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What We Have Learned About Best Practices for Recruitment and Retention in Multicenter Pregnancy Studies

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Abstract

For thirty years, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units (MFMU) Network has had significant impact on clinical practice in obstetrics. The MFMU Network has conducted 50 randomized clinical trials and observational studies designed to improve pregnancy outcomes for mothers and children. Each center has a designated clinical research nurse coordinator who coordinates the day-to-day operations of each trial and leads a research team that is responsible for recruitment, and retention, of participants. Some of the lessons learned by the nurse coordinators over the past 30 years are described with examples from recent studies. Best practices that we have amassed from our experience are also described.

Introduction

It is well known that multicenter clinical research studies that can change clinical practice require adequate numbers of participants to answer the scientific questions. Retention of those subjects is critical to minimize the loss of important data collected. The MFMU Network consists of 12-14 leading academic research institutions with access to approximately 150,000 annual deliveries and an infrastructure capable of handling multiple, large randomized clinical trials and observational studies concurrently. Because of the pace of recruitment and the volume of studies we have conducted, we have had to ‘learn our lessons’ rather quickly. However, given the complexity of conducting good clinical research, we have found that no one technique to recruit and bring patients back works for all studies and at all centers.

It is acknowledged by the MFMU investigators that the coordinators are ‘the backbone’ of the Network. Study success relies heavily on them as they play the primary role in all of the

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following facets of conducting and managing our studies: IRB submission, training and supervising study staff, maintaining regulatory files, monitoring study performance, supervising data entry, ensuring data quality, resolving data queries, maintaining study supplies, and most importantly, recruiting, enrolling and retaining subjects.

One of the strengths of the Network is that the nurse coordinators are integrated into the organization. The MFMU Network Steering Committee is the decision-making body and consists of the clinical center, data coordinating center, and NICHD principal investigators. The Steering Committee meets quarterly and all of the nurse coordinators attend this meeting. The meeting provides an opportunity for the coordinators to meet separately face-to-face for several hours to share problems, accomplishments, and materials; problem-solve issues hindering recruitment and follow-up; and refine strategies in real time to maximize opportunities.

Each study is supervised by a protocol subcommittee which includes a subset of the Network clinical center principal investigators, the NICHD Project Scientist, representation from the data coordinating center and two nurse coordinators. The subcommittee assures that all aspects of the research are considered in study design. The two coordinators actively participate in protocol and operations development with a keen focus on the feasibility of recruiting and retaining pregnant women. Once the study begins the subcommittee monitors progress of the study; takes part in central outcome review, if required; discusses problems; clarifies study procedures; and recommends changes to the protocol or manual of operations to the Steering Committee. The two nurse coordinators are the liaison with the other coordinators and bring issues and problems for resolution to the subcommittee.

We have found that active monitoring is the key in establishing best methods for each individual study. Regular, ongoing scrutiny of screening, enrollment and follow-up efforts helps to ensure that efforts are commensurate with trial design and execution. Once studies are ongoing, weekly recruitment updates and monthly summaries provide a useful snapshot of screening and recruitment efforts. A quarterly report has more detailed information on data quality, protocol adherence, compliance and retention. This article is intended to share some of the MFMU recruitment and retention strategies employed by the nurse coordinators. Following are some examples from specific trials.

Randomized Trial of 17 Alpha Hydroxyprogesterone Caproate (17-OHPC) for Prevention of Preterm Birth in Nulliparous Women with a Short Cervix (SCAN)

This double-blinded trial was conducted to determine whether 17-OHPC treatment reduces the risk of preterm delivery in nulliparous women with a short cervix.¹ Nulliparous women were approached to consent for a screening transvaginal ultrasound to measure cervical length. The ultrasound was performed by a study-certified sonographer. This trial is an example of one where large volume screening in prenatal clinics is required. One of the most helpful components for recruitment is support from the OB/GYN department - for example if sonographers and physicians take the time to introduce their patients to the research staff.

While the clinic staff wish to be supportive, they do not always have the time to answer study-related questions in detail. Providing a constant presence of research staff members in the clinics to answer study questions generally ensures seamless and effective screening and recruitment.

Screening a large volume of women also required more staff to be involved in the recruiting process. The same staff person was unable to recruit and be available for the real time ultrasound. A second research staff member had to oversee the ultrasound process to make sure it was carried out within protocol and by a study certified sonographer. This should be taken into account when planning.

