PregSource℠: Crowdsourcing to Understand Pregnancy Observations of Daily Living from Pregnant Women

Protocol Number: T-CH-0901: PregSource℠

ClinicalTrials.gov number: NCT02577536

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Version Date: 2015 December 8

Protocol Details

Total requested accrual	100,000 Subjects (estimated)
Project Uses Ionizing Radiation:	No
IND/IDE required:	No
Durable Power of Attorney	No
Multi-institutional Project	No
Data and Safety Monitoring Board:	No
Technology Transfer Agreement:	No
Samples are being stored:	No
Flesch-Kincaid reading level of consent form:	8.0

Contents

ABSTRACT

Objective
To better understand the range of physical and emotional experiences and alterations in behavior that women have during pregnancy and after giving birth, the impact of these experiences on women's lives, and the perinatal challenges encountered by special sub-populations of women.

Study Population/Eligibility Criteria
Pregnant women age 18 to 70, all races and ethnicities.

Design Type
PregSource℠: Crowdsourcing to Understand Pregnancy (PregSource℠) will use a longitudinal, crowd-sourcing, citizen science approach, asking pregnant women regularly and directly about their pregnancies. Participants will enter information throughout gestation and the early infancy of their babies into online surveys and trackers via a website and/or mobile applications ("apps"). In exchange, participants will be able to track their pregnancy data over time, print out reports to share with their healthcare team, and view summaries of de-identified data to see how they compare to other women. In addition, PregSource℠ will provide participants with links to trusted, evidence-based information from partner organizations about pregnancy management, issues, and complications.

Participants may also be a potential pool of recruits for clinical studies. Based on information they enter, eligible women who are interested in participating in clinical studies may be sent contact information about observational or interventional studies. Their contact information will not be shared directly with researchers.

After a critical mass of data is collected, de-identified data will be available to approved researchers for analysis.

Outcome Measures
PregSource℠ is an online research registry for collecting information about the natural history and range of normative experiences of pregnancy from the primary source: pregnant women. It, therefore, does not have specific outcome measures beyond descriptive data on women's experiences and pregnancy outcomes.

SECTION 1. STATEMENT OF PROBLEM

In 2009, the U.S. Centers for Disease Control and Prevention (CDC) reported an estimated 6,369,000 pregnancies – 102 pregnancies per 1,000 women – resulting in 4,131,000 live births and 1,087,000 fetal losses (Curtin SC, et al 2013). While many of these women are seen by physicians, and hundreds of research studies are conducted, we know more about pregnancy complications, than about the natural history of human pregnancy. There is limited to no information on normal pregnancy despite its prevalence as the majority of studies are performed on specific conditions. Furthermore, even those tend to be case series and not representative of the population. In a review of clinicaltrials.gov there are no ongoing studies characterizing normal pregnancy. Information collected in any systematic way from the patient's point of view about how pregnancy affects the lives of women in our modern world is also missing, such as:

- How many women get morning sickness? How long does it generally last? At what gestational ages does it tend to occur? Does it have any impact on maternal weight?
- How does being pregnant affect women's sleep, energy levels, and mood? How do these change over the course of the pregnancy?
- What is the impact of pregnancy and pregnancy symptoms on women's lives? How easy is it to stick to your doctor's orders for diet, exercise, and special treatments?
- How is being pregnant more challenging for certain women (e.g., women with physical and intellectual disabilities)?

We believe that PregSource℠: Crowdsourcing to Understand Pregnancy (PregSource℠) will help us gather information directly from pregnant women as they experience it, so that we can help answer some of these questions. According to Project HealthDesign, "Lay people engage in health practices and health behaviors every day, not just during visits to clinicians. They revealed that they attend not only to signs and symptoms of illness as directed by clinicians, but also to the idiosyncratic, highly personal thoughts, behaviors, attitudes, sensations, and environmental conditions that inform them about their health state and alert them to take action related to health. These observations of daily living (ODLs) complement traditional signs and symptoms of disease (e.g., blood pressure, shortness of breath) and highlight the personal experience of health and disease (Brennan 2010)."

