 80% response rate (we achieved a 71% response rate in our pilot). Therefore maximum anticipated enrollment is  $200 \times 3 \times 32 \times 0.8 = 15,360$ .

##### 3.4.1.1.1 Eligible nurses and physicians will meet the following inclusion criteria:

- Employed full-time by the hospital, affiliated practice, or affiliated university in a role that involves the care of children with bronchiolitis hospitalized on non-intensive care inpatient units
- Fluent in English

##### 3.4.1.1.2 Eligible administrators will meet the following inclusion criteria:

- Oversee the care of bronchiolitis on a local level (e.g. nurse manager) or a hospital level (e.g. Chief Quality and Safety Officer)
- Fluent in English

**3.4.1.1.3 Nurses, physicians, and administrators will be excluded if they meet any of the following exclusion criteria:**

- No exclusion criteria

**3.4.1.2 Population 1b**

Hospital staff who participate in qualitative interviews In Aim 2, we will conduct semi-structured interviews with physicians and nurses who provide care to bronchiolitis patients in participating units with a maximum anticipated enrollment of 64.

**3.4.1.2.1 Eligible nurses and physicians will meet the following inclusion criteria:**

- Directly or indirectly involved in the care of bronchiolitis patients or EMO Trial operations at the site of interest during the trial period
- Fluent in English

**3.4.1.2.2 Nurses and physicians will be excluded if they meet any of the following exclusion criteria:**

- No exclusion criteria

**3.4.2 Population 2a**

*Bronchiolitis patients directly observed while not receiving supplemental oxygen ("in room air," for primary trial outcome).* Since the goal of the deimplementation strategies is to align practice with existing national guidelines, we aim to improve the care of children age 2-23 months old with bronchiolitis who are in room air, have not received supplemental oxygen in the preceding hour, and do not have history of apnea or cyanosis during the current illness.

We calculate maximum anticipated enrollment as follows based on our target of 90 patients/participating hospital/phase plus a 10% margin:

Phase 1:  $90 \times 45 = 4050$

Phase 2:  $90 \times 32 = 2880$

Phase 3:  $90 \times 32 = 2880$

Phase 4:  $90 \times 16 = 1260^*$

*\*despite increasing the sites to 16 from 14, we are intentionally not changing the previously calculated 1260 maximum anticipated enrollment, as we do not expect to exceed this number.*

Total maximum anticipated enrollment =  $11,070 \times 1.10 = 12,177$

**3.4.2.1 Eligible patients will meet the following inclusion criteria:**

- Infants and children 2 months through 23 months old
- Hospitalized on non-ICU, non-emergency department, non-step down units participating in the trial
- Cared for by generalist inpatient services (e.g. general pediatrics, hospital medicine)
- Primary diagnosis of bronchiolitis in most recent physician progress note
- Not actively receiving supplemental oxygen ("in room air")

- Last documented receipt of supplemental oxygen >1 hour prior to direct observational data collection

**3.4.2.2 Patients will be excluded if they meet any of the following exclusion criteria:**

- Documented apnea or cyanosis during the current illness
- Extreme prematurity (<28 weeks completed gestation)
- Cardiac disease
- Pulmonary hypertension
- Chronic lung disease
- Home oxygen requirement
- Neuromuscular disease
- Immunodeficiency
- Cancer
- Covid-19 / SARS-CoV-2-related illness (known or suspected, including multisystem inflammatory syndrome in children [MIS-C])

**3.4.3 Population 2b**

*Bronchiolitis patients directly observed while receiving supplemental oxygen (for underuse evaluation).* In Aim 3, we are seeking to identify potential unintended consequences of deimplementation strategies aiming to reduce continuous SpO<sub>2</sub> monitoring in bronchiolitis patients who are in room air. One potential unintended consequence is underuse of monitoring in higher risk patients. In Aim 3, we define underuse as failing to continuously monitor bronchiolitis patients receiving ≥2L/min supplemental oxygen or ≥2L/min of supplemental room air flow via any respiratory support device (a marker of more severe disease). We will measure it using the same in-person bedside observational data collection methods as in Aim 1, but use them in this distinct population of patients receiving oxygen.

We calculate maximum anticipated enrollment as follows based on 35 patients/participating hospital/phase plus a 10% additional margin:

Phase 1: 35\*45 = 1575

Phase 2: 35\*32 = 1120

Phase 3: 35\*32 = 1120

Phase 4: 35\*16 = 490

*\*despite increasing the sites to 16 from 14, we are intentionally not changing the previously calculated 490 maximum anticipated enrollment, as we do not expect to exceed this number.*

Total maximum anticipated enrollment = 4305\*1.10 = 4736

**3.4.3.1 Eligible patients will meet the following inclusion criteria:**

- Infants and children 2 months through 23 months old
- Hospitalized on non-ICU, non-emergency department, non-step down units participating in the trial
- Cared for by generalist inpatient services (e.g. general pediatrics, hospital medicine)
- Primary diagnosis of bronchiolitis in most recent physician progress note
- Actively receiving ≥2L/min supplemental oxygen or 21% room air flow

**3.4.3.2 Patients will be excluded if they meet any of the following exclusion criteria:**

- Extreme prematurity (<28 weeks completed gestation)

- Cardiac disease
- Pulmonary hypertension
- Chronic lung disease
- Home oxygen requirement
- Neuromuscular disease
- Immunodeficiency
- Cancer
- Covid-19 / SARS-CoV-2 (known or suspected)

#### 3.4.4 Population 3

*Parents or guardians of bronchiolitis patients who participate in qualitative interviews.* In Aim 2, we will conduct semi-structured interviews with parents or guardians of children hospitalized with bronchiolitis who were found to be in room air during Aim 1 data collection. Maximum anticipated enrollment 20.

##### 3.4.4.1 Eligible parents or guardians will meet the following inclusion criteria:

- Their child was hospitalized for bronchiolitis on a unit participating in the trial during the most recent bronchiolitis season
- Their child was found to be in room air during Aim 1 data collection
- Fluent in English

##### 3.4.4.2 Parents or guardians will be excluded if they meet any of the following exclusion criteria:

- They are an employee of the hospital or a hospital volunteer

#### 3.4.5 Population 4

*Clinical Decision Support (CDS) Coaches who participate in qualitative interviews.* In Phase 4 we will conduct semi-structured interviews with CDS Coaches. Maximum anticipated enrollment: 10

##### 3.4.5.1 Eligible CDS Coaches will meet the following inclusion criteria:

- They were a CDS Coach for one or more sites during Phase 2 and/or Phase 3.
- Fluent in English

##### 3.4.5.2 Eligible CDS Coaches will be excluded if they meet any of the following exclusion criteria:

- No exclusion criteria

## 4 STUDY PROCEDURES

### 4.1 Description of interventions (deimplementation strategies)

#### 4.1.1 Unlearning (both study arms)

##### 4.1.1.1 Educational outreach

Educational outreach will focus on communicating core messages to staff including the national guidelines, the evidence and rationale underlying the guidelines, and talking points to use if parents ask about monitoring, using language adapted from a successful parent-focused intervention.<sup>68</sup> The educational materials used in our pilot trial will be reviewed and updated with input from the Advisory Committee and Family Advisors, to ensure the parent perspective is represented and to navigate any issues related to family-facing communications. Outreach to clinicians will include several formats: (1) in-person educational outreach sessions delivered in site-specific forums (e.g., staff meetings, safety huddles<sup>69,70</sup>) and led by the Site PI or designee and/or a nurse partner (depending on

audience). Sessions will occur weekly during day and night shifts in the month prior to the start of active deimplementation, with refresher sessions monthly for the remainder of P2. (2) Handouts and posters locally adapted with each hospital's institutional logos and design standards, posted in key locations (e.g. unit break room). (3) Short educational videos and messaging distributed using an email marketing platform (e.g., Constant Contact<sup>71</sup>) that enables measurement of open rates, clicks, and message engagement. All educational messaging will be designed to minimize the likelihood of psychological reactance by minimizing choice-restricting language, using a collaborative tone, and emphasizing justification for recommendations.<sup>60</sup> All messaging will be field tested with clinicians in virtual focus groups prior to launch.

#### 4.1.1.2 Audit & Feedback

Audit & feedback will match our successful pilot study methods<sup>55</sup> and will include two levels: (1) weekly unit-level feedback and (2) real-time 1:1 feedback to clinicians. Weekly unit-level feedback will be based on findings from direct observation of bronchiolitis patients in room air, as described in Aim 1 methods. Each week, the Data Coordinating Center (DCC) will compute the prior week's continuous SpO<sub>2</sub> overuse rate and distribute these data to sites in the form of a pdf visual dashboard that includes comparisons over time and between hospitals. The dashboard will then be shared locally with clinicians in person (through educational outreach channels) and via email. In contrast, real-time 1:1 feedback will occur at the clinician level. When collecting data on an individual patient, data collectors encountering guideline-discordant continuous monitoring are empowered to briefly ask any available clinician responsible for that patient's care, in a nonjudgmental way, about indications for monitoring that patient. The clinician is ultimately responsible for deciding if any changes are indicated. In our 6-hospital pilot,<sup>55</sup> real-time feedback was provided for 73% of eligible patients, demonstrating feasibility.

#### 4.1.2 Substitution (experimental arm only)

The substitution strategy includes a clinical pathway integrated into the EHR.

##### 4.1.2.1 Clinical pathway

Clinical pathways guide clinicians step-by-step through evidence-based care.<sup>72</sup> Guidelines state that continuous SpO<sub>2</sub> monitoring should be used in bronchiolitis only if the patient is actively receiving supplemental oxygen or previously experienced apnea or cyanosis.<sup>14</sup> For patients continuously monitored due to a supplemental oxygen requirement, guidelines recommend transitioning to intermittent SpO<sub>2</sub> measurement within 1 hour of achieving saturations ≥90% in room air.<sup>14</sup> During Year 1 of the trial, clinician stakeholders, Family Advisors, and our Advisory Committee will participate in a virtual guideline-to-pathway translation exercise led by Co-I Schondelmeyer, who led the Delphi process resulting in the BEEP guidelines<sup>14</sup> and has prior experience translating guidelines to pathways.<sup>49,73–75</sup> Based on the existing guidelines, the new Eliminating Monitor Overuse (EMO) pathway will clearly specify (a) situations when it is appropriate to initiate intermittent SpO<sub>2</sub> measurement (the alternative practice) instead of continuous SpO<sub>2</sub> monitoring, and (b) when it is appropriate to discontinue continuous SpO<sub>2</sub> monitoring and transition to intermittent SpO<sub>2</sub> measurement. We will make the pathway available via web link exclusively to hospitals randomized to the unlearning + substitution arm.