Once enrolled, flexibility was the key to providing consistent follow-up on a weekly basis. Some centers were able to offer home visits which require additional nurses for staffing or contracting with home health agency nurses to complete home visits. Offering transportation to and from weekly visits was also conducive to retention.

Randomized Clinical Trial of Treatment for Mild Gestational Diabetes Mellitus (GDM)

The purpose of this randomized trial was to determine whether women with mild GDM (fasting glucose < 95 mg/dl) should be treated with usual GDM care, i.e. diet, glucose monitoring, and insulin as needed as opposed to normal obstetric care. Women who failed the required one- hour clinical glucose screening test between 24 and 30 weeks gestation and met all other eligibility criteria were potentially eligible for the trial. They were then asked for consent to undergo an oral glucose tolerance test for analysis at a central laboratory. They were informed that if they were found to have mild GDM and still satisfied all other eligibility criteria, they would be randomized, without requesting further consent, either to usual GDM care or to normal obstetric care, without knowing the results of the test. Moreover, they had to agree that if even if they did not have mild GDM, they might be selected to be part of the usual obstetric care group. The rationale for this complex design is described in Thom et al. in this issue and in Landon et al.² Given that all of the study information was contained in a single consent document, initially the study was somewhat difficult to explain to the patients.

Since these women needed a diagnostic three-hour GTT anyway, the OGTT itself was not a barrier to recruitment. Some centers used their Clinical Research Center (now CTSA) facilities and staff for the three-hour test. This method had multiple advantages for the patient including use of a private room with TV and bed, as well as receiving lunch upon completion of the test. Other centers performed the GTT using clinical space available at their centers. Patient reimbursement for time and transportation were also provided.

The blood samples were sent to the central laboratory and results forwarded directly to the data coordinating center. Women who were designated as having mild GDM according to their OGTT results were randomized by the coordinating center to usual GDM care or to standard obstetric care. A matching sample of women who passed the OGTT test was also enrolled by the coordinating center into the usual obstetric care arm. The clinical center staff

were notified when a woman was assigned to usual GDM care, in which case they knew that the woman had been diagnosed with mild GDM, or if she had been enrolled in the usual obstetric care arm. If she was in the latter group, neither the research staff nor the patient knew whether she did or did not have mild GDM. After a patient was assigned to be part of usual GDM care or normal obstetric care, the research staff re-explained the study group she was in to the patient, and questions were answered using a standardized script. Only one woman in the usual GDM care group decided not to proceed with the study.

This trial was difficult to recruit for because care providers were concerned that their patients with mild GDM were being treated as though they did not if they randomized to the usual obstetric care arm. The PI at each center educated the multiple providers about the rationale for the trial, the study procedures, and the importance of following the study protocol. The Protocol Subcommittee Chair who led the trial and other physician members of the subcommittee made themselves available to travel to the centers to give Grand Rounds and educate local obstetricians. Support from private physicians, as always, was crucial to the success of the trial and retention of study patients. We have found that providers who support and understand the study are more likely to refer patients. Likewise, patients are more willing to participate if their provider is supportive and understands the study.

The primary outcome required determination of neonatal hypoglycemia by heel stick conducted within two hours of birth, hyperinsulinemia from cord blood and hyperbilirubinemia determined from a blood sample before 24 hours of age. As with any study procedures needed at the time of delivery or shortly thereafter, success depends on being notified of the participant coming in for delivery. Techniques include asking patients to call (or these days, to text) upon admission to the Labor and Delivery (L&D) Unit, placing posters and/or fliers around the unit to remind clinical staff to notify research staff when a study participant arrives, flagging electronic medical with a research notification or an electronic notice, and flagging paper medical records with brightly colored paper. Ensuring successful follow-up for the GDM trial was labor intensive and required on-call research personnel for nights and weekends.

Gestational Diabetes Mellitus (GDM) Follow-Up Study

The Gestational Diabetes Mellitus Follow-up Study (GDM FU) was a follow-up to the GDM trial above. The study was designed to evaluate whether treatment of mild GDM confers sustained offspring health benefits, including a lower frequency of obesity in the treated mothers' children at 5 to 10 years of age.³ Height, weight, blood pressure, waist circumference, fasting glucose, fasting insulin, triglycerides, and HDL cholesterol were measured.