PregSource℠ is an initiative run by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, to learn about women's experiences with pregnancy, to collect observations of daily living and healthcare information about their pregnancies. It is an online research registry for collecting information about the natural history and range of normative experiences of pregnancy from the primary source: pregnant women. Its goal is to collect data that will help inform future studies on pregnancy and other health areas, which we discuss below in more detail. It is neither designed nor intended to determine clinical effectiveness or cost-effectiveness of health care products and services, measure or monitor safety and harm,

measure quality of care, or diagnose or treat any disease or condition. The purpose of PregSource℠ is to inform future research – not necessarily to perform empirical research – by learning about:

- Women's physical and emotional experiences during pregnancy and after giving birth;
- How pregnancy affects their lives; and
- Special challenges of some women, such as women with disabilities or chronic health conditions.

PregSource℠ can give us an overall picture of what women experience during pregnancy based on information from the women themselves.

Crowdsourcing Methodology

To do this, PregSource℠ will harness the innovative power of crowdsourcing and citizen science (Swan M 2012) by asking pregnant women to contribute their personal observations of daily living to our database. Promoted recently by the White House Office of Science and Technology Policy (OSTP), "Crowdsourcing is a process in which individuals or organizations request voluntary contributions from a large group of unknown individuals ("the crowd")(The White House, Web log post, December 2, 2014)." OSTP includes initiatives that incorporate and improve upon crowdsourcing as part of the Second Open Government Federal Action Plan. The Office also notes that "Citizen science and crowdsourcing are powerful tools that can help Federal agencies: advance and accelerate scientific research through group discovery and co-creation of knowledge; increase science literacy and provide students with skills needed to excel in science, technology, engineering, and math; improve delivery of government services with significantly lower resource investments; and connect citizens to the missions of federal agencies by promoting a spirit of open government and volunteerism." PregSource℠ is designed to do all of these.

PregSource℠ will use a longitudinal, crowd-sourcing, citizen science approach, asking pregnant women directly about their pregnancies. Participants will enter information throughout gestation and the early infancy of their babies into online surveys and trackers via a website and/or mobile applications ("apps"). This research registry will enable us to collect data and experiential trends on issues and topics for which no baseline data currently exist, and that can inform current and future research projects among pregnant women (Wang et al 2015). Because of the Internet-based design of the study, it may not enroll a nationally representative sample. But by surveying a broad cross-section of women about their experiences in near real-time, data from PregSource℠ might confirm (or contradict) some of the information that currently exists about pregnancy topics such as nausea, weight gain, and sleep quality and duration. For instance, one of the key findings from the 2009 IOM pregnancy weight gain guidelines were that "Currently available data sources are inadequate for studying national trends in GWG [gestational weight gain], or postpartum weight, or their determinants (IOM 2009)." PregSource℠ can provide data on GWG trends and other baseline data that investigators can use to inform their observational studies and interventional trials on such topics and can potentially aid in recruitment.

By collecting information directly from the primary source (pregnant women), PregSource℠ requires minimal infrastructure cost, while simultaneously maximizing delivery of evidence-based pregnancy information from experts.

Participants answer questionnaires about their experiences over the course of their pregnancy, recovery, and their baby's development – observations of daily living that are usually available only from periodic, time-constrained clinical visits. Women with certain pre-pregnancy conditions (e.g., physical disabilities) and those who develop pregnancy complications (e.g., gestational diabetes) will be asked additional questions about their pregnancy experiences, outcomes, and recovery. The anytime/anyplace access to participants improves data collection by recording events as they occur throughout pregnancy. This type of access to participants in research is unprecedented and not feasible in other types of research designs.

In addition to utilizing the power of the crowd, PregSource℠ aims to capitalize on the new trend of the "quantified self," people aiming to improve their personal health by using technology to record their daily activities and biometrics. Many women now are currently tracking their menses, fertility, and other health data using apps, wearable devices such as FitBit and Apple Watch, and other websites (Swan M 2009, Wolf G 2009, Appelboom G et al 2014). Given the 300+ pregnancy-related apps currently available, we believe that pregnant women are particularly interested in tracking their data. We also believe that they will be willing to donate their data for scientific research, if we: provide them with easy-to-use trackers and questionnaires, and incentivize them to keep using them over the course of their pregnancy with educational materials, comparison summary data, and tools that capture what they are interested in tracking, in addition to data that are of empirical research value. Finding out how many women are willing to do so, and best practices and lessons learned along the way, in and of itself, will provide meaningful information for future crowdsourcing research efforts in pregnancy and other health areas.