##### 4.1.2.2 EHR integration

Table 2. Guiding principles for pathway EHR integration.	
Right information	When to initiate intermittent measurement instead of continuous monitoring When to transition from continuous monitoring to intermittent measurement after supplemental oxygen is discontinued
Right people	Physicians who order monitoring Nurses who monitor patients for clinical changes and place or remove monitoring equipment
Right channels	EHR and Clinical Pathways Program webpage (via web link exclusively to

	unlearning + substitution arm hospitals)
Right points in workflow	Hospital admission, supplemental oxygen management, rounds
Right format(s) may include, but not be limited to, any combination of:	<ul style="list-style-type: none"> <li>• EHR-embedded link to pathway website presented to clinicians at appropriate points in workflow (minimum standard)</li> <li>• Order set for bronchiolitis monitoring that guides physicians to appropriately order (a) guideline-concordant monitoring initiation and (b) transition to intermittent measurement, and clearly communicates instructions to staff</li> <li>• Clinical reminder / alert that notifies nurses that continuous monitoring may no longer be indicated based on a documented discontinuation of supplemental oxygen</li> </ul>

We have developed guiding principles that will facilitate a standard approach to EHR integration while also allowing flexibility in format (Table 2). This pragmatic approach is directly aligned with recommendations for research involving flexible EHR-based strategies.<sup>76</sup> Flexibility is essential to the success of this strategy because EHR software, configuration, resources, and context vary between hospitals; it would be unrealistic to expect all hospitals to integrate pathway recommendations in exactly the same way.<sup>76</sup> Instead of standardizing the software itself, we will standardize the process and function of the intervention (an approach promoted by the UK Medical Research Council).<sup>77,78</sup>

Since integrating pathways into the EHR is a form of clinical decision support (CDS), we have standardized the process of EHR integration around the “Five Rights of CDS,” aiming to ensure delivery of (1) the right information, (2) to the right people, (3) in the right intervention format, (4) through the right channels, (5) at the right point in workflow.<sup>79,80</sup> We have set a very feasible minimum standard for pathway EHR integration that requires minimal effort to ensure that all hospitals have at least the most basic form of CDS in place at the start of the active deimplementation period (P2): an EHR-embedded link to the clinical pathway website inserted into the EHR at appropriate points in workflow (e.g. within monitoring order forms and nursing vital sign flowsheets). For sites that have some form of existing CDS providing the “right information,” the goal

**Table 3.** Measures and timing of measurement throughout the trial. Details of each measure in Section 5.

Measure	Aim	P1	P2	P3	P4
Use of continuous pulse oximetry (to calculate penetration, sustainability, and underuse)	1,3	X	X	X	X
Acceptability	1		X		
Routinization & institutionalization	2		X	X	
Implementation climate	2		X		
Implementation leadership	2		X		
Psychological reactance	2		X		
Fidelity	1		X		
Cost	1		X	X	
Qualitative inquiry (staff & parents)	2			X	X
Length of hospital stay	3	X	X	X	
Oxygen supplementation duration	3	X	X	X	
Safety monitoring	N/A	X	X	X	X

of the EHR-integration will be to optimize the EHR CDS to better fit the local context and maximize the capability of the CDS based on the EHR and local infrastructure.

In order to match local capabilities to EHR CDS formats, we have partnered with the national Pediatric CDS Collaborative (PCC). Following randomization, each site assigned to the unlearning +

substitution arm will be matched with an EHR integration “coach” from PCC who has experience implementing CDS across institutions. Each coach will facilitate integration of the clinical pathway into the local EHR by liaising directly with the Site PI, local clinicians, and informatics staff to ensure that CDS meeting the criteria in Table 3 is built on time and in a way that matches local capabilities. Because EHR interventions should be optimized over time to meet the evolving needs of clinicians, coaches will continue meeting with the site team members through the end of P3 to assist with optimizations and software updates, or to align with new bronchiolitis guidelines (should they emerge). The flexibility and ongoing optimization of the EHR-integrated pathway is a pragmatic strength of this proposal entirely consistent with the foundations of implementation science and clinical informatics, and one that will result in locally-developed EHR integration that matches local workflows.<sup>76</sup>

## 4.2 Procedures within each study phase (see also Table 3)

### 4.2.1 Baseline Phase (P1)

- Measure baseline use of continuous SpO<sub>2</sub> monitoring in patients with bronchiolitis who are in room air using direct observation
- Medical record review
- Measure length of hospital stay in bronchiolitis patients
- Measure oxygen supplementation duration in bronchiolitis patients
- Underuse of continuous SpO<sub>2</sub> monitoring in patients with bronchiolitis who are receiving ≥2L/min supplemental oxygen or ≥2L/min of supplemental room air flow via any respiratory support device (are inappropriately unmonitored).
- Measure baseline EHR CDS alignment with the 5 rights using same approach used to assess fidelity in P2
- Cluster-randomize hospitals with the lowest baseline penetration to either: the unlearning only arm (educational outreach with A&F) or the unlearning + substitution arm (adding an EHR-integrated clinical pathway to facilitate the transition from continuous SpO<sub>2</sub> monitoring to intermittent SpO<sub>2</sub> measurement when clinically appropriate).

### 4.2.2 Active Deimplementation Phase (P2)

- Deimplementation strategies (interventions) are deployed
  - unlearning only arm: educational outreach with A&F
  - unlearning + substitution arm: educational outreach with A&F + an EHR-integrated clinical pathway to facilitate the transition from continuous SpO<sub>2</sub> monitoring to intermittent SpO<sub>2</sub> measurement when clinically appropriate
- Measure use of continuous SpO<sub>2</sub> monitoring in patients with bronchiolitis who are in room air using direct observation
- Medical record review
- Measure acceptability using questionnaire
- Measure routinization & institutionalization using questionnaire
- Measure implementation climate and leadership using questionnaire
- Measure psychological reactance using questionnaire
- Measure fidelity to each deimplementation strategy
- Assess costs associated with delivering each deimplementation strategy
- Measure length of hospital stay in bronchiolitis patients
- Measure oxygen supplementation duration in bronchiolitis patients
- Underuse of continuous SpO<sub>2</sub> monitoring in patients with bronchiolitis who are receiving ≥2L/min supplemental oxygen or ≥2L/min of supplemental room air flow via any respiratory support device (are inappropriately unmonitored).

- At the end of P2, unlearning (educational outreach with A&F) interventions are withdrawn from both arms.

#### 4.2.3 Sustainability Phase (P3)

- Substitution (EHR-integrated pathway) is maintained exclusively in the unlearning + substitution arm
- Measure use of continuous SpO<sub>2</sub> monitoring in patients with bronchiolitis who are in room air using direct observation
- Medical record review
- Measure routinization & institutionalization using questionnaire
- Assess costs associated with delivering each deimplementation strategy
- Qualitative interviews aiming to better understand mechanisms of practice change in response to each deimplementation strategy
- Qualitative interviews of parents/guardians of children hospitalized with bronchiolitis to explore their perceptions of, and reactions to, deimplementation activities
- Measure length of hospital stay in bronchiolitis patients
- Measure oxygen supplementation duration in bronchiolitis patients
- Underuse of continuous SpO<sub>2</sub> monitoring in patients with bronchiolitis who are receiving  $\geq 2$ L/min supplemental oxygen or  $\geq 2$ L/min of supplemental room air flow via any respiratory support device (are inappropriately unmonitored).
- Calculate primary outcome of sustainability of guideline-concordant deimplementation (calculated based on use of continuous SpO<sub>2</sub> monitoring in patients with bronchiolitis who are in room air over time)
- Validate suctioning data by communicating with a clinical staff member to confirm data entries in the EHR are correct

#### 4.2.4 Exploratory Phase (P4)

- Identify the hospitals that meet criteria for participation in the exploratory data collection phase
  - We will create four groups consisting of four hospitals each based on the following characteristics: (1) Freestanding/Non-freestanding Children's Hospitals and (2) pre-existing CDS presence/no pre-existing CDS presence
    - If there are  $\leq 4$  hospitals available in that group, invite all of them,
    - If there are more than 4, we would first filter out hospitals that did not meet the criteria of statistical significant drop in overuse between P1 and P2 (Experienced a significant increase in penetration of guideline-concordant care between P1 and P2)
    - If still have  $>4$  remaining, we would filter out hospitals that did not meet the 90% penetration sustainment margin (Maintained the increased penetration at  $\geq 90\%$  of the P2 percentage [an established margin<sup>37</sup>] through P3)
    - If still have  $>4$  remaining, we would sort the hospitals by the numeric gap between the hospital's measured P3 penetration and the P2 90% margin and select the 4 with the smallest gap (best sustainment)
- Measure use of continuous SpO<sub>2</sub> monitoring in patients with bronchiolitis who are in room air using direct observation
- Medical record review
- Qualitative interviews aiming to better understand mechanisms of practice change in response to each deimplementation strategy
- Qualitative interviews of parents/guardians of children hospitalized with bronchiolitis to explore their perceptions of, and reactions to, deimplementation activities
- Underuse of continuous SpO<sub>2</sub> monitoring in patients with bronchiolitis who are receiving  $\geq 2$ L/min supplemental oxygen or  $\geq 2$ L/min of supplemental room air flow via any respiratory support device (are inappropriately unmonitored).

## 5 STUDY EVALUATIONS AND MEASUREMENTS

### 5.1 Measure use of continuous SpO<sub>2</sub> monitoring in patients with bronchiolitis who are in room air using direct observation

We will perform direct observation of continuous SpO<sub>2</sub> monitoring in order to measure its use, as we have done successfully in prior studies.<sup>24,55</sup> As in the prior studies, we will simultaneously assess cardiorespiratory (electrocardiographic) monitoring. We must directly observe because our prior research has shown that analyzing orders for monitoring does not accurately capture actual monitoring status.<sup>81</sup> Research staff at each hospital will perform cross-sectional observational data collection rounds during the study periods. During these data collection rounds, trained research staff walk to each hospital unit with eligible children. On the unit, staff determine the continuous monitoring status of each patient based on either (a) going to the bedside and visually examining the waveforms displayed on the monitor, or (b) going to a central monitoring station that displays the waveforms of multiple patients on the unit and visually examining the waveforms displayed on the monitor for the eligible child. Repeated over time, this method captures repeated cross-sections of penetration of guideline-concordant care, which is used to subsequently calculate the primary outcome of sustainability (see Statistical Considerations). *Repeated measures in the same patient are permitted as long as they are separated by at least 6 hours.*

We have previously shown that, in hospitals that use the Epic EHR and have physiologic monitor integration with the EHR, examining the EHR for the presence of monitor data is a valid method for assessing the bedside monitoring status. The following approaches are permissible alternatives to direct in-person observation to determine continuous monitoring status:

- In hospitals with physiologic monitor device integration with the EHR, visualizing device-integrated monitor data in EHR flowsheets, reports, or real-time waveform displays.
- In hospitals with clinical remote monitor viewing applications approved for clinical use at their institution (e.g. Airstrip, Philips, GE, Sickbay, Etiometry), visualizing remote monitor data in flowsheets, reports, or real-time waveform displays.

During the observational rounds, as in our prior studies, we will also assess/confirm the supplemental oxygen / flow status (current device, flowrate, %FiO<sub>2</sub>) since the hospital chart may not always be perfectly accurate. This assessment may be performed using any of the following methods:

- Visual assessment at the bedside
- Asking a clinician caring for or overseeing the care of the patient (e.g. nurse, charge nurse, physician, respiratory therapist, medical assistant) either in-person, by telephone, or through a hospital-approved clinical communication / messaging platform (e.g. Epic SecureChat, TigerText, Voalte, Ascom).