This study presented unique challenges as the trial was not designed to follow up the participants long term. Contact had not been maintained with participants after delivery hospitalization and the 6-week post-partum period. Each site requested IRB approval to contact subjects for an unplanned follow-up. Initial efforts to re-establish contact with participants included searching the electronic medical records for updated contact information for patients who re-entered the system after completion of the original GDM

study. For those who did not re-renter the system with updated contact information, the challenge was much greater.

Because of the increased popularity of the cell phone during the same period, many participants no longer had active home phone numbers. According to the National Health Interview Survey (NHIS) report (2013) there was an almost 40% increase from 2003-2013 among adults living in households with only wireless telephone service.⁴ According to the report 53% of Hispanic adults rely on wireless-only service. Of note, the GDM FU potential study population was 59% Hispanic. In addition, due to the ever-changing competition among cell phone service providers, many people change cell phone numbers often as more affordable options become available. For the participants who had cell phone numbers at initial study enrollment, there was a substantial chance that they no longer had the same cell phone number years later. Thus, the challenge began as to the best method to locate and contact these patients.

Along with the advances of cell phones to Smartphones, the popularity of social media also grew. While people may often disconnect from one phone number to another, they often maintain their connection to social media; therefore, Web-based search engines and social media were also used as resources to regain contact. Checking pediatric or obstetrical records for other visits helped us find patients too. These databases often had information found in public records which then helped with the process of locating these participants. To simplify this process, the data coordinating center purchased credits with a search engine company (Accurint®) to use in searching for these participants. As with all MFMU Network studies, the coordinators shared insights regarding what resources had proven to be most successful. In the end, 76% of the families were successfully contacted.

With respect to recruitment, our goal was to make participation as convenient as possible. Some centers offered Saturday appointments to accommodate mothers and their children who did not want to miss work or school to attend the exam. For those women who had moved, protocols were set in place so that patients could be seen at a more convenient Network center. When this was not possible, special considerations for travel reimbursement and hotel accommodations were made for those individuals who were no longer near a study center. Of those who were contacted we were able to achieve a 75% rate of participation.

In summary, persistence and various tracking methods were essential to our success in contacting participants 5 to 10 years after their participation in the original randomized trial. For this older trial we had not originally asked women if they would be willing to be contacted for future research. Today when we obtain consent for a trial that does not involve long term follow-up, we always ask the participant if she would be willing to be contacted in the future for additional research. It is always important to collect up-to-date contact information. We have found that multiple family contacts, especially parents, grandparents, and friends are the most useful.

Combined Antioxidant and Preeclampsia Prediction Study (CAPPS)

CAPPS was a randomized trial of antioxidants (Vitamins C and E) to reduce complications of pregnancy associated hypertension.⁵ The CAPPS participants were enrolled in the first or early second trimester of the pregnancy. For all placebo-controlled trials, the Network has a policy of requiring a 1-week 'run-in' or test period to ensure that the medication is palatable, and to confirm the candidate's willingness to take part. Each participant was given a supply of placebo capsules in a single-blind manner and asked to return within 14 days for a compliance check. If she took more than half the required amount of pills she was deemed compliant, and allowed to enroll in the randomized trial. Of those who were eligible and consenting 27% were excluded from randomization as a result of the run-in. The reasons for exclusion because of the compliance run-in were consent withdrawal, lost contact, failure to return and failure take the required dose. While the compliance run-in period was difficult to plan and schedule, we feel that it is useful to eliminate women who would potentially withdraw or not continue taking the study medication during the trial.

This study used large black capsules of vitamin C and E or placebo. And we learned that the physical properties of the medication matters to patients. Many women complained about the size of the capsules and difficulty in swallowing them as well as the unappealing black/dark color. We learned that it was important to educate the women in advance by showing a sample of the pills and explaining that the pills were about the size of an average prenatal vitamin. It was also explained to the potential study participants that the pills had to be dark colored so that everyone would be blinded to what was inside and to protect the integrity of the medication from the light. They were gel coated to make them easier to swallow. In order to increase compliance, we recommended that they take them at the same time as the daily prenatal vitamin.