In exchange, participants will be able to track their pregnancy data over time, and print out reports to share with their healthcare team. They will also be able to view summaries of PregSource℠ data to see how they compare to other women – "Am I the only one that still has morning sickness at 6 months of pregnancy?" In addition, PregSource℠ participants will receive relevant information about evidence-based medical guidelines and practices that are already published by government and non-government health care societies and organizations. Participants will be clearly told that if they have any concerns about their pregnancy or about what they learn in PregSource℠, they should discuss their concerns with their health care provider.

Participants may also be a potential pool of recruits for clinical studies. Based on information they enter, eligible women interested in participating in clinical studies, would be sent contact information about observational or interventional studies. Their contact information will not be shared directly with researchers.

After a critical mass of data has been collected, de-identified data from PregSource℠ will be made available to approved researchers for analysis. De-identified data will be housed in the Research Data Patient Repository (RDPR).

By gathering information directly from pregnant women, researchers will have access to a large dataset to better understand pregnancy from the participant's point of view and potentially find ways to improve healthcare and wellness for all pregnant women.

SECTION 2. STUDY OBJECTIVES AND OUTCOME MEASURES

2.1. PRIMARY OBJECTIVE

To better understand the range of physical and emotional experiences and alterations in behavior that women have during pregnancy and after giving birth, the impact of these experiences on women's lives, and the perinatal challenges encountered by special sub-populations of women. The protocol will be positioned to address numerous questions. Initially, it will focus on eight areas with the ability to expand to many other areas once the foundation is developed.

2.2. SECONDARY OBJECTIVES

To measure the impact that pregnancy symptoms and treatments have on women's lives. Examples of the overarching questions and measures include:

- Nausea and vomiting during pregnancy – to identify how often this affects pregnancy, its timing, treatments, and impact on weight
    - How often and at what gestational age do nausea and vomiting begin/improve?
    - Impact on weight
    - Treatments
- Physical disabilities and pregnancy – to identify how many pregnancies may be affected by physical disabilities
    - What disability?
    - Impact on pregnancy
    - Impact of pregnancy on the condition
- Weight gain in pregnancy – to identify weight gain patterns in pregnancy and compare to Institute of Medicine guidelines
    - Pre-pregnancy weight and height
    - Weight weekly or monthly
    - Plot weight gain on the appropriate IOM guideline chart
- Activity/Exercise in pregnancy – to identify exercise patterns in pregnancy including type and amount of exercise, impact on pregnancy
    - Evaluation of moderate and high impact activities across pregnancy
- Sleep in pregnancy – to identify sleep patterns in pregnancy including number of hours, sleep quality, and sleep position
    - Sleep pattern prior to pregnancy
    - Number of hours (on average) sleep per night
    - Quality of sleep
    - Prevalence of sleep apnea
    - Sleep position
- Mood in Pregnancy – to identify general mood in pregnant women throughout gestation. This will be done via a Mood Tracker and mood may be entered as often as necessary. We will use the validated Positive and Negative Affect Schedule (PANAS)

(Watson D and Clark LA 1994; Thompson ER 2007). This measure has also been used to access psychological stress among women with and without reproductive failure (Coughlan C et al 2014). It may collect mood descriptions such as excited, irritable, angry, jittery, etc.

