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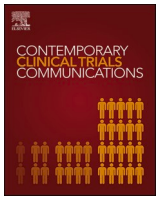

# Direct-to-participant recruitment of mothers and infants: A strategic approach during challenging pandemic times

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ABSTRACT

Under traditional circumstances, most clinical trials rely on in-person operations to identify, recruit, and enroll study participants and to complete study-related visits. During unusual circumstances, such as the COVID-19 pandemic, the typical clinical trial model is challenged and forced to explore alternative approaches to implementing study recruitment, participant enrollment, and data collection strategies. One such alternative is a direct-to-participant approach which leverages electronic resources and relevant technological devices (*e.g.*, smart phones) available to researchers and patients. This approach functions under the assumption that a participant has access to a device that connects to the internet such as a smart phone, tablet, or computer. Researchers are then able to transition a typical paper-based, in-person model to an electronic-based, siteless, remote study. This article describes the challenges clinicians and researchers faced when implementing a direct-to-participant study approach during the COVID-19 pandemic. The lessons learned during this study of infant populations could help increase efficiency of future trials, specifically, by lessening the burden on participants and clinicians as well as streamlining the process for enrollment and data collection. While direct-to-adult

*Abbreviations:* CDW, Clinical Data Warehouse; DCRI, Duke Clinical Research Institute; IRB, Institutional Review Board; Pediatrix, Pediatrix Medical Group; REDCap, Research Electronic Data Capture.

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participant recruitment is not a novel approach, our findings suggest that studies attempting to recruit the infant population may benefit from such a direct-to-participant approach.

## 1. Introduction

COVID-19, a severe acute respiratory disease caused by the SARS-CoV-2 virus [1], spread rapidly across the globe resulting in world-wide lockdowns that started in March 2020 [2,3]. The COVID-19 pandemic triggered the need to develop alternative approaches for recruitment and operations in clinical research studies. Lessons learned from COVID-19 clinical trials may improve future study protocols [4,5].

Conducting clinical research in the infant population has inherent challenges [6–9]; the COVID-19 pandemic created yet another layer of challenges for researchers. Non-essential research was limited and in-person office visits were halted. Staff resources were redirected to manage developing COVID-19 response units. Researchers at the Duke Clinical Research Institute (DCRI), evaluating the outcomes of infants affected by COVID-19, sought to adjust and adapt their procedures to maintain study efficacy via a direct-to-participant approach. This approach leverages electronic resources and relevant technological devices (e.g., smart phones) and electronic data capture systems available to researchers and patients. Researchers are then able to transition a typical paper-based, in-person model to an electronic-based, siteless, remote study.

This article discusses the specific methods and implementation of a direct-to-participant approach used to recruit and retain study participants. Implementation of the direct-to participant approach eased study management by decreasing in-person logistical complications. Less burden was placed on clinical and research staff as participants experienced alternate access to study scheduling and participation via mobile applications and electronic consents and surveys.

## 2. Methods

### 2.1. Participants

We included mothers and their infants discharged from hospitals managed by The Pediatrix Medical Group (Pediatrix) across the United States that met the following criteria: (1) mothers of infants or infants positive for SARS-CoV-2 by hospital discharge; or (2) infants born on or after June 1, 2020, to a mother positive for SARS-CoV-2 during pregnancy or birth hospitalization. Mothers or infants who died during the birth hospitalization were excluded. We sought to enroll 200 mother-infant pairs. The study was approved by the Duke University Health System Institutional Review Board (IRB).

### 2.2. Study design

We leveraged the infrastructure of the DCRI and Pediatrix to capture important outcomes in infants and mothers affected by COVID-19. This observational study consisted of both retrospective and prospective recruitment of eligible mother-infant pairs and collected data from multiple electronic sources:

1. REDCap (Research Electronic Data Capture) database hosted at Duke University School of Medicine [10,11];
2. Medical records from the mother and infant requested via fax by the study team through a medical records release form and/or shared electronically by the participant via the Pulse by Pluto Health mobile application [12];
3. Pediatrix BabySteps Clinical Data Warehouse (CDW) which sources data from Pediatrix's BabySteps, a proprietary electronic clinical documentation system used to create all of the providers' clinical notes during daily practice [13].

To avoid delays with study site activation, Pediatrix hospitals were not considered study sites but instead were considered referring locales, which allowed the DCRI to serve as the study coordinating center with no participants enrolled from the Duke University Health System. Referring locales did not share protected health information with the DCRI coordinating center. Each referring locale was required to receive their local IRB acknowledgement of recruitment referral activities, specifically recruitment phone calls, prior to referring their patients to the Duke study coordinator. As such, interested Pediatrix hospitals did not have to endure the often-lengthy single IRB process required to enroll interested participants as part of a multi-site study. Instead, Pediatrix hospitals alerted local IRBs of their involvement and activities as a referring locale, and the Duke IRB was the IRB of record.