As with other studies, there were many initially interested women who notified the research staff that they would not participate because their spouse or family members did not want them in a research study. To circumvent this, participants were asked to include family members and significant others in the consent process and some were provided with a simplified overview of the consent form to share with them ahead of the randomization process. Every attempt should be made to provide materials that are simple and brief. The majority of the women also needed a dating ultrasound which was paid for by the study and was a prime opportunity to encourage the spouse or family members to be involved. At this time, research staff reviewed the consent form with the participant and her family members, and answered all their questions. Nevertheless, research staff need to be cognizant of patient stressors, information overload, and possible study fatigue which may affect compliance. Every attempt was made to meet participants for the compliance check and randomization, as well as to arrange subsequent study visits at a prenatal visit to minimize the research visit burden and increase recruitment and retention.

Randomized Trials of Thyroxine Therapy for Subclinical Hypothyroidism or Hypothyroxinemia Diagnosed During Pregnancy (TSH)

The TSH study consisted of two parallel trials designed to determine whether thyroxine compared with placebo given to women with subclinical hypothyroidism or hypothyroxinemia affects I.Q. as measured by the Wechsler Preschool and Primary Scale of Intelligence in their children at age five.⁶

The most noteworthy challenge in this trial was the five-year follow-up required to obtain the study's primary outcome cited above. The children also underwent neurodevelopmental testing annually. Participating centers' research personnel went to great lengths to track subjects and keep them engaged throughout the five years. Face-to-face interaction at routine clinic appointments, as well as birthday and holiday cards, "thinking of you" notes, E-mail messages, and newsletters are just some of the methods used. Even when patients move abroad, attempts should be made to keep in touch with them.

Many subjects moved not only to different states but to other countries. For those who moved, maintaining contact and tracking subjects required elaborate methods, creativity, and above all, perseverance. We found that persistence in calling cell phone numbers that were previously documented as "disconnected" to see if they were reactivated resulted in many successful contacts. Some subjects agreed to return to their centers of origin while others were agreeable to follow-up in places within close proximity of their new residences. In addition, we had several study examiners who were willing to travel to the families' homes to conduct the testing. Allowing these kinds of variations in the follow-up procedures were crucial in ensuring excellent follow-up of these patients.

One would think that the endeavors outlined above would be more than enough to ensure follow-up for most TSH subjects, if not all. However, for a number of subjects who had returned to Mexico, follow-up in the U.S. was neither an option, nor were examiners willing to travel there for safety reasons. We had to think 'outside the box'. For these families we set up a site in Mexico, (El Centro Medico ABC Hospital), where TSH follow-up visits would be conducted by a Mexican examiner who was certified for the study. The long and challenging process from concept to actualization was worth the effort. The follow-up coordinator in Dallas, TX served as the liaison to facilitate communication between the participants, the examiner and ABC Hospital staff. This was important because there was already an established rapport and trust between the participants and the follow-up coordinator, that was a key factor in maintaining contact throughout the 5-year follow-up period. To bring these recruits back in trials with long-term follow-up, the importance of a long-term, dedicated and organized follow-up coordinator who has already established a trusting relationship with the patient and who is persistent but tolerant cannot be overstated. This strategy has been used effectively in the Network for many trials. For this trial, remarkably, a Network-wide follow-up rate of more than 90% at 5 years of age was achieved.

Antenatal Late Preterm Steroids (ALPS)

The ALPS trial was a randomized trial to evaluate whether administration of antenatal corticosteroids versus placebo to women at high risk of delivering at 34 to 36 weeks of gestation (the late preterm period) reduces the need for neonatal respiratory support.⁷

Since the literature supports standard of care corticosteroid use for women likely to deliver less than 34 weeks gestation, we found that requesting consent in the late preterm period 34 – 36 weeks gestation was less complicated than other studies and somewhat reassuring to parents. The majority of recruitment for this trial took place on L&D. Our experience with in-patient trials has shown us that timing of consent is always crucial, and we found this trial to be no different. For eligible women, consenting usually took place on L&D units due to preterm rupture of membranes or preterm labor. The timing of consent was very challenging in this setting because women were often experiencing anxiety and/or pain. It was often necessary to delay consenting for a more convenient time, while staying mindful of the time constraints for enrollment (patients were excluded if delivery was expected in less than 12 hours). The care teams, physician and nurse, were instrumental in providing insight to the appropriate timing of the consent. It was much less challenging to obtain informed consent from patients who had a planned induction or cesarean because this provided time before the delivery to conduct the consent process in a relaxed environment, usually in the clinic setting rather than in the rushed L&D setting.