#### 5.1.1 Medical record review

After direct observational data collection rounds, staff perform chart review for demographics and other covariates used in previous research:

- Local hospital medical record number (required for tracking across admissions)
- Local hospital patient admission /account number (required for tracking within admissions)
- Date of birth (required for accurately tracking and validating age in days over time)

- Patient initials (as a secondary means of verifying the patient's identity in the databases)
- Hospital
- Admission date and time
- Discharge date and time
- Unit name
- Bed number
- Patient age
- Patient sex
- Patient race and ethnicity
- Patient primary diagnosis and chronic conditions
- Forms of chronic neurologic impairment (e.g. static encephalopathy, cerebral palsy, hydrocephalus, spina bifida, epilepsy/seizure disorder, hypotonia, other form of neurologic impairment)
- Technology dependence (e.g. short-term feeding tube, long-term feeding tube, central venous line, renal dialysis)
- History of ICU stay earlier in this admission, with dates and times of ICU stays
- Patient gestational age
- Characteristics of supplemental oxygen administration (flow rate, fraction of inspired oxygen, oxygen delivery device, maximum support during hospitalization), also including dates of initiation, adjustment, discontinuation, last documented time on supplemental oxygen.
  - Admission weight in Kilograms
  - High Flow Nasal Canula (HFNC) use:
    - Characteristics of patient at time of initiation: time/date, initial flow rate, initial FiO<sub>2</sub>, SpO<sub>2</sub>, Respiratory Rate (RR)
    - Characteristics of patient prior to initiation: Mode of oxygen delivery, time/date SpO<sub>2</sub> last documented and SpO<sub>2</sub> rate, time/date RR last documented and RR
    - Respiratory or general exam flowsheet: time/date of flowsheet, characteristics observed (head bobbing, grunting, altered mental status), and any free text notes
    - Physical exam clinical note (e.g., event note, progress note, RRT documentation or nurse/RT flowsheet assessment): time/date of note, general exam and respiratory exam findings, and any free text notes

- Blood gas: time/date of sample, pH, CO<sub>2</sub>, source (venous/arterial/capillary/unknown)
- Highest documented HFNC flow rate and highest documented FiO<sub>2</sub>
- Last documented time/date of HFNC and/or time/date of transition to LFNC or room air
- Final flow rate, last documented FiO<sub>2</sub> 21%, time/date of change to FiO<sub>2</sub> 21%
- Laboratory testing and imaging studies that may indicate other forms of medical overuse (e.g. respiratory viral testing, chest x-rays), including results of those studies.
- Medication administration that may indicate other forms of medical overuse (e.g. bronchodilators).
- Characteristics of enteral, intravenous, subcutaneous, and other forms of fluid administration
- Limited English Proficiency status of family, as evidenced by chart review suggesting that there is a language barrier, limited English proficiency, interpreter needed, interpreter previously used to communicate with this family, that the preferred language of patient/family is something other than English, or other similar documentation.
- Role composition / staffing model of the team caring for the patient, for example, the team was comprised of attending physicians supervising nurse practitioners, vs. the team was comprised of an attending physician supervising residents and medical students; the nurse:patient ratio was 1:3, the respiratory therapist:patient ratio was 1:8.
- Unit characteristics including unit census, cohorting of bronchiolitis patients in specific respiratory care areas, and the presence of oxygen weaning protocols.
- How long have they been off respiratory support (e.g. supplemental oxygen or room air flow), according to the chart?
- Are any pulse oximetry measurements documented in the chart since the patient has been off respiratory support (e.g. supplemental oxygen or room air flow) as an indication that intermittent SpO<sub>2</sub> measurement is taking place?
- Primary site where patient receives primary care
- Post-hospitalization Primary Care follow-up recommendations and subsequent appointment information
- Characteristics of instances of respiratory suctioning, including the date/time of suctioning, the route of suctioning (e.g. nasal), the role of the person performing the suctioning (e.g. respiratory therapist), and any comments about clinical sequelae of the suctioning documented in the EHR (e.g. "improved" or "coughing")

## 5.2 Questionnaires

Site PIs will prepare lists of the nurses and physicians who provide care for bronchiolitis patients on the units participating in the study, as well as administrators who oversee the medical care and safety for bronchiolitis patients at institutional and unit levels. Questionnaires will be distributed electronically and managed centrally from the DCC using REDCap.

For hospitals that elect not to provide the DCC with staff contact information for questionnaire distribution, the site PIs or their designees will distribute a survey link to the relevant stakeholder groups or administer the questionnaire (without any PHI) on paper for subsequent entry into REDCap.

Questionnaire items are included in the eIRB appendix. We will submit amendments to the IRB for any changes to the questionnaire prior to distribution. No questionnaire items will involve PHI.

### 5.2.1 Measure acceptability using questionnaire

Acceptability among nurses and physicians will be measured using items adapted from the 4-item Acceptability of Intervention Measure (AIM)<sup>56</sup> previously used in our pilot study. We have also included items from our pilot study questionnaire covering feasibility, appropriateness, and perceived safety. See appendix in eIRB.

### 5.2.2 Measure routinization & institutionalization using questionnaire

We will use an adapted version of the valid and reliable Slaghuys measurement instrument for sustainability of work practices to assess the potential mediators: routinization & institutionalization.<sup>57</sup> The instrument assesses two closely related but conceptually distinct processes: routinization, in which clinicians develop new routines such that the practice change becomes part of their everyday work, and institutionalization, in which the organization embeds the practice change into its existing systems and structures. See appendix file for draft questionnaire items.

### 5.2.3 Measure implementation climate and leadership using questionnaire

We will administer the Implementation Climate Scale to understand whether the environment expects, supports, and rewards deimplementation of continuous SpO<sub>2</sub> monitoring.<sup>58</sup> We will measure implementation leadership using the Implementation Leadership Scale to understand leader behaviors (e.g., proactive, knowledgeable, and supportive of deimplementation).<sup>59</sup>

### 5.2.4 Measure psychological reactance using questionnaire

We will measure psychological reactance in clinicians using the same multiple choice instruments used in seminal reactance work<sup>60</sup> adapted as necessary to this deimplementation trial to assess (1) perceptions of threats to freedom in response to deimplementation messaging, (2) emotional responses, and (3) cognitive responses.<sup>60,62,63</sup>

## 5.3 Measure fidelity to each deimplementation strategy

Deimplementation fidelity is the extent to which educational outreach, A&F, and the EHR-integrated clinical pathways are performed per protocol. Fidelity data for educational outreach and A&F will be extracted from intervention logs maintained by Site PIs and entered into a data collection form. Fidelity data for the EHR integration will be assessed (at baseline as a benchmark of pre-existing EHR CDS and then later in P2 as a fidelity measure) using local EHR screenshots and descriptions uploaded by each site to assess alignment of the actual EHR interface with each informatics guiding principle in Table 2. Each principle will be scored independently by 2 clinical informaticists as being fully met, partially met, or not met for each hospital.

#### **5.4 Assess costs associated with delivering each deimplementation strategy**

Cost of delivering each of the strategies will be assessed using a Time-Driven Activity Based Costing method,<sup>84</sup> based on who (personnel completing the task) does what (specific activities performed), when (timing), and how often (the frequency, intensity, and/or duration of the activity). First, we will create a step-by-step process map that carefully specifies activities within the unlearning and substitution strategies. We will specify the names of specific strategies (e.g., conducting A&F sessions), actions (specific procedures that need to be performed, e.g., holding weekly unit-based in-person group discussion) and actors (who is involved in the procedures, e.g., EHR coach, clinician) in each strategy. Second, we will determine frequency and duration of each of these actions. Once we determine how many times an actor participated in a given action and the duration of the action, multiplying frequency and duration will yield total time spent by the actor on a given action. Multiplying this by the actor's hourly wage rate will yield total cost incurred by that actor to perform that specific action. The total cost of an action is the sum of costs incurred by each actor who participated in that action. In this way, we will determine cost of each action in each implementation strategy. Adding up the cost of each action of a specific implementation strategy will yield the total cost of personnel resources for that strategy. For non-personnel resources, we will itemize consumable equipment, supplies (training materials, assessment and evaluation materials, office supplies, etc.). Cost of each item will be determined from administrative records. Personnel and non-personnel costs will be added together to determine overall unlearning and substitution strategy costs. In this way, we will discretely outline the entirety of the unlearning and substitution process and assign resource use and costs to these processes to a high degree of specificity. We expect there to be communication-related actions that are not protocolized, such as staff responding to emails, making phone calls and holding in-person meetings to provide assistance as needs arise. To estimate frequency and duration of these type of actions, we will choose a defined period during active implementation and ask staff to save their emails and record their scheduled phone calls and in-person meetings on their calendar so we can determine an estimate of the frequency of communication. We will also ask them to provide an estimate of the average duration of these communications.

#### **5.5 Clinical outcomes**

We will measure the primary clinical outcome of LOS and the secondary clinical outcome of oxygen supplementation duration in the cohort of patients whose data were collected in Aim 1, using chart review performed at each site after hospital discharge.

##### **5.5.1 Measure length of hospital stay (LOS) in bronchiolitis patients**

LOS is defined as the time interval in minutes from admission to an inpatient or observation hospital unit until discharge from an inpatient or observation hospital unit.

##### **5.5.2 Measure oxygen supplementation duration in bronchiolitis patients**

Total oxygen supplementation duration is defined as the total minutes during the entire admission that the patient received any supplemental oxygen or supplemental flow of room air via any respiratory support device (e.g. high flow nasal cannula, ventilator).

#### **5.6 Qualitative interviews aiming to better understand mechanisms of practice change in response to each deimplementation strategy**

Our qualitative inquiry aims to better understand mechanisms of practice change in response to each deimplementation strategy. Using a deviance approach,<sup>85,86</sup> we will conduct semi-structured interviews with nurses and physicians who provide care to bronchiolitis patients at the end of P4 (the exploratory study phase that examines sustainability 2 years after withdrawal of educational outreach and A&F) as well as with CDS Coaches. In collaboration with site PIs, eligible clinicians will be identified purposively from staff rosters and invited to participate in interviews by telephone call, texting, and/or emailing to discuss the process of deimplementation as experienced by stakeholders. Purposive sampling will seek to obtain a wide range of nurse and physician experience levels, nurse

and physician supervisory vs front line care roles, nurse shift (day vs night shift), and physician care model (teaching service vs attending-only hospitalist model). Interviews will explore mechanistic relationships between (a) the strategies, (b) the findings of the quantitative measures above, and (c) sustainability. Interviews will be conducted by telephone or using teleconferencing software (e.g. Zoom, BlueJeans, Teams). Interviews will be recorded. The participant will be permitted to choose the format (telephone vs teleconferencing software with audio-only vs teleconferencing software with audio and video). The informed consent process will include discussion that if the participant elects to conduct the interview with video on, the video will also be recorded.

The staff member's email address will be collected in order to send a recruitment email. They will be provided a copy of their consent form by email or mail. In order to provide the staff member with a copy of their consent form, we will also collect their mailing address if mail is their preferred means of receiving that document.

A sample interview guide is attached. As is standard practice in qualitative research, the interview guide will be a fluid document that will be modified and updated as we proceed with interviews. We will not submit amendments to the IRB for changes to the interview guide unless there are major changes in the scope. No interview questions will involve PHI.