### 2.3. Participant recruitment

Initially, study participants were only recruited prospectively from Pediatrix in-patient postpartum units using local electronic health records to monitor COVID-19 diagnosis of the mother and/or newborn during birth hospitalization. Once an eligible mother-infant pair was identified, dedicated clinicians at referring Pediatrix locales discussed the study with the family and shared the study flyer with the study website link, QR code, website access code, and contact information for the study team. This method did not yield a high recruitment rate as initially anticipated by the research team, and thus, additional recruitment methods were explored.

In the second quarter of 2021, we updated the eligibility criteria to include retrospective recruitment of eligible mother-infant pairs from participating Pediatrix locales. Pediatrix locales identified eligible mother-infant pairs in their electronic health record and the CDW from June 2020 through the time they received local IRB acknowledgement of retrospective recruitment, but no later than June 2022. Eligible individuals were contacted by the referring locales via phone, and if they expressed interest in study participation, they were transferred to the study phone number at the DCRI to share their contact information with the virtual study coordinator. Direct transfer of phone call from the referring locale to DCRI, when possible, facilitated a "warm handoff" that resulted in increased likelihood of participation. Retrospective recruitment training for referring locales began in July 2021; study enrollment increased from August 2021 through March 2022 as shown in Fig. 1.

With the addition of retrospective recruitment, referring locales shared the study flyers (English/Spanish) on the Pediatrix website, in Pediatrix hospital/clinic waiting areas, and directly with eligible mothers at their clinic visits or after labor and delivery. Flyers directed potential participants to the study website to review detailed study information and watch an overview video featuring study investigators with English audio and Spanish subtitles.

In order to encourage participation, in April 2022, the study protocol was amended to include an electronic gift card upon completion of the enrollment questionnaire as compensation for participant time. This initiative further improved the enrollment process and increased participation (Fig. 1).

## 3. Results

### 3.1. Sample size and outcomes relative to the method

The study enrolled 96 mother-infant participant pairs from October 2020 to September 2022. Pediatrix identified 38 locales for prospective referrals. Of the 38 referring locales, 16 (42 %) also participated in

retrospective referrals which consisted of referral phone calls to eligible patients. If the mother expressed interest in the study, the referring locale would share the study flyer via email and/or text, and if the mother agreed, the locale would also transfer the mother to the study phone line to speak with the virtual study coordinator or leave a voicemail with their contact information. Across the 16 referring locales, a total of 1016 calls were made in which 305 (30 %) mothers agreed to receive more information about the study, 232 (23 %) mothers declined, and 479 (47 %) were considered lost to follow-up.

### 3.2. Data collection

Critical components to the direct-to-participant recruitment and retention approach were the methods and platforms used for data collection. All study data, including the consent form and medical records release form, were collected remotely via REDCap electronic data capture tools hosted at Duke University School of Medicine [10,11]. Eligible mothers were given a REDCap website link and a study code to enter at the bottom of the study welcome page. Once the code was entered, participant contact information was collected in the event the study team needed to contact them throughout the informed consent process. After entering their contact information, eligible participants were guided through the electronic consent process, ending with the electronic signing of the medical record release form for participant mother and their infant. Once the participant mother completed this process, they received an email with their signed consent document, medical records release form, along with a link to their unique enrollment questionnaire in REDCap.

The enrollment questionnaire collected information about the participant mother's medical providers from first obstetric visit through their participant infant's first year of birth and, if known at the time, the infant's medical providers from birth through 12 months of age. The participant mother's contact information was verified, and limited demographic information, such as the mother's educational level, race, ethnicity, and marital status was also collected. After enrollment, participant mothers received a REDCap notification when their infant turned 6 months and 12 months of age to complete follow-up surveys.

Once participant infants turned 12 months of age, the study team requested medical records for participant mother (from first obstetric visit through infant's first year of birth) and participant infant (from birth through 12 months of age) via fax based on the information provided at the time the enrollment questionnaire was completed.

At study start-up, the study team intended to use the Pulse by Pluto Health mobile application allowing participants to directly share their medical record electronically, but this was ultimately not included in the initial consent form. The Pulse by Pluto Health mobile application is a Health Insurance Portability and Accountability Act compliant platform with access to electronic medical data from select healthcare networks nationwide [12]. At the time of writing, the team successfully incorporated the use of Pulse by Pluto Health via an IRB amendment and with the addition of a consent addendum. Participants that opted-in and shared their medical records via the Pulse by Pluto Health mobile application received an additional electronic gift card as compensation for time spent.