A Randomized Trial of Fetal ECG ST Segment and T Wave Analysis as an Adjunct to Electronic Fetal Heart Rate Monitoring (STAN)

The purpose of this trial was to determine whether fetal ST segment analysis as an adjunct to conventional electronic fetal heart rate monitoring would decrease the risk of fetal compromise. This randomized trial - the largest of the Network's trials to date - required the enrollment of over 11,000 women in L&D units. Women were randomized either to an 'open' STAN monitor, that included ST segment analysis of the fetal ECG, in addition to usual fetal heart rate parameters or to a 'masked' fetal heart rate monitor which functioned exactly as a conventional fetal heart rate monitor. Further details are available in the primary report.⁸ Prior to initiation of this study all obstetric care providers, that is both physicians and nurses, who might have any direct patient care or management involvement, had to undergo initial training and certification at a level that exceeded existent FDA requirements.

Buy-in from faculty and institutional support was very important in recruitment efforts and was accomplished through Grand Rounds and training sessions. The trial required more L&D coverage by research staff than initially expected, and with adequate coverage, recruitment increased. Gaining the support of the clinical staff was also critical. Maintaining appropriate staffing was challenging yet crucial to ensuring that every possible eligible subject has an opportunity for consent and randomization.

The study requirement to use a specific fetal scalp electrode was met with some resistance from physicians and staff in institutions where the use of fetal scalp electrodes was not common practice. This provided many educational opportunities for the network

investigators and research staff and was critical for the ongoing success of the study. Over time, the investigators' and nurse coordinators' persistent outreach, training and education, informative lunch sessions, and availability 24/7 generated the acceptance and trust needed to result in referrals and study completion.

Randomized Trial to Prevent Congenital Cytomegalovirus (CMV)

The CMV study is an ongoing randomized double-masked placebo-controlled clinical trial designed to determine if monthly treatment with CMV hyperimmune globulin (Cytogam ®) will lower the rate of transmission of CMV to infants born to mothers with a primary CMV infection identified in early pregnancy. CMV screening was well received at most centers. Women were willing to add an extra tube of blood to routine labs for peace of mind to rule out this potentially devastating virus. The sheer screening numbers needed to identify women with primary CMV has been a daunting challenge.

Notifying women of positive results is difficult. The primary caregiver is often notified first and then the woman is called by the nurse coordinator. These calls are often alarming to patients; in fact many admitted to searching the internet for more information as soon as the call was over. Emphasis during the call is placed on getting a consult with Maternal-Fetal Medicine and an ultrasound and not on the trial. When the women come in, if they are still eligible (for example, no signs of fetal CMV infection on ultrasound) the trial is described in more detail in a face to face meeting with the research nurse. The Network has created an informational video that is helpful for the women and their families. Most patients do not decide on participation without consulting family members and partners, as well as their physicians.

The CMV trial is an inconvenient and complex study as it involves monthly infusions and a large time commitment both for treatment and follow-up. Some women are afraid to undergo the infusions or unproven treatment during their pregnancy when exposure to CMV does not mean that their offspring will be automatically affected; the fetal infection rate is 40% with primary maternal CMV infection. Nevertheless, the consent rate for the CMV trial has been if anything, somewhat higher than anticipated.

An Observational Study of Hepatitis C Virus in Pregnancy (HCV)

HCV is an ongoing observational study to understand risk factors associated with transmission of the virus from pregnant mother to her child. Mass screening for this study has been quite efficient as we used a single blood draw and tube to test for both CMV (above) and HCV viruses. This was beneficial to the patient as it lessened the amount of blood required and eliminated the need for a second needle stick if the studies were not combined. Some Network centers were able to utilize a single consent form for both CMV and HCV screenings. This decreases the burden on the patients and means that the sample collection procedure can be described more simply.

Subjects' willingness to participate in the HCV study has not been problematic. Reasons for consenting are mostly altruistic. Major reasons for declining include incarceration, relocation, or planned delivery outside of a MFMU Network hospital; or transportation

issues. Patients consider this a complex study and often wish to involve spouse or other family members before agreeing to enroll. Engagement of family members in recruitment and follow-up process is crucial for getting buy-in from the perspective enrollee. Providing simplified informational materials for family members and allowing women some time to have discussions about it with them is more likely to ensure a commitment to participate from the women.