- Medications in pregnancy – to identify how many medications women are taking, reasons for their use, and how many are taken without clinician recommendation
    - Any medications used (weekly query) with triggers of those input in prior week to allow a continuation or stopping of that medication
    - Reason for the medication being used
    - Did a medical provider recommend the medication or is it being used over the counter?
- Alternative "medications"/herbal supplement use in pregnancy – to identify how many and what alternative medications/herbal supplements women are taking, reasons for their use, and how many are taken without clinician recommendation
    - Any herbal supplements or alternative medications used?
    - If yes, at what gestational age and for how long?
    - Reason for use
- Number of ultrasounds in pregnancy – to identify how many ultrasounds are being performed in pregnancy, the reasons, and how many are performed without clinician recommendation
    - Any ultrasounds during pregnancy?
    - Reason for the ultrasound

2.3. OUTCOME MEASURES

PregSource℠ is a research registry for gathering longitudinal, observational data from women during their pregnancies. It, therefore, does not have specific outcome measures beyond descriptive data on women's experiences and pregnancy outcomes.
It will provide the following benefits:

- Allow participants to compare their personal health situation to the summarized, de-identified information from other participants, and links to evidence-based information sources
- Provide de-identified data to approved researchers for analysis on etiology, natural history, and/or treatment effectiveness on issues related to pregnancy
- Identify pregnant women who may be eligible and interested in participating in clinical studies and trials

Below is a sample of outcome measures that PregSource℠ will collect and analyze.

2.3.1. Primary Outcome Measures

- Gestational age of delivery
- Birthweight of baby
- Maternal gestational weight gain
- Health of baby and mom

2.3.2. Secondary Outcome Measures

- Proportion of pregnant women who experience nausea and vomiting in pregnancy across gestation
- Proportion of pregnancies that are impacted by physical disabilities
- Weight gain patterns in pregnancy with a comparison to IOM guidelines
- Exercise patterns in pregnancy including type and amount of exercise, impact on pregnancy
- Sleep patterns in pregnancy including number of hours, sleep quality, and sleep position
- How many medications women are taking, reasons for their use, and how many are taken without clinician recommendation
- How many alternative medications /herbal supplements pregnant women are taking, reasons for their use, and how many are taken without clinician recommendation
- Number of ultrasounds in pregnancy

In the future, additional measures may be added, such as assessments of maternal mental health, stress, chronic conditions such as hypertension and diabetes, and assessment of maternal diet and other environmental factors.

SECTION 3. STUDY POPULATION

This will be a prospective cohort study, collecting information from women of child-bearing age who are pregnant. The study will include healthy volunteers, as well as those with pre-conception medical conditions and/or pregnancy complications. Because it will be online, there is no limit to the number of participants who can join. It will be focused on women in the United States, but because it will be online, women in other countries may also participate.

3.1. INCLUSION CRITERIA

- Women who are pregnant and over 18 and under 70 years of age.

3.2. EXCLUSION CRITERIA

- Males
- Women who are not pregnant
- Minors under age 18
- Women over the age of 70
- Women who are unable to provide consent for themselves

SECTION 4. STUDY DESIGN AND METHODS

4.1. STUDY OVERVIEW

PregSource℠ is a participant opt-in research registry. A pregnant woman can go online to the Website or download the app to join directly at a time of her choosing. PregSource℠ will not provide medical advice, treatments, or evaluations, for either clinical or research purposes, and the participant will not be required to visit a doctor, complete any medical examinations, or provide biological samples in order to participate.

Registry questions cover the time period from pre-conception through pregnancy and the post-partum period until 36 months, including neonatal outcomes. A participant can remain in the study as long as she chooses. It is possible, but not required, that she could remain in the study between pregnancies, entering information for multiple pregnancies.

PregSource℠ will be run on a web-based platform under contract with Lockheed Martin Management Systems Designers, Inc. and its affiliated subcontractor, PatientCrossroads, Inc. (collectively referred to as "Contractor"). The platform will capture participant information using condition-specific elements, as well as existing Common Data Elements (http://www.nlm.nih.gov/cde/).

4.2. RECRUITMENT

4.2.1. Recruitment Strategy

We do not anticipate contacting potential participants directly, and will not have access to medical records to identify women for inclusion. Potential enrollees may learn of the study from many sources, including: the NICHD Website, the PregSource℠ Website (or downloading the PregSource℠ app), our partner organizations[1], a participant's doctor or midwife (via professional organizations), or by word of mouth from friends, family members, and other participants.