#### **5.7 Qualitative interviews of parents/guardians of children hospitalized with bronchiolitis to explore their perceptions of, and reactions to, deimplementation activities**

We will conduct semi-structured interviews with parents or guardians of children hospitalized with bronchiolitis who were found to be in room air during Aim 1 data collection. Eligible parents or guardians will be identified purposively from bronchiolitis patients' trial records during P3 and invited to interview by telephone call, texting, and/or emailing during the 8 weeks following discharge in order to explore their perceptions of, and reactions to, SpO<sub>2</sub> deimplementation activities. Purposive sampling will seek to obtain a wide range of patient ages since parents' perspectives likely differ for very young infants (e.g. 2-3 months old) compared to older children (e.g. 18-23 months old). Purposive sampling will also be used to optimize diversity among the participants. In order to optimize diversity across racial and ethnic groups, we will first recruit 5 patients, then assess the racial makeup of the sample, and target for the distribution of all 15 patients to be 1/3 Hispanic Black, 1/3 Non-Hispanic Black, and 1/3 Other. Interviews will be conducted by telephone or using teleconferencing software (e.g. Zoom, BlueJeans, Teams). Interviews will be recorded. The participant will be permitted to choose the format (telephone vs teleconferencing software with audio-only vs teleconferencing software with audio and video). The informed consent process will include discussion that if the participant elects to conduct the interview with video on, the video will also be recorded.

Parent or guardian names, email addresses, and telephone numbers will be collected for recruitment purposes. They will be provided a copy of their consent form by email or mail. In order to provide the parent or guardian with a copy of their consent form, we will collect the parent/guardian's email address and/or mailing address, depending on their preferred means of receiving that document.

A sample interview guide is attached. As is standard practice in qualitative research, the interview guide will be a fluid document that will be modified and updated as we proceed with interviews. We will not submit amendments to the IRB for changes to the interview guide unless there are major changes in the scope. No interview questions will involve PHI.

#### **5.8 Underuse of continuous SpO<sub>2</sub> monitoring in patients with bronchiolitis who are receiving $\geq 2\text{L/min}$ oxygen (are inappropriately unmonitored).**

We will also collect additional data to capture any underuse of monitoring in higher risk patients that could plausibly occur in response to deimplementation. We define underuse as failing to continuously monitor bronchiolitis patients receiving  $\geq 2\text{L/min}$  supplemental oxygen or  $\geq 2\text{L/min}$  of supplemental room air flow via any respiratory support device (a marker of more severe disease)<sup>5</sup> and will measure it using the same in-person bedside observational data collection methods used to observe patients in room air during Aim 1 (and in practice, sites will likely perform these

observational rounds for this distinct population simultaneously with observational rounds for Aim 1). See Section 5.1 above for data collection methods.

### 5.9 Monitoring for Equitable Deimplementation

The DCC will perform monthly surveillance for signals in the data that may suggest hospital- or study-level inequities in deimplementation stratified by patient race and ethnicity and generate descriptive reports throughout the trial. These reports will be periodically reviewed by the investigative team and DSMB.

## 6 STATISTICAL CONSIDERATIONS

### 6.1 Primary Endpoint

The primary endpoint is the sustainability of guideline-concordant deimplementation of continuous SpO<sub>2</sub> monitoring.

### 6.2 Secondary Endpoints

Secondary endpoints will include the following:

- The changes in penetration of guideline-concordant care within each study arm
- The acceptability, feasibility, appropriateness, and perceived safety of deimplementation among staff, compared between nurses and physicians
- The mediation effects of routinization and institutionalization
- The moderation effects of implementation climate, implementation leadership, and psychological reactance
- Fidelity to each deimplementation strategy
- Costs associated with delivering each deimplementation strategy
- The relationship between penetration of guideline-concordant care and length of hospital stay (LOS) in bronchiolitis patients
- The relationship between penetration of guideline-concordant care and oxygen supplementation duration in bronchiolitis patients
- Themes from qualitative interviews
- Underuse of continuous SpO<sub>2</sub> monitoring in patients with bronchiolitis who are receiving  $\geq 2$ L/min supplemental oxygen or  $\geq 2$ L/min of supplemental room air flow via any respiratory support device.
- Exploration of deimplementation inequities

### 6.3 Statistical Methods

#### 6.3.1 PRIMARY ENDPOINT: Sustainability of guideline-concordant deimplementation of continuous SpO<sub>2</sub> monitoring

We will analyze sustainability as a longitudinal difference in differences comparison between study arms of the change in penetration between baseline (P1) and the phase after withdrawal of educational outreach and A&F (P3), expressed as (P3-P1 | Arm 2) - (P3-P1 | Arm 1). Penetration is defined as the percentage of bronchiolitis patients in room air who are receiving guideline-concordant care: appropriately not being continuously SpO<sub>2</sub>-monitored. In order to make this

comparison, we will use the patient-level direct observation data that includes the binary outcome of monitored vs. unmonitored. We will use generalized hierarchical mixed-effects models with logit link for longitudinal binary outcome data. We will include hospital- and patient-specific random intercepts and slopes to account for clustering. We will apply spline-based piecewise regression in the mixed-effects models to allow for estimation of trajectories over time, with the start of each phase being the pre-specified knots. The model will include two time variables, one indicating the week number and one indicating the phase (i.e. P1, P2, P3). The interaction between spline-specific slope and intervention will be included in the model to assess the difference in differences between study arms. To account for differences in patient-level factors that cannot be accounted for by the cluster-randomization, we will adjust for the same covariates used in previous research, including age, gestational age, time since weaning from supplemental oxygen, presence of an enteral feeding tube, neurologic impairment, and overnight observation. Statistical contrasts at the hospital level will be made using postestimation marginal effects. These methods facilitate estimation of standardized (for patient-level characteristics) sustainability and the effect of adding the substitution strategy to the unlearning strategy. We will perform a sensitivity analysis considering the hospital unit as an additional level of clustering in the hierarchical model.

### **6.3.2 The changes in penetration of guideline-concordant care within each study arm**

Penetration during active deimplementation will be analyzed using a similar model to that described above for sustainability, with contrasts of interest within each study arm (not differences in differences): P2-P1 | Arm 1; P2-P1 | Arm 2.

#### **6.3.2.1 Exploratory analysis of penetration including prior years of EMO**

In winter 2018-19 we conducted the original EMO observational study in 56 sites,<sup>24</sup> and in winter 2019-20 we conducted a pilot study in 6 sites. In this exploratory analysis we will include deidentified penetration data available from the prior studies with data from the trial and analyze penetration within-hospital over time using longitudinal regression in hospitals participating in the trial to gain further insight into longitudinal penetration with and without intercurrent interventions.

### **6.3.3 The acceptability of deimplementation among staff, compared between nurses and physicians**

Acceptability (ordinal measure) will be analyzed using ordered logit regression, with comparisons between professions (nurse vs. physician). The same approach will be applied to other questionnaire items assessing feasibility, appropriateness, and perceived safety (see appendix questions in eIRB).

### **6.3.4 The mediation effects of routinization and institutionalization of the practice change on the relationship between the deimplementation strategies and sustainability, penetration**

Mediation analysis allows us to separate the direct effects of an exposure from effects that occur via an intermediate variable (indirect effects). For each outcome (penetration and sustainability) we will perform separate mediation analyses for routinization and institutionalization, each based on dimension-specific scores on the adapted Slaghuis questionnaire. Mediation will be tested using the product of coefficients approach for multilevel mediation analysis,<sup>87-89</sup> which we have used in previous studies.<sup>90-92</sup> In this approach, the total effect of the deimplementation strategy is parsed into direct and indirect effects.

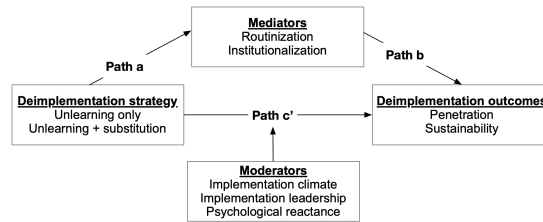


Figure 2. Mediators and moderators.

As shown in Figure 2, “Path a” represents the effect of the deimplementation strategy on the hospital-level mediators. “Path b” represents the effect of the hospital-level mediators on the outcomes. An unbiased estimate of the mediated effect is derived via the product of the “a” and “b” paths (i.e.,  $a*b$ ) from these analyses.<sup>88,89,92</sup> We will test the statistical significance of the mediated effects using the joint

significance test.<sup>93</sup> We will use Monte Carlo simulation methods to derive confidence intervals.<sup>93–96</sup> Given recent developments in the causal mediation analysis literature,<sup>97</sup> we will estimate the indirect effect using both the conventional method described here and using the counterfactually-defined causal effects approach for cluster-randomized studies.<sup>97,98</sup> Models will be estimated in Mplus which permits estimation of both types of effects and includes Monte Carlo simulation facilities for conducting sensitivity analyses useful for evaluating the tenability of embedded assumptions.<sup>99</sup> Moderators of the strategies’ effects will be tested separately by adding terms for each moderator and its interaction with the deimplementation strategy to the Aim 1 models only during the active implementation period.

### 6.3.5 The moderation effects of implementation climate, implementation leadership, and psychological reactance among staff on the relationship between the deimplementation strategies and sustainability, penetration

Moderators will be tested by adding terms for each moderator and its interaction with the strategy to the Aim 1 regression models for penetration and sustainability (Path c’).

### 6.3.6 Fidelity to each deimplementation strategy

Deimplementation fidelity (descriptive) to the unlearning strategy will be calculated as the number of educational outreach and A&F sessions delivered in each hospital divided by the number expected in the protocol during each week and averaged over all weeks of the active deimplementation period. Fidelity to the substitution strategy will be assessed as the extent to which the clinical pathway is integrated according to the “5 Rights” guiding principles; each principle will be scored as being fully met, partially met, or not met and summarized for each hospital.

### 6.3.7 Costs associated with delivering each deimplementation strategy

Analysis for costs is descriptive and the data resulting from the Time-Driven Activity Based Costing method<sup>84</sup> described will be summarized for each of the strategies using descriptive statistics.

### 6.3.8 The relationship between penetration of guideline-concordant care and length of hospital stay (LOS) in bronchiolitis patients in each study phase

The hospital-level penetration for each phase (P1, P2, P3) will be the primary exposure variable. Penetration will be combined with patient-level data that includes LOS. We will use generalized mixed-effects regression to model the LOS (assuming a gamma distribution with a log link function to account for the expected skewed nature of LOS data) and use hospital-specific random intercepts to account for within-hospital clustering. We will estimate the change in LOS for each 5% change in penetration using postestimation marginal effects.

### 6.3.9 The relationship between penetration of guideline-concordant care and oxygen supplementation duration in bronchiolitis patients in each study phase

The hospital-level penetration for each phase (P1, P2, P3) will be the primary exposure variable. Penetration will be combined with patient-level data that includes duration of oxygen supplementation. We will use linear mixed-effects regression to model the duration of oxygen

supplementation (assuming a normal distribution) and use hospital-specific random intercepts to account for within-hospital clustering. We will estimate the change in oxygen supplementation for each 5% change in penetration using postestimation marginal effects.

#### 6.3.10 Themes from qualitative interviews

Interview transcripts will be loaded into NVivo software. Analysis will follow an integrated approach using the CFIR as a starting framework while also allowing new concepts to emerge and become part of the coding scheme. This approach uses an inductive process of iterative coding to identify recurrent themes, categories, and relationships. After initial exploration of the data, a comprehensive coding scheme is developed and applied to all data in order to produce a highly granular descriptive analysis. Two trained team members will separately double-code a sample of the transcripts to assess the reliability of the coding scheme. Disagreements in coding will be resolved through team discussion.