By far the biggest issue with the HCV Study has been infant follow-up to obtain blood samples at two months and five months of age. Since these infants are high risk, it is preferable that they be followed by a pediatric infectious disease specialist. Scheduling their study visits with a coinciding clinical appointment has been helpful in maintaining subject retention. In this population, working with authorities in custody cases or foster care can help with follow-up.

As with other follow-up after neonatal discharge, it is important to establish a strong rapport with research subjects and to design effective aids for them to stay in touch, including, for instance, 'contact information sheets' and 'research staff contact cards.' Follow-up coordinators make every effort to check in regularly with patients to ensure correct contact information and to remind them of future appointments. Some centers have a single phone number, single pager number, or an OB research email address where subjects can easily provide updated contact information. Contact information obtained at delivery, however, may not be current at the time of infant two-month visit. Telephone attempts and internet searches often lead to dead ends.

Even with known contact information, these subjects often do not show up for their scheduled pediatric appointments. In attempts to collect research information, coordinators have driven to patients' homes and to pediatric appointments out of town, only to wait on a patient who never shows or to find out they no longer live there.

With perseverance, subjects thought to be lost to follow up, can be relocated. Examples include mobile phones which may have been turned off due to a patient not paying her bill, but then turned back on a few months later. Sometimes a patient may be incarcerated or in a homeless shelter for a period of time and then reached at a later date.

In this population, working with authorities in custody cases or foster care can help with follow-up. One example is a biological mother who gave her infant up for adoption. The enrolling center has been successful in communicating with the prospective adoptive parents, the Department of Social Services and obtaining the social workers consent for the infant's continued study participation.

Discussion

Strategies for successful recruitment and retention vary from study to study and from center to center. Regular interaction of research personnel, especially the nurse coordinators, allows discussion of the implementation and progress of trials, the exchange of ideas and solutions to issues; and generates questions for the protocol subcommittees to enhance the study design or operations.

Buy-in of others such as clinic staff or obstetric providers is vital to recruitment efforts. Educational information such as printed materials, brochures, flyers and posters are important not only to provide information to the potential enrollees, but increase awareness of the trials and educate hospital personnel including the administration. Engagement of family members in recruitment is essential. Simplified informational materials for family members and allowing women some time to have discussions about it with them is more likely to ensure a commitment to participate.

Once enrolled, first and foremost is to develop the ability to keep enrolled subjects in the study and follow them up, whether they are in L&D or at home years later. Failure to collect as much contact data as possible could mean the difference between capturing valuable data and losing the patient to follow-up, jeopardizing the study results. We found that no participants should be 'written off' because in some cases, persistence in relocating patients has proven effective.

Logistical factors affecting subject retention include (among others) family involvement and support, and mobility. As with all studies, engaging and educating family members early on and being available in a supportive, caring manner can mean the difference between retaining or losing them. This requires a structured format and current contact information to check-in with trial participants regularly.

It is important to design flexible recruitment and retention plans, and if possible, for instance, to coincide with prenatal visits (CAPPS) or school vacations (GDM FU Study). Allowing follow-up during weekend home visits or allowing patients to go to another center also eases the burden for busy families and enhances their commitment. Providing a budget for travel reimbursement for patients who move away and are willing to come to a Network center or for examiners to visit the patients facilitates follow-up has been very fruitful in terms of follow-up. Providing incentives that are not coercive, such as transportation reimbursement, child care while the mother is with staff, gift cards to help defray out-of-pocket expenses for the participant show that the participant's time and effort are valued.

Conclusion

The MFMU Network, with its longstanding multicenter clinical trial infrastructure of university-based perinatal centers and dedicated, experienced perinatal research teams, has successfully completed many randomized trials and observational studies for three decades. We've learned that multiple strategies work best to answer the scientific questions proposed by the investigators. Each study brings new challenges and lessons learned in enrolling and retaining pregnant women in perinatal research. The importance of flexibility in addressing these challenges is paramount. By using strategies outlined here and developing new ones as needs arise, we hope to continue to provide and follow-up adequate numbers of participants to answer clinically-relevant obstetrical questions, furthering the mission of the MFMU to reduce perinatal morbidity related to preterm birth, fetal growth abnormalities and maternal complications.

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