In addition, NICHD's Public Communications Branch will draft posts about PregSource℠ for NICHD's social media outlets (https://www.facebook.com/nichdgov and https://twitter.com/nichd_nih).

The Website will provide information that explains the purpose of data collection, what participation involves, risks and benefits, alternatives to participation, an explanation of how

[1] Partner organizations include: the American Academy of Pediatrics; the American College of Obstetricians and Gynecologists; the American College of Nurse-Midwives; American Society for Reproductive Medicine; Office of Research on Women's Health; , Centers for Disease Control and Prevention; Health Resources and Services Administration ; Lamaze International, Preeclampsia Foundation; Obstetric and Neonatal Nurses; Office of Behavioral and Social Sciences Research ; the March of Dimes; and the Society for Maternal-Fetal Medicine and several NIH institutes such as NCCIH, NHLBI, NIEHS, NINR and NIMHD.

the data will be used, and contact information for any questions about the research or their rights as a research subject.

4.2.2. Recruiting Non-English Speakers

We will launch the main PregSource℠ website and app in English first. After that, the full website, main consent form, app, and questionnaires will be translated into additional languages, starting with Spanish.

We anticipate launching a fully translated Spanish version of PregSource℠ within 12 months of the launch of the English version. Creating a syntactically and culturally appropriate Spanish version means going beyond a straight word-for-word translation to also incorporate nuances in vocabulary, tone, idioms, and approach. The process is more akin to creating an entirely new website and application than to providing information in a different language because all PregSource℠ content will be affected: from questionnaires and consent documents to help information and system error messages to color schemes and images.

This effort will be led by the NICHD Office of Communications, which has successfully led several other similar projects including the creation of the Spanish version of DS-Connect®: The Down Syndrome Registry and the Spanish subsite of the main NICHD website. The plan outlined below is based on the team's experience with other similar projects.

1. After English website and app are launched, identify, program, and get IRB approval for additional modifications as needed. (15 weeks)
2. Outline translation requirements (i.e., setting freeze date for English content, identifying neutral Spanish words and phrases for use throughout, selecting a neutral Spanish editing style guide, listing staff roles and responsibilities, developing draft deliverable schedule, etc.). (2 weeks)
3. Freezes English version of website and/the app, inventory English content, and pulls into spreadsheet with appropriate technical information. (3 weeks)
4. Provides spreadsheet to American Translation Association-certified translator(s), who then translate the content. This activity comprises the bulk of the timeframe and includes some review and discussion with subject matter and other experts to ensure original intent of questions/content is maintained. (10 weeks)
5. Translator(s) return translated content to programmers, who then build the new website and application in a development or production environment. (7 weeks)
6. Once the site and/app are fully programmed, translators, technical experts, subject matter experts, security experts, and others review the content and function of the site and/app and make any necessary changes. Obtain IRB approval for revisions. (5 weeks)
7. Beta testing begins with different users focused on different aspects of the site/app: some are reviewing for content clarity, others for user experience, and others for overall function and security. All teams discuss suggested changes before they are incorporated. (4 weeks)
8. Final translated content is sent to the IRB for review and approval. (3 weeks)

9. Once approved, the site/app moves from development/production environment to live environment and technical and security experts verify technical and security functions. The English version content is unfrozen. (3 weeks)
10. Maintenance and minor revisions are ongoing as users work in and through the English and Spanish versions. Plans for any changes should include both English and Spanish versions. Analysis of functionality and use is also ongoing for both English and Spanish versions (currently using Google Analytics, but specific tools may change over time).

4.2.3. Recruitment Advertising

Recruitment and retention are critical to the success of a project like PregSource℠, and we intend to employ multiple strategies and tactics at different times throughout the project to achieve our target goals. The tactics may vary from creating radio and transit ads, to providing materials and information for intermediaries (in this case, care providers), to working with and through online and in-person communities, to utilizing sponsored referrals. The specific tactics used will depend on many factors, such as the signup rates, the survey completion rates, participant demographic coverage, and the geographic areas in which we will focus our initial efforts.