#### 6.3.11 Underuse of continuous SpO<sub>2</sub> monitoring in patients with bronchiolitis who are receiving $\geq 2\text{L}/\text{min}$ oxygen (are inappropriately unmonitored) within each study arm, across all study phases

We will examine underuse of continuous SpO<sub>2</sub> monitoring during P1, P2, and P3 as the percentage of patients with bronchiolitis observed receiving  $\geq 2\text{L}/\text{min}$  supplemental oxygen or  $\geq 2\text{L}/\text{min}$  of supplemental room air flow via any respiratory support device who are inappropriately unmonitored. We will analyze underuse longitudinally and by study arm using similar patient-level mixed-effects logistic regression models as in the primary analysis for Aim 1.

#### 6.3.12 Exploration of deimplementation inequities

Deimplementation inequities will be explored by including patient sex, race, and ethnicity in all regression models (including potential interactions with other exposure variables).

### 6.4 Sample Size and Power

*Winter 2020-2021 saw very low bronchiolitis volumes due to public health measures to contain the SARS-CoV-2 pandemic. If bronchiolitis patient volumes are lower than a typical bronchiolitis season during Phase 1 of this trial, we will re-run power calculations after Phase 1 based on that data and may amend the protocol based on those revised, updated calculations.*

#### 6.4.1 Aim 1 Sample Size and Power

The trial's overall power analysis is based upon the primary deimplementation outcome (sustainability), consistent with hybrid type III. We expect that the pilot study's pre-post effect size of 30 percentage points likely overestimates the effect size expected in this trial. Based on NIH guidance, we have used data from our pilot trial primarily to assess feasibility and understand important design effects (e.g. clustering). Therefore, we have placed greater emphasis on incorporating clinically meaningful differences of 15-20 percentage points (%pts) that, based on consensus of our research team and experts within PRIS, could reasonably impact future guidelines and policy. In this trial, power is primarily driven by the number of hospitals, the variation across hospitals, and the within-hospital correlation over time. The degree of correlation can be expressed as either the intra-cluster correlation coefficient or the between-cluster coefficient of variation. While the two approaches are equally valid, we have used the between-cluster coefficient of variation method in our calculations because it is more flexible and is more readily understood. Table 4 below outlines detectable effect sizes at 80% power based on 12 hospitals/arm remaining at the end of P3 (16 randomized/arm minus 4/arm assuming 25% dropout).

Table 4. Aim 1 primary outcome power calculations. Calculated using PASS 2020, v20.0.1.	
Hypothesis	Effect size at 80% power for n=12 hospitals/arm
Primary (sustainability). When comparing the difference in penetration between P3 and P1, Arm 2 will have a	Power is 80% to detect a difference in differences of <u>16 %pts between P1 and P3</u>

greater difference than Arm 1, expressed as: (P3-P1   Arm 2) - (P3-P1   Arm 1)	<u>among study arms</u> . Using footnote parameter ranges, effect size range is 12-20 %pts.
<b>Secondary (penetration).</b> Each arm will experience greater penetration during P2 compared to P1, expressed as: P2-P1   Arm 1, and P2-P1   Arm 2	Within each arm, power is 81% to detect a difference of <u>12 %pts between P1 and P2</u> . Using footnote parameter ranges, effect size range is 9-16 %pts.
Arm 1 = unlearning only. Arm 2 = unlearning + substitution. <u>Parameters informed by preliminary data:</u> approximately 50% monitored in P1, average 90 patients/hospital/phase, 2-sided alpha=.05, moderate within-hospital correlation across phases of 0.6 (range 0.5-0.7), moderate-high between-hospital standard deviation of 15 %pts (range 13-17). <u>Feasibility note:</u> In the pilot trial, each hospital collected data on an average of 118 unique patients during 1 season.	

#### 6.4.2 Aim 2 Sample Size and Power

##### 6.4.2.1 Quantitative

We have performed a conservative power calculation for mediation effects in logistic regression (since our primary dataset is patient-level with the binary outcome of monitored vs. unmonitored for each patient) using PASS. We assume 12 hospitals/arm, 30 clinician responses/hospital to the adapted Slaghuys questionnaire, correlation of 0.3 between the deimplementation strategy arm indicator variable and the mediator, and penetration in the unlearning only arm of 55% during P3. Using these parameters, we will have 80% power to detect an indirect mediation effect of 1.25, which is interpreted as a 1.25-fold increased odds of guideline-concordant care penetration with each 1 SD increase in the mediator (the dimension-specific score on the adapted Slaghuys questionnaire). This is a conservative estimate because the calculation does not account for the additional power that will be gained due to the two measurement time points in each hospital used for the sustainability outcome.

##### 6.4.2.2 Qualitative

We estimate that we will need to conduct 48 clinician interviews to achieve thematic saturation with 12 interviews across each of the 4 possible profession and sustainability subgroups (nurse/physician, high/low sustainability). We expect thematic saturation after performing 15 parent interviews since there are no subgroup analyses planned.

#### 6.4.3 Aim 3 Sample Size and Power

For the primary clinical outcome of LOS, we performed a power analysis informed by estimates of LOS from prior clinical trials and observational studies, based on a median LOS of 36 hours, interquartile range 20-52 hours, and a clinically important difference in LOS of 6 hours between lowest and highest quartiles of penetration observed in the study. With an estimated 90 patients per phase per hospital across 3 phases and a minimum of 24 hospitals, we will have 80% power to detect a difference in LOS of 2.4 hours between the lowest and highest quartiles of penetration (alpha=.05). The underuse outcome requires in-person data collection in a new population distinct from Aim 1. With surveillance of 35 patients/hospital receiving  $\geq 2\text{L/min}$  supplemental oxygen or  $\geq 2\text{L/min}$  of supplemental room air flow via any respiratory support device observed within each phase, we will have 80% power to detect a clinically significant 23 %pt difference in underuse of monitoring from 5% at baseline in P1 to 28% in P2 or P3, assuming a within-hospital correlation of 0.4. Other Aim 3 outcomes are descriptive.

#### 6.5 Interim Analysis

An analysis is required and planned immediately after P1 (prior to any interventions) in order to obtain baseline penetration of guideline-concordant care for each participating hospital and confirm sites with adequate bronchiolitis volumes, infrastructure, and capability to conduct subsequent randomization based on these results.

We also propose interim analyses following active deimplementation (Phase 2) and sustainability (Phase 3) phases in order to provide the DSMB with up-to-date data for these meetings in order to assess safety and feasibility.

In addition, the DSMB will, at their discretion, be able to request additional interim analyses.

There are no pre-specified stopping rules for efficacy or safety for this project focused on aligning practice with the standard of care.

## **7 SAFETY MANAGEMENT**

### **7.1 Clinical Adverse Events**

Clinical adverse events (AEs), any untoward or unfavorable medical occurrence in a human subject; including any abnormal sign, symptom or disease that is temporally related to the research, whether or not it is related to the subject's participation in the research, will be monitored throughout the study. See details in Section 8 describing the proactive adverse event surveillance plan.

### **7.2 Adverse Event Reporting**

Since the study procedures are not greater than minimal risk and the purpose of the interventions is to align practice with existing guidelines and the standard of care, SAEs are not expected. If any unanticipated problems related to the research involving risks to subjects or others happen during the course of this study (including SAEs) they will be reported to the IRB in accordance with CHOP IRB SOP 408: Unanticipated Problems Involving Risks to Subjects. Unanticipated Problems are any incidents, experiences, or outcomes that are unexpected (in terms of the nature, severity or frequency), related to a subject's participation in the research, and suggest that the research places subjects or others at greater risk of harm than was previously known or recognized. Serious Adverse Events (SAEs) in the context of this study are AEs that meet any of the following conditions: (1) results in death; (2) is life-threatening (places the subject at immediate risk of death from the event as it occurred); (3) requires prolongation of existing hospitalization; (4) results in persistent or significant disability/incapacity; (5) based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition above.

AEs that do not meet prompt reporting requirements will be summarized in narrative or other format and submitted to the IRB at the time of continuing review (if continuing reviews are required), or will be tracked and documented internally by the study team but not submitted to the IRB (if continuing reviews are not required).

## **8 STUDY ADMINISTRATION**

### **8.1 Treatment Assignment Methods**

#### **8.1.1 Randomization**

This cluster-randomized trial uses covariate constrained randomization to randomize at the hospital level, accounting for important covariates. See details in Section 3.2.

#### **8.1.2 Blinding**

There is no blinding in the trial.

### **8.2 Data Collection and Management**

The Clinical Research Computing Unit (CRCU) at the University of Pennsylvania will serve as the DCC.

### **8.2.1 Database**

All research data for this trial will be stored in an electronic database that is managed by the Research Technologies Department (RTD) of the CRCU. The database will be hosted on secure computing servers and will be restricted to only those individuals who are authorized to work on the trial. Individual user accounts with passwords will be used to restrict access to the database. Specific privilege assignments within the database will also be employed to limit the types of functions that authorized users can perform to those functions that are appropriate for their role in the trial. Additional measures to prevent unauthorized external access to the database environment will be employed using network firewall technologies. The CRCU team will work closely with the investigators and to design, develop, and test a database to support the requirements of the study and to promote data security and integrity. Electronic audit trails of changes to database contents will be incorporated into the design and will capture and record those changes automatically. In addition to the trial database where actual results will be maintained, a development database will be created. The development database is a working environment that facilitates the development, testing, troubleshooting, enhancement, and training for the data management system (DMS) without adversely affecting the integrity of the collected project data.

### **8.2.2 Data Entry and Data Quality Module**

The CRCU will configure a database to allow remote data entry (RDC) from the participating trial sites. The RDC module will be available to any computer with a persistent internet connection and will be run using standard web browser software. Data entry checks will be included in the entry screen designs where appropriate to limit the opportunity for erroneous entries due to mistyping. Such data entry checks would include value range comparisons, valid data type checks, required value checks, and skip pattern enforcement. This data entry module will be configured for single data entry. Validation rules will be defined by CRCU clinical data management personnel, working closely with the investigators, to identify data items that may have been collected incorrectly or entered into the database inaccurately. Clinical site personnel will review the results of the data validation queries and take any required corrective action for invalid data. Queries will be recorded and tracked in the data quality module. Corrections identified for individual data items will be managed by the clinical sites. All changes made will be recorded in an electronic audit trail and documented using change control procedures.

### **8.2.3 Reports Dashboard Module**

Reports Dashboard Module: Using RStudio Connect software, the CRCU will create a dashboard specific to the functional needs of the trial. The dashboard will make it possible to connect to a variety of data sources, and explore the objects and data inside the connection. CRCU will design and program standard report templates that can be scheduled to be executed/distributed on proscribed timetables. Assigned users will be able to share and collaborate on study data for purposes of conducting site audits, monitoring the trial progress and safety, providing individual and overall feedback to sites and committees, and assessing data entry metrics and data quality assessments.

### **8.2.4 Testing**

Prior to deployment and use by the clinical sites and CRCU personnel, the database and DMS will be subjected to extensive functional testing. This testing is conducted according to a written test plan and is intended to verify the proper functioning of all components of the DMS. Any components that do not function as they were intended will be identified and evaluated by the development team to determine appropriate corrective action. Testing will also include an evaluation by user representatives for adherence to the requirements established by the intended users for the DMS. Successful completion of these user acceptance tests will mark the end of development and predicate the deployment of the DMS for use in storing and managing active trial data.