## 4. Discussion/conclusion

The direct-to-participant recruitment method provided the opportunity to enroll eligible mothers and their infants. As such, mothers completed the consent process, medical records release forms, enrollment, and follow-up questionnaires on behalf of their infants. The use of the direct-to-participant recruitment method in the pediatric population was novel, and we noted a few barriers. For example, some mothers expressed concern regarding the time commitment involved with the study. Taking the initiative to complete the consent form without a site study coordinator beside them could have been an additional barrier. The study team attempted to mitigate this concern by providing support over the phone to complete questionnaires and by sending periodic survey reminders via REDCap. Overall the direct-to-participant approach was successful for study implementation and recruitment in an infant population during the COVID-19 pandemic. Some of the challenges included attempting to recruit participants and maintain study engagement during major life changing events such as a pandemic and birth of a child.

As the study progressed, we attempted different recruitment approaches and incentives to increase study enrollment, participation, and retention which strengthened the initial study method. The addition of referring locales led to an increase in participant enrollment. The addition of participant compensation not only aided enrollment numbers, but also incentivized already enrolled participants to participate in the Pulse by Pluto Health Mobile Application [5,12]. The use of Pulse by Pluto Health also provided the research team the opportunity to view medical data that may have not been requested through the manual medical record fax request process.

In adapting to the COVID-19 pandemic, we learned that a direct-to-participant approach in the infant population could increase recruitment efficiency, lessen the burden on participants and clinicians, and streamline the process for enrollment and data collection. While direct-

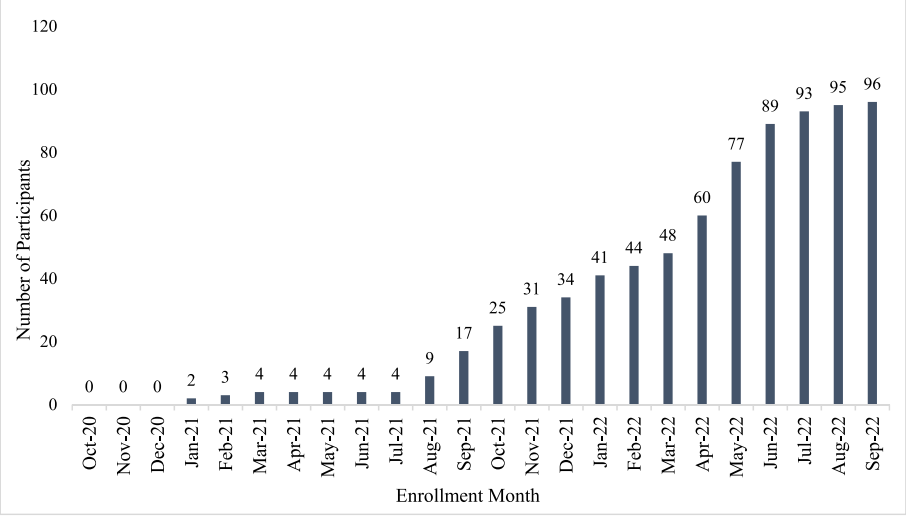


**Fig. 1.** Cumulative enrollment by month from October 2020–September 2022.

to-adult participant recruitment is not a novel approach, our findings suggest that studies attempting to recruit the infant population would benefit from a direct-to-participant approach.

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The Funder has no role in the design of the study and collection, analysis, or interpretation of the data.

## CRediT authorship contribution statement

**Stefany Olague:** Project administration, Visualization, Writing – original draft, Writing – review & editing. **Helen Boyle:** Project administration, Resources, Writing – original draft. **Imtiaz Ahmed:** Investigation, Writing – review & editing. **Basharat Buchh:** Investigation, Writing – review & editing. **Giang Sinh T. Truong:** Investigation, Writing – review & editing. **Brent Reyburn:** Investigation, Writing – review & editing. **Clarissa DeLeon:** Investigation, Writing – review & editing. **Grace C. Lin:** Investigation, Writing – review & editing. **Kaashif A. Ahmad:** Investigation, Writing – review & editing. **Barbara Carr:** Investigation, Writing – review & editing. **Meghali Singhal:** Investigation, Writing – review & editing. **Melissa Althouse:** Investigation, Writing – review & editing. **Raymond Castro:** Investigation, Writing – review & editing. **Anthony Rudine:** Investigation, Writing – review & editing. **Evelyn Rider:** Investigation, Writing – review & editing. **Melissa L. Macomber-Estill:** Investigation, Writing – review & editing. **Bradley Doles:** Investigation, Writing – review & editing. **Jenelle F. Ferry:** Investigation, Writing – review & editing. **Hector Pierantoni:** Investigation, Writing – review & editing. **Savannah Sutherland:** Investigation, Writing – review & editing. **Reese H. Clark:** Conceptualization, Data curation, Investigation, Methodology, Resources, Writing – review & editing. **Courtney K. Blackwell:** Conceptualization, Methodology, Writing – review & editing. **P. Brian Smith:** Conceptualization, Funding acquisition, Methodology, Supervision, Writing – review & editing. **Daniel K. Benjamin:** Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Writing – original draft, Writing – review & editing. **Rachel G. Greenberg:** Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Writing – original draft, Writing – review & editing.

## Declaration of competing interest

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

## Data availability

No data was used for the research described in the article.

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