The NICHD will rely on its many Partners to help engage their constituents and encourage women to participate. For example:

- The American College of Obstetricians and Gynecologists, the Society for Maternal-Fetal Medicine, and the Association of Women's Health, Obstetric, and Neonatal Nurses, have already agreed to recommend that their members promote PregSource℠ and will share NICHD-provided materials and information with their members to make this promotion easy and cost-effective.
- The Health Resources and Services Administration, the Centers for Disease Control and Prevention, and the March of Dimes have indicated that they will promote the website/app through their local chapters and regional maternal and child health offices and departments.

We plan to create an array of items for multiple channels and types of media that we will share with all of our partners and will make them publically available to non-partners. These will include (but are not limited to): social media messages and graphics, slides that can be inserted into presentations, flyers that are easily reproducible, text that can be dropped into a newsletter or conference program, digital badges that women can include in their social media profiles indicating that they are participating, posters for clinics and provider offices, emails that can easily be distributed over existing listservs and distribution lists, designs for displays that can be used at health fairs or in birthing classes, posting information about the site/app in online resources such as clinicaltrials.gov and ResearchMatch, etc.

NICHD will also issue press releases via the NICHD and/or NIH Communications Offices. NICHD's Website will also post a description of the research registry, along with a link to the main website, and include information in appropriate lists of similar registries and trials, such as the

NIH List of Registries webpage (http://www.nih.gov/health/clinicaltrials/registries.htm). Similar registry descriptions may be available in electronic and/or printed handouts.

In addition, according to the Pew Research Center, when Americans look for health information online, three-quarters of them begin by using a search engine (Fox 2013). If recruitment is slow, Google AdWords and other online mechanisms may be used to boost the online profile of PregSource℠ in such searches.

Concurrent to the culturally appropriate translation process, the NICHD will develop a promotion plan for the Spanish version of the site and app. The promotion plan will involve PregSource℠ partners and other organizations, such as the National Hispanic Medical Association (NHMA) and the National Hispanic Nurses Association (NHNA), as well as community groups, such as the Mary's Centers for Maternal and Child Care, and other agencies, such as the HHS Office of Minority Health. Specific tactics for promoting the Spanish website's availability include (but are not limited to): contributing information and visuals for NHMA, NHNA, and others to include in their newsletters, electronic updates, and other communications with their constituents for providers to share with their patients; creating online assets that NICHD and PregSource℠ partners can incorporate into their websites and social media accounts; sending out announcements and notices using outlets such as Hispanic PR Newswire; conducting some face-to-face outreach at Mary's Centers and other community venues; and asking Gobiernousa.gov (the official web portal of the United States Government in Spanish) and other resource sites to include information about PregSource℠ on their sites. The messages and materials will be ready to share when the Spanish site/app are launched.

If during data monitoring (see Section 7.2.4, Monitoring Recruitment and Sample Population), PregSource℠ identifies under-represented groups, we will develop and implement similar targeted recruitment and outreach efforts to enroll participants in these groups.

4.2.4. Anticipated Accrual Rate

There is no limit on the number of participants in PregSource℠. At this time it is difficult to estimate accurately how many women may choose to register, how many will enter – and continue to enter – data throughout their pregnancy, and what the accrual rate is likely to be. The immediate goal is to accrue 10,000 participants within 2 years of launch.

4.2.5. Recruitment Replacement Strategy

If a participant decides to withdraw her information from the database, no specific effort will be made to replace that individual.

4.3. SCREENING

A potential participant will self-register online via the Website or app without providing proof of eligibility (e.g., a medical diagnosis). The Website will provide general information about the registry on a Frequently Asked Questions webpage.

Participants must complete the online consent form before they can enter data.

4.4. STUDY PROCEDURES

4.4.1. Consent Documents and Process

Who obtains consent. Informed consent will be collected electronically via the Internet; study staff will not obtain verbal or in-person informed consent. Each subject will read, complete, and submit an online consent form herself.

Consent procedure. To join the study, a participant will need to:

1. Create an account by going online to the PregSource℠ Website, https://PregSource.nih.gov. The Website can be accessed via computer or the app. Apps will be available for downloading in both iPhone and Android versions. The participant will need to choose a unique user name and a password.