### **8.2.5 Operations and Administration**

RTD personnel will provide database administration services for the life of the project and will maintain the database in an appropriate manner for the retention period required by regulation and institutional policies. Database administration includes user account maintenance, database security and performance monitoring and tuning. RTD staff will also perform operational tasks as necessary. Such tasks may include electronic data loading, database software management, and process documentation.

### **8.2.6 Maintenance**

RTD staff will maintain the DMS over the life of the study. Any modifications made to the DMS will be conducted in accordance with change control procedures. RTD will work closely with study investigators and CDM personnel to identify desired modifications and to assess the impact of any proposed modifications.

### **8.2.7 User Training**

CRCU staff will provide training annually, prior to the start of each phase, for trial personnel associated with data collection. This session will cover correct handling of all data collection instruments and use of the data entry system. Training webinars will be conducted during study implementation at the sites. Site users will be instructed to perform mock data entry for the data management system training certification process.

### **8.2.8 User Support**

CRCU will interface with the participating sites (vary by year) to provide assistance with problem solving related to use of the remote data entry system, as needed.

### **8.2.9 Reports**

CRCU will generate periodic reports on subject accrual, study progress, adverse events and data quality will be generated and provided to investigators, reviewers, and any study quality and safety monitoring boards as may be specified by the protocol and applicable regulations. CRCU staff will collaborate with the biostatistics team on reports for the DSMB, Interim Analysis and Annual Continuing Reviews and other NHLBI mandated reports.

### **8.2.10 Sharing Data with Analytic Core**

The CRCU will work closely with biostatistics faculty and staff to ensure that data analysis needs are addressed during the design phase of the data collection instruments and the trial DMS. CRCU staff will grant read-only access to the study data for biostatisticians to perform interim and final analyses. Data dictionaries and any other relevant information will be provided to the biostatisticians to facilitate their analyses.

### **8.2.11 Database Lock**

CRCU staff will lock the database once all data have been collected. Study data will be packaged for data sharing purposes. A snapshot of the database will be taken and stored in a secure folder.

## **8.3 Confidentiality**

All data and records generated during this study will be kept confidential in accordance with Institutional policies and HIPAA on subject privacy. The Investigator and other site personnel will not use such data and records for any purpose other than conducting the study.

No identifiable data will be used for future study without first obtaining IRB approval. The investigator will obtain a data use agreement between provider and any recipient researchers before sharing a limited dataset.

### **8.3.1 Record Retention Policy Reconciliation**

In accordance with their local retention of records policies, the DCC will retain all information from this study for 6 years after the study is completed, after which PHI will be removed from the data set.

We recognize that other relying sites may have different record retention requirements. For this reason, the DCC will provide all data submitted from relying sites to the DCC back to each Site PI in the form of “study close out packages” for each site at final data lock using a Penn IT approved secure method, allowing each site to meet their local record retention requirements. We will not submit Site-Specific IRB Amendments describing each site’s record retention requirements.

## **8.4 Regulatory and Ethical Considerations**

### **8.4.1 Data and Safety Monitoring Plan**

#### **8.4.1.1 Data and Safety Monitoring Board**

A locally-appointed Data and Safety Monitoring Board (DSMB) will oversee this clinical trial. The purpose of the DSMB is to monitor safety and ensure participant welfare throughout the trial. The DSMB will advise the Federal funding agency (NHLBI) and the Principal Investigators regarding the continuing safety of study subjects and the continuing validity and scientific merit of the study. The DSMB will be responsible for monitoring accrual of study subjects, adherence to the protocol, assessments of data quality, performance of individual clinical sites, and review of SAEs should they occur.

Proposed DSMB members will undergo conflict of interest review by the Compliance Operations and Conflict of Interest (COI) Department at Children’s Hospital of Philadelphia. The investigative team will provide the Department with the names and contact information of proposed DSMB members. Upon receiving this information, the Department will distribute COI disclosure forms to the proposed members for completion. Upon receipt of the forms, the Department will review any potential conflicts and seek clarification from each individual as needed. In accordance with FDA guidance on the structure and operation of clinical trial data monitoring committees, DSMB members should be independent of all entities sponsoring, organizing, conducting, or regulating the trial. They should not have any significant financial interest in the study’s conduct or outcome, nor be involved in the study design, nor work at the MPIs’ home institutions, nor serve as a Site PI for this trial during their period of DSMB membership. The Department will review COI forms to determine whether any consultancies, relationships with medical device companies, research support, financial interests, or any other relationships exist that could be construed as introducing potential bias to their role as a DSMB member. If any consultancies or financial interests of a proposed member may be viewed as potentially materially impacting their objectivity, they will not be invited to serve on the DSMB. Each DSMB member will be responsible for informing the sponsor and DSMB Chair if any relevant changes in financial interest or other developments affecting potential or perceived conflict of interest develop during the duration of DSMB membership.

The investigators will draft a DSMB charter to guide its function for the trial and the charter will be reviewed, revised as necessary, and approved by the DSMB. The Data Coordinating Center (DCC) will send reports to DSMB members prior to each DSMB meeting. The DSMB will have the final say in determining meeting intervals.

In its meetings the DSMB will review outcome data, safety data, equitable deimplementation data, and subject accrual. We propose convening one DSMB meeting with interim analysis planned following each of the 4 phases included in the trial: baseline measurement, active deimplementation, sustainability, and exploratory (when all enrollment will be complete), along with meetings scheduled ad hoc as necessary. An interim analysis will be provided by the Analytic Core to the DSMB after each of the phases listed above. In addition, the DSMB will, at their discretion, be able to request additional interim analyses. The DSMB can recommend whether or not to terminate enrollment in the trial because of potential safety concerns or study feasibility issues. At the final meeting following completion of subject enrollment, the DSMB will review final subject accrual and safety data to include in a written report.

#### 8.4.1.2 Adverse Event Surveillance, Reporting, and Management

The risks of this trial are minimal as it involves deimplementation strategy interventions intended to align clinical practice with established evidence, national guidelines, and recommendations for high quality bronchiolitis care. This is primarily an implementation trial, rather than a trial focused on efficacy or effectiveness. The interventions are assigned at the cluster (hospital) level to staff who are caring for patients with bronchiolitis on participating units. In this section we describe potential adverse events in patients that may result from changes in staff physiologic monitoring practices, which may or may not be attributable to the deimplementation strategy interventions.

Since the interventions are assigned at the hospital level to staff who are caring for patients with bronchiolitis, we will perform surveillance for adverse events in all bronchiolitis patients hospitalized on units participating in the study. This also includes (a) patients who were not subjects of data collection because the intervention is applied to staff working on participating units and could impact the care of patients with bronchiolitis even if they are not reviewed during data collection rounds, and (b) patients who may not have had their care impacted in any way by the trial interventions because they are applied to staff members, not directly to patients.

On a monthly basis during each post-randomization phase (P2, P3, and P4), site investigators will perform surveillance for (a) readmission of bronchiolitis patients within 7 days of discharge from units participating in the trial and (b) code blue and rapid response team activations in bronchiolitis patients hospitalized on units participating in the study that have the potential to meet “unanticipated problems involving risk to subjects” criteria. In order to establish a baseline for these events prior to any deimplementation interventions, we will also ask each site that will be continuing on to P2 to perform retrospective surveillance using data from their highest data collection volume month in P1. Using existing local patient safety databases and reports (e.g., local code blue and rapid response team activation logs, readmission reports), site investigators will review the charts of each bronchiolitis patient who was readmitted or was the subject of a code blue or rapid response team call. Readmission reviews will initially determine if the patient was hypoxemic to <85% at the time of re-presentation to the emergency department. Code blue and rapid response team activation reviews will initially determine if the patient was unmonitored and subsequently found to be hypoxemic to <85% at the time of the event when SpO<sub>2</sub> monitors were applied. Readmissions and code blue/rapid response team activations meeting those initial criteria will be considered study AEs, whether or not they are related to the research intervention. Site investigators will complete a report form assessing the items in the CHOP IRB “Unanticipated Problems Decision Tree” to analyze relatedness, unexpectedness, and seriousness. Relatedness will be assessed through chart review and speaking with staff involved in the patient’s care if necessary to determine if the event was at least possibly related to the study interventions, summarized as “there is a reasonable possibility that the event may have been caused by the trial interventions.” See additional details below in the Section “Risk of deimplementation procedures” for context to inform assessment of relatedness, unexpectedness, and seriousness. Site investigators will report events that meet “unanticipated problems involving risk to subjects” criteria to the DCC and their local IRBs in accordance with the regulatory timelines indicated below and local IRB policies.

SAE and Unanticipated Problem reporting will adhere to the NHLBI SAE and Unanticipated Problem Event Reporting Timelines illustrated in the table below and available at <https://www.nhlbi.nih.gov/grants-and-training/policies-and-guidelines/nhlbi-adverse-event-and-unanticipated-problem-reporting-policy>. Investigators must also take into account local IRB reporting timelines if they are shorter than NHLBI Policy. Relying sites’ local IRB policies with shorter reporting timelines for SAEs and Unanticipated Problems supersede longer timelines in the NHLBI guidance.

#### SERIOUS ADVERSE EVENT AND UNANTICIPATED PROBLEM REPORTING TIMELINES

Event Type	<p><b>When Event is Reported</b></p> <p><i>Shown in italics: Reconciliation between local IRB Policy and NHLBI Policy based on applying the policy with the shorter reporting timeframe using CHOP as an example. Other relying sites' local IRB reporting requirements may differ. Relying sites' IRB policies with shorter reporting timelines for SAEs and Unanticipated Problems supersede longer timelines in the NHLBI guidance.</i></p>	By Whom Event is Reported	To Whom Event is Reported
<p><b>Fatal or life-threatening unexpected, suspected serious adverse reactions</b></p>	<p><b>NHLBI Policy:</b> Within 7 calendar days of initial receipt of information.</p> <p><b>CHOP IRB Policy:</b> SAEs that involve a CHOP subject and involve the death of the subject or are considered life-threatening need to be reported to the IRB within 1 business day of discovery (telephone, fax, email, eIRB) with a full report submitted in eIRB within 48 hours of the initial notification. All unanticipated problems involving subjects external to CHOP must be reported to the CHOP IRB within 7 business days of receipt of the report from the study sponsor, data coordinating center or overall study PI.</p> <p><i>Policy reconciliation: Refer to CHOP Policy for reporting events involving CHOP subjects to CHOP IRB. Refer to NHLBI policy for all other reporting and reports to CHOP IRB regarding subjects external to CHOP. Relying sites' IRB policies with shorter reporting timelines for SAEs and Unanticipated Problems supersede longer timelines in the NHLBI guidance.</i></p>	<p>Investigator</p> <p>Sponsor or designee<sup>1</sup></p>	<ul style="list-style-type: none"> <li>Local/internal IRBs</li> <li>NHLBI and/or Data Coordinating Center (DCC)</li> <li>FDA (if IND study)</li> </ul>
<p><b>Non-fatal, non-life-threatening unexpected, suspected serious adverse reactions</b></p>	<p><b>NHLBI Policy:</b> Within 15 calendar days of initial receipt of information.</p> <p><b>CHOP IRB Policy:</b> All other unanticipated problems involving CHOP subjects must be reported within 7 business days of discovery. All unanticipated problems involving subjects external to CHOP must be reported to the CHOP IRB within 7 business days of receipt of the report from the study sponsor, data coordinating center or overall study PI.</p> <p><i>Policy reconciliation: Refer to CHOP Policy for reporting to CHOP IRB. Refer to NHLBI policy for all other reporting. Relying sites' IRB policies with shorter reporting timelines for SAEs and Unanticipated Problems supersede longer timelines in the NHLBI guidance.</i></p>	<p>Investigator</p> <p>Sponsor or designee</p>	<ul style="list-style-type: none"> <li>Local/internal IRBs/Institutional Officials</li> <li>NHLBI and/or DCC</li> <li>FDA (IND/Marketed Products)</li> <li>All participating investigators</li> </ul>
<p><b>Unanticipated adverse device effects</b></p>	<p><b>NHLBI Policy:</b> Within 10 working days of investigator first learning of effect.</p> <p><b>CHOP IRB Policy:</b> All other unanticipated problems involving CHOP subjects must be reported within 7 business days of</p>	<p>Investigator</p>	<ul style="list-style-type: none"> <li>Local/internal IRBs</li> </ul>

	<p>discovery. All unanticipated problems involving subjects external to CHOP must be reported to the CHOP IRB within 7 business days of receipt of the report from the study sponsor, data coordinating center or overall study PI.</p> <p><i>Policy reconciliation: Refer to CHOP Policy for reporting to CHOP IRB. Refer to NHLBI policy for all other reporting. Relying sites' IRB policies with shorter reporting timelines for SAEs and Unanticipated Problems supersede longer timelines in the NHLBI guidance.</i></p>	Sponsor or designee	<ul style="list-style-type: none"> <li>NHLBI and/or DCC</li> <li>FDA (if IDE study)</li> </ul>
<b>Unanticipated Problem that is not an SAE</b>	<p><b>NHLBI Policy:</b> Within 14 days of the investigator becoming aware of the problem.</p> <p><b>CHOP IRB Policy:</b> All other unanticipated problems involving CHOP subjects must be reported within 7 business days of discovery. All unanticipated problems involving subjects external to CHOP must be reported to the CHOP IRB within 7 business days of receipt of the report from the study sponsor, data coordinating center or overall study PI.</p> <p><i>Policy reconciliation: Refer to CHOP Policy for reporting to CHOP IRB. Refer to NHLBI policy for all other reporting. Relying sites' IRB policies with shorter reporting timelines for SAEs and Unanticipated Problems supersede longer timelines in the NHLBI guidance.</i></p>	Investigator	<ul style="list-style-type: none"> <li>Local/internal IRBs/Institutional Officials</li> <li>NHLBI and/or DCC</li> </ul>
<b>All Unanticipated Problems<sup>2</sup></b>	<p><b>NHLBI Policy:</b> Within 30 days of the IRB's receipt of the report of the unanticipated problem from the investigator.</p>	<p>IRB</p> <p>Investigator<sup>3</sup></p>	<ul style="list-style-type: none"> <li>OHRP</li> <li>External IRBs</li> </ul>

**NHLBI Policy Footnotes:**

1. Designee is appointed by the sponsor; for example, DCC, CRO.
2. Per OHRP guidance: only when a particular AE or series of AEs is determined to meet the criteria for an UP should a report of the AE(s) be submitted to the IRB at each institution under the HHS regulations at 45 CFR part 46. Typically, such reports to the IRBs are submitted by investigators.
3. Investigators should also take into account local IRB guidance if reporting timelines for UPs are shorter than OHRP guidance

One or more medical monitor(s) will be appointed by the PIs in consultation with the DSMB. The medical monitor(s) will assess all Adverse Event and Unanticipated Problem reports sent to the DCC by site investigators, reviewing and electronically signing each report. The monitor will then follow the CHOP IRB "Unanticipated Problems Decision Tree" to determine the appropriate course of action, keeping in mind the expected natural history and outcomes outlined below in the Section "Risk of deimplementation procedures." Reports that suggest that subjects or others are placed at a greater risk of harm than initially anticipated will be accompanied by an Action Plan that outlines the steps that will be taken to mitigate the newly identified risk(s).

#### **8.4.2 Risk Assessment**

Risks are not greater than minimal in this study.

##### **8.4.2.1 Risks of direct observation and medical record review**

The primary risk of direct observation and medical record review procedures is breach of confidentiality of the data collected. These risks are mitigated by using the measures described above. In addition, each participant will be assigned a study identification number. This number will be used instead of names and other private information in any data exported from the primary database.

##### **8.4.2.2 Risks of questionnaires**

The primary risk of questionnaire procedures is breach of confidentiality of the data collected. These risks are mitigated by using the measures described above. In addition, each participant will be assigned a study identification number. This number will be used instead of names and other private information in any data exported from the questionnaire database.

##### **8.4.2.3 Risks of qualitative interviews**

The risks of qualitative interview procedures include:

- Breach of confidentiality (from data or audio recording)
- Momentary embarrassment or discomfort

These risks are mitigated by using the measures described above. In addition, each participant will be assigned a study identification number. This number will be used on data collection forms and in the database instead of names and other private information. A separate list will be maintained that will link each participant's name to the study identification number for future reference and communication. To mitigate risk of embarrassment or discomfort, subjects will be informed that they do not have to answer any questions that make them too uncomfortable. For the recording of the interview, no one other than the research team, the person who takes notes during the interview, and the transcription company will hear the recordings. If someone's name is mentioned, it will not be included on any notes or transcription. And if there are confidentiality concerns related to specific questions, the subject may elect to skip any question or stop the interview at any time.

##### **8.4.2.4 Risks of deimplementation procedures**

The risks of deimplementation procedures include:

- Clinicians extending their practice beyond the recommendations delivered in this trial and deimplementing monitoring in patient populations for whom deimplementation is not recommended (e.g. patients requiring supplemental oxygen)
- Missed episodes of desaturation in patients not requiring supplemental oxygen, which in some situations could represent patient deterioration

Brief episodes of desaturation are common and expected in bronchiolitis patients during recovery from acute illness, and is rarely associated with adverse outcomes. A landmark 2016 study by Principi and colleagues enrolled 118 infants with bronchiolitis at the time of emergency department discharge.<sup>101</sup>

Given that there are 3 sets of national recommendations that promote using less continuous monitoring in stable bronchiolitis, this study is not introducing any additional risk than would be introduced if clinical leaders initiated efforts into routine clinical care to align their hospitals' practice with the existing national guidelines. The trial simply aims to determine the best way to integrate and sustain this practice by showing clinicians' their own data, providing information/education on the existing recommendations, and providing decision support in the EHR. All decisions about changes to monitoring are made by the primary medical team, not the researchers.

In addition, we have outlined above a plan to perform surveillance for (a) readmission of bronchiolitis patients within 7 days of discharge from units participating in the trial and (b) code blue and rapid response team activations in bronchiolitis patients hospitalized on units participating in the study. In our pilot study, no episodes of deterioration were attributable to the deimplementation interventions.

#### **8.4.3 Potential Benefits of Trial Participation**

##### **8.4.3.1 Direct**

There are no direct benefits to participation in this study.

##### **8.4.3.2 Indirect**

The study outlined in this proposal will generate important knowledge that will advance the fields of implementation science and hospital medicine, specifically advancing methods to promote sustainable deimplementation of ineffective medical practices in the hospital setting.

Patients, their families, and the health professionals caring for them have the potential to indirectly benefit from higher quality, guideline-concordant health care. This may produce fewer monitor alarms, and thereby fewer interruptions from alarms that may break the concentration of health professionals and contribute to errors, wake patients from sleep, or cause unnecessary anxiety in patients and their loved ones. The patients also may have a lower risk of harm due to a reduction in the probability of the clinicians caring for them experiencing the alarm fatigue that can result from high alarm rates. Patients may also benefit by not having their hospital stays prolonged unnecessarily due to the overdiagnosis of inconsequential mild hypoxemia.

#### **8.4.4 Risk-Benefit Assessment**

Based on the discussion above and the lack of deviation from standard clinical care, the benefits of this study far outweigh the minimal risks. Given that the risks of the study are minimal, it is reasonable to proceed with the project.

#### **8.5 Recruitment Strategy**

##### **8.5.1 Recruitment of hospital sites**

Recruitment of US and Canadian hospital sites for this trial commenced in fall 2020 while the PIs were preparing the grant proposal. At that time a message was sent to all PRIS Network hospitals inviting them to express preliminary interest in participating in the trial. A total of 67 sites expressed interest and 52 sites signed a letter of support included in the grant proposal. Post-award, we will reach out to all sites that initially expressed interest in 2020 as well as additional PRIS sites that previously participated in EMO projects but did not express initial interest in 2020. Sites from outside the PRIS Network referred to our team will also be considered for inclusion.

Among sites that previously participated in the original 56-hospital EMO observational study,<sup>24</sup> we will exclude sites that:

- Failed to collect sufficient data in original EMO observational study<sup>24</sup> (<20 observations)

- Had baseline adjusted overuse <30% in original EMO observational study.<sup>24</sup> We chose this cut point because, of the prior EMO sites that collected sufficient data in the original EMO observational study<sup>24</sup> and did not partake in the pilot study (n=43), if we took all, the average baseline among prior EMO hospitals would be 45% overuse. The power calculation assumes a baseline of 50% overuse. If we exclude hospitals with <30% baseline overuse from the trial, the average baseline among prior EMO participants would be 52% overuse (48% penetration), aligned with the power calculation.

All sites that participated in the 6-hospital pilot study will be invited to participate regardless of their baseline overuse percentage.

If we fail to engage at least 50 sites in commencing the IRB reliance and data use agreement process, we will perform additional outreach to PRIS Network sites and may consider expanding to direct recruitment outside of the PRIS Network (e.g. in the American Academy of Pediatrics Value in Inpatient Pediatrics Network).

## **8.5.2 Recruitment of individuals**

### **8.5.2.1 Patients for in-person observational rounds**

For the data collection in-person observational rounds, site investigators will identify all patients currently admitted to their hospital's non-ICU, non-emergency department, non-step down units with bronchiolitis by reviewing the census of each unit that cares for children with bronchiolitis and examining the charts of patients meeting age criteria to determine if they are eligible.

### **8.5.2.2 Staff for questionnaires**

The DCC will electronically distribute the staff questionnaire measures to the following health care professional types who worked on an intervention unit in a role involving the care of patients with bronchiolitis during the intervention period:

- Attending physicians
- Resident physicians
- Nurses

Site PIs will prepare lists of the nurses and physicians who provide care for bronchiolitis patients on the units participating in the study, as well as administrators who oversee the medical care and safety for bronchiolitis patients at institutional and unit levels. Site PIs will submit these lists of staff email addresses of these potential subjects to the DCC, who will import these into the survey distribution system.

### **8.5.2.3 Staff for qualitative interviews**

For the qualitative interviews, using a deviance approach,<sup>85,86</sup> we will conduct semi-structured interviews with nurses and physicians who provide care to bronchiolitis patients (the exploratory study phase that examines sustainability 2 years after withdrawal of educational outreach and A&F) as well as with CDS Coaches. In collaboration with site PIs, eligible clinicians will be identified purposively from staff rosters and invited to participate in interviews by telephone call, texting, and/or emailing to discuss the process of deimplementation as experienced by stakeholders. Purposive sampling will seek to obtain a wide range of nurse and physician experience levels, nurse and physician supervisory vs front line care roles, nurse shift (day vs night shift), and physician care model (teaching service vs attending-only hospitalist model). Interviews will explore mechanistic relationships between (a) the strategies, (b) the findings of the quantitative measures above, and (c) sustainability.