2. Review and complete the online consent form.

Consent documents. A Frequently Asked Questions (FAQs) document will be available on the Website to help address questions participants may have, such as: what is the purpose of the study, what does participation involve, what are the known risks and benefits of participation, how will the data be used, and contact information for further questions. A copy of the electronically signed consent responses will be saved in each participant's Profile for future reference. The PregSource℠ Privacy Policy and Terms and Conditions will also be available on the Website. In addition, Coordinators will be available via email (posted on the "Contact Us" webpage) during regular business hours to answer questions.

Consent to re-contact for follow-up. After completing the consent and registration process, a participant will be asked, as part of completing her account profile, whether she is willing to be contacted by PregSource℠ staff about studies and clinical trials she may be eligible to participate in. The original consent will be part of her account profile, and she will be able to change her Contact and Sharing Preferences at any time.

4.4.2. Account Profile Set up and Health History Questionnaire

Once registered and consented, a participant can begin to enter information after reading the PregSource℠ Privacy Policy and Terms and Conditions of use, then completing her Account Profile and taking an initial Health History questionnaire to collect data on:

- Contact information and preferences (email, text, etc.), including an optional alternate contact[2]
- Demographics and socioeconomics -- NIH-required race/ethnicity data, general family income ranges, education levels

[2] Alternate Contacts will be contacted only in cases when repeated attempts to gather final pregnancy outcome information have been unsuccessful.

- Interest in participating in a clinical trial. The participant will be asked for her consent to allow the PregSource℠ coordinators to contact her regarding future opportunities for participation in a clinical trial or research study.
- Pre-pregnancy general health – height, weight, a checklist for chronic conditions (e.g., diabetes, lupus), medications
- Reproductive health – contraceptive use, previous pregnancy histories, infertility, use of assisted reproductive technologies
- Current pregnancy health – gestational age, number of fetuses, date of first prenatal visit, prenatal visits completed, any diagnoses received or test results.

A participant will access PregSource℠ questionnaires online and/or via a mobile app to enter her own data. She will be able to download apps (e.g., via the iTunes or Android online app stores) to a smartphone or tablet, and connect these to her online account.[3] The apps, as well as the Website, will let her access and enter data into online surveys and trackers. A participant will also be sent reminders and push notifications, asking her to update her information.

All questionnaires will be constructed using "Smart Survey Design" – i.e., using conditional or skip logic to add or skip questions that are not relevant, based on previous answers. Aggregated data will help us analyze response frequencies for survey questions.

4.4.2.1. Trackers

Each participant can enter data in a set of health "trackers" – online or in-app software diaries that capture daily or weekly information over the course of pregnancy about her weight, nausea symptoms, mood, and sleep. Additional trackers may be added at a later date for tracking nutrition, exercise, and pain. She can enter data in the trackers as often as she chooses. We anticipate that for trackers such as nausea, sleep, and mood, a participant might enter data on a daily basis; while weight data might be entered only once a week or even once a month. Most trackers will collect data on timing, duration, severity/intensity, and related issues. A 2013 report by Citrix[4], a software company that tracks app usage, shows pregnancy related apps to have wider usage. Many of the available trackers have been used and/or validated in the pregnant population[5]. Recent research articles[6] have demonstrated the use of web-based methods to collect relevant health related information from pregnant women.

Unless otherwise indicated in her Account Profile, a participant will be reminded on a weekly basis to update her information, if she has not entered new data within the past two weeks.

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[3] Participants will not be required to use the apps. The apps will be available as a potentially more readily available means of accessing the questionnaires and trackers.

[4] Nick Bilton, New York Times, Auguest 26, 2015

[5] Hämeen-Anttila K, Nordeng H, Kokki E, Jyrkkä J, Lupattelli A, Vainio K, Enlund H. Multiple information sources and consequences of conflicting information about medicine use during pregnancy: a multinational Internet-based survey. J Med Internet Res. 2014 Feb 20;16(2).

[6] Wise LA, Mikkelsen EM, Rothman KJ, Riis AH, Sørensen HT, Huybrechts KF, Hatch EE. A prospective cohort study of menstrual characteristics and time to pregnancy. Am J Epidemiol. 2011 Sep 15;174(6):701-9

We anticipate including the following trackers:

Weight tracker. Weight would likely be entered weekly/monthly. Data collected includes:

- Weight (in pounds or kilograms)[7]

Nausea tracker. The Nausea Tracker could be entered as often as necessary, collecting data on:

- Date
- Timing (morning, afternoon, all day)
- Duration
- Severity (just nauseous, vomited)

Sleep tracker. In addition to asking about a participant's sleep patterns and apnea diagnosis prior to pregnancy in the initial health questionnaire, the Sleep Tracker may collect data on:

- Number of hours of sleep each night
- Quality of sleep (slept soundly, tossed and turned, etc.)
- Sleep position (back, stomach, right side, left side)

Activity tracker. Activity could be entered as often as necessary. It may collect data on:

- Intensity of physical activity
- Duration of physical activity

Mood tracker. The Mood Tracker could be entered as often as necessary. We will use the validated Positive and Negative Affect Schedule (PANAS) (Watson D and Clark LA 1994; Thompson ER 2007). This measure has also been used to access psychological stress among women with and without reproductive failure (Coughlan C et al 2014). It may collect:

- Mood description

As per Section 7.1.1.1 Safety: "If a participant enters data indicating a health or safety concern, the database will send an automated notice to her that she may want to contact her doctor for advice. The database may also refer her to related factsheets and websites with further information." In PregSource℠, after a participant enters data for the PANAS, the platform will calculate raw scores for both positive affect (PA) and negative affect (NA). Crawford (2010) reported norms for the PA and NA scores on the PANAS instrument. Because the data were not normally distributed, they converted the data into percentiles. The Crawford nomogram will be used to convert raw scores into percentiles. Participants who score >95th percentile for NA and/or <5th percentile for PA will be considered to have affect that deserves further attention by a clinician. Participants with scores in these ranges will receive a notification stating that their mood may indicate a problem that they may want to discuss with their care provider. Participants will also receive a follow-up message 2 weeks after the initial notification

[7] Height data would be collected in the Initial Health Questionnaire, so that BMI can be calculated. We would ask in the Gestational Age monthly questionnaires if there was any change in height (not likely for adults, but may change for teenagers).

reminding them that their mood tracker indicated a concern that may warrant discussion with their health care provider.

Medications in pregnancy tracker. The Medications Tracker may ask if the women have:

- Taken any medications for specific conditions
- When they stopped taking the medication
- Reason for the medication being used

Alternative therapies tracker. The Alternative Therapies Tracker may ask women if they are taking any alternative medications or herbal supplements, reasons for their use, and how many are taken without clinician recommendation:

- Any herbal supplements or alternative medications used?
- If yes, which therapies?
- Reason for use

4.4.2.2. Gestational Age Questionnaires

Once a month, PregSource℠ will send each participant an email, text, or app push notification, with a link to a new questionnaire relevant to her current week of gestation. For example, at 25 weeks of gestation, we may ask whether she has felt her baby move yet. At the end of each questionnaire, if the participant has not entered data into the health trackers in the past month, she will be taken to the appropriate trackers to enter information. This process will allow PregSource℠ to reduce duplication of questions, and capture changes over time in a consistent manner (e.g., all weight data will be entered into the Weight tracker).

If a participant does not complete her monthly questionnaire, she will receive a reminder once a week to do so via email or text to review the information she has entered into the database and provide any appropriate updates to her information.

Gestational-age questionnaires will continue monthly through pregnancy and then quarterly up to 36-months post-partum to capture information on maternal recovery and neonatal and infant outcomes and development.

4.4.2.3. Sub-group Questionnaires

Based on answers to previous questions, a participant with a special condition or complication may be asked to complete additional questionnaires. Such questionnaires will collect more detailed information about her health history, current pregnancy status, and special challenges and issues. Sub-groups may include women with:

- Disabilities (physical or intellectual