### **8.5.2.4 Parents or guardians for qualitative interviews**

For the qualitative interviews of families, eligible parents or guardians will be identified purposively from bronchiolitis patients' trial records during P3 and invited to interview by telephone call, texting, and/or emailing during the 8 weeks following discharge in order to explore their perceptions of, and

reactions to, SpO<sub>2</sub> deimplementation activities. Purposive sampling will seek to obtain a wide range of patient ages since parents' perspectives likely differ for very young infants (e.g. 2-3 months old) compared to older children (e.g. 18-23 months old).

## **8.6 Informed Consent/Assent and HIPAA Authorization**

### **8.6.1 Population 1: Hospital Staff**

Population 1 includes all hospital staff who are exposed to the interventions by being present on participating hospital units or overseeing bronchiolitis care during active deimplementation, sustainability, and exploratory phases. These hospital staff members are considered third parties to the research. They are not considered research subjects and informed consent is not required unless they participate in study questionnaires or qualitative interviews (and thereby fall into hospital staff research subject subpopulations 1a or 1b, outlined below).

#### **8.6.1.1 Population 1a**

*Hospital staff who complete study questionnaires.* Informed consent will be obtained for the questionnaires administered to health care professionals. We request a waiver of documentation of consent. The first section of the electronic questionnaire webpage will include the required elements of consent and a statement that completion of the questionnaire indicates willingness to participate. Specific language is included in the eIRB application attachments. HIPAA Authorization is not necessary for the questionnaire portion of the study; names and email addresses of health care professionals are being collected in order to distribute and manage the questionnaire but are not considered PHI because they do not relate to the health of an individual. The potential subjects will have ample time to review the consent language, minimizing the likelihood of coercion.

We seek to enroll subjects under IRB SOP 501 8(a) to allow recruitment of employees and trainees who are under the supervision of the investigator(s), including those who report to Site PIs as participants in study questionnaires. This waiver is appropriate because employees and trainees (e.g. residents and fellows) working in Pediatric Hospital Medicine are by design the subjects of this aspect of the research and are the same specialty as the Site PIs in most cases. Investigators will not have access to data or reports that would allow them to know which employees or trainees chose to participate or not participate. The research could not practicably be carried out without the waiver or alteration. The intent is to obtain a large, unbiased sample of clinicians to obtain insights on care related to pulse oximetry monitoring in bronchiolitis that will then help us understand the mechanisms (mediators and moderators) of the interventions. The research could not practicably be carried out without the waiver or alteration, as approximately 25% of sites have Site PIs with some form of leadership role that would prohibit us from recruiting subject cohorts at their sites, which would threaten the above research goal. The study could not practicably be carried out without the Waiver of Documentation of Consent as subjects will not be seen in person.

#### **8.6.1.2 Population 1b**

*Hospital staff who participate in qualitative interviews.* Informed consent will be obtained for the qualitative interviews of staff. We request waiver of documentation under 45 CFR 46.117©(1)(ii). Interviews will be conducted by telephone or using teleconferencing software (e.g. Zoom, BlueJeans, Teams). The investigator will obtain consent following the same requirements as written consent but the subject will not sign a consent form. The form employed uses the CHOP consent template but substitutes the usual signature page with the IRB's documentation of verbal consent page. The study will be explained as outlined in the consent form and the subject will be given ample opportunity to ask questions, and will be provided with extra time to think about it if requested (to minimize the likelihood of coercion). If interested in participating, the documentation of verbal consent page of the form will be completed and the interview will proceed. HIPAA Authorization is not necessary for the staff interviews; names and email addresses of health care professionals are being collected in order to manage the interview process but are not considered PHI because they do not relate to the health of an individual.

We seek to enroll subjects under IRB SOP 501 8(a) to allow recruitment of employees and trainees who are under the supervision of the investigator(s), including those who report to Site PIs as participants in study interviews. This waiver is appropriate because employees and trainees (e.g. residents and fellows) working in Pediatric Hospital Medicine are by design the subjects of this aspect of the research and are the same specialty as the Site PIs in most cases. Investigators will not have access to data or reports that would allow them to know which employees or trainees chose to participate or not participate. The research could not practicably be carried out without the waiver or alteration. The intent is to conduct semi-structured interviews aiming to better understand mechanisms of practice change in response to each deimplementation strategy. The research could not practicably be carried out without the waiver or alteration, as approximately 25% of sites have Site PIs with some form of leadership role that would prohibit us from recruiting subject cohorts at their sites, which would threaten the above research goal. The study could not practicably be carried out without the Waiver of Documentation of Consent as subjects will not be seen in person.

### 8.6.2 Populations 2a and 2b

*(2a) Bronchiolitis patients directly observed while not receiving supplemental oxygen ("in room air," for primary trial outcome) and (2b) Bronchiolitis patients directly observed while receiving supplemental oxygen (for underuse evaluation).*

Waivers of consent/ assent and of HIPAA Authorization are requested.

The research meets the criteria of 45 CFR 46.116(d), as illustrated below:

- Risks are not greater than minimal in this study. The primary risk is breach of privacy and confidentiality. The risk will be minimized by keeping all data and records confidential in accordance with institutional policies on subject privacy. The investigators will not use data or records for any purpose other than conducting the study.
- The waiver or alteration will not adversely affect the rights and welfare of the subjects because PHI will only be accessed by IRB approved study staff performing data collection, and we have taken extensive precautions by using a professional DCC to minimize risk of PHI exposure.
- The research could not practicably be carried out without the waiver or alteration. The intent is to obtain a large, unbiased sample of patients with bronchiolitis to obtain insights on hospital-level practices and systems of care related to pulse oximetry monitoring in bronchiolitis. The research could not practicably be carried out without the waiver or alteration, as it will not be feasible to locate and contact the families of all of the patients who are being monitored in room air with bronchiolitis. All of the patients admitted to study sites with bronchiolitis who are monitored in room air are required in order for this to be an unbiased sample representative of the population with adequate sample size.
- There will not be any pertinent patient-level information that would benefit the patient directly after participation so none of the subjects will be provided with additional information after participation.

We also request a waiver of HIPAA Authorization for the patient subjects. The study presents no more than minimal risk to the privacy of individuals. The research meets the criteria of 45 CFR 46.116(d), as illustrated below:

(A) The use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:

(1) An adequate plan to protect the identifiers from improper use and disclosure;

- *We have provided an adequate plan to protect identifiers from improper use and disclosure above.*

(2) An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and

- *We have provided a plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research that is also consistent with institutional record retention policies.*

(3) Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by this subpart;

- *Protected health information will not be reused or disclosed to any other entity except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by this subpart.*

(B) The research could not practicably be conducted without the waiver or alteration; and

- *The research could not practicably be conducted without the waiver as described above in waiver of consent request.*

(C) The research could not practicably be conducted without access to and use of the protected health information.

- *The research could not practicably be conducted without access to and use of protected health information needed to track patients over time and to track the dates of admission and data collection at each site during the trial.*

### 8.6.3 Population 3

*Parents or guardians of bronchiolitis patients who participate in qualitative interviews.* Informed consent will be obtained for the qualitative interviews of parents and guardians. We request a Waiver of HIPAA Authorization for Recruitment Purposes for Population 3, the parents/guardians of bronchiolitis patients whose contact information we have proposed collecting so that we may contact them and invite them to participate in the qualitative interviews. The study presents no more than minimal risk to the privacy of individuals. The research meets the criteria of 45 CFR 46.116(d), as illustrated below:

(A) The use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:

(1) An adequate plan to protect the identifiers from improper use and disclosure;

- *We have provided an adequate plan to protect identifiers from improper use and disclosure above.*

(2) An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and

- *We have provided a plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research that is also consistent with institutional record retention policies.*

(3) Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by this subpart;

- *Protected health information will not be reused or disclosed to any other entity except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by this subpart.*

(B) The research could not practicably be conducted without the waiver or alteration; and

- *The research could not practicably be conducted without the waiver because subjects will not be met in person during the hospitalization due to the design of the data collection procedures for the patients (populations 2a and 2b).*

(C) The research could not practicably be conducted without access to and use of the protected health information.

- *The research could not practicably be conducted without access to and use of protected health information needed to contact the parents/guardians to recruit them to participate.*

We also request waiver of documentation under 45 CFR 46.117(c)(1)(ii). Interviews will be conducted by telephone or using teleconferencing software (e.g. Zoom, BlueJeans, Teams). The investigator must obtain consent following the same requirements as written consent but the subject does not sign a consent form. The form substitutes the usual signature page with the IRB's documentation of verbal consent page. The study will be explained as outlined in the consent form and the subject will be given ample opportunity to ask questions, and will be provided with extra time to think about it if requested (to minimize the likelihood of coercion). If interested in participating, the documentation of verbal consent page of the form will be completed and the interview will proceed. HIPAA Authorization will be obtained using the same process with documentation on the same form.

#### 8.6.4 Population 4

*Clinical Decision Support (CDS) Coaches who participate in qualitative interviews.* In Phase 4 we will conduct semi-structured interviews with CDS Coaches. Informed consent will be obtained for the qualitative interviews. We request waiver of documentation under 45 CFR 46.117(c)(1)(ii). Interviews will be conducted by telephone or using teleconferencing software (e.g. Zoom, BlueJeans, Teams). The investigator will obtain consent following the same requirements as written consent but the subject will not sign a consent form. The form employed uses the CHOP consent template but substitutes the usual signature page with the IRB's documentation of verbal consent page. The study will be explained as outlined in the consent form and the subject will be given ample opportunity to ask questions, and will be provided with extra time to think about it if requested (to minimize the likelihood of coercion). If interested in participating, the documentation of verbal consent page of the form will be completed and the interview will proceed. HIPAA Authorization is not necessary for the interviews; names and email addresses are being collected in order to manage the interview process but are not considered PHI because they do not relate to the health of an individual.

We seek to enroll subjects under IRB SOP 501 8(a) to allow recruitment of employees and trainees who are under the supervision of the investigator(s), including those who report to Site PIs as participants in study interviews. This waiver is appropriate because CDS coaches, employees, and trainees (e.g. residents and fellows) working in Pediatric Hospital Medicine are by design the subjects of this aspect of the research and are the same specialty as the Site PIs in most cases. Investigators will not have access to data or reports that would allow them to know which employees or trainees chose to participate or not participate. The research could not practicably be carried out without the waiver or alteration. The intent is to conduct semi-structured interviews with CDS Coaches who participated in the design and development of decision support for bronchiolitis patients aiming to better understand mechanisms of practice change in response to each deimplementation strategy. The research could not practicably be carried out without the waiver or alteration, as approximately 25% of sites have Site PIs with some form of leadership role that would prohibit us from recruiting subject cohorts at their sites, which would threaten the above research

goal. The study could not practicably be carried out without the Waiver of Documentation of Consent as subjects will not be seen in person.

### 8.7 Payment to Subjects/Families

Staff and parent/guardian participants in qualitative interviews will each be paid \$25 for their time and effort. No other subjects will be paid for their participation.

## 9 PUBLICATION

Peer-reviewed publication is planned. No identifiable information will be used in publication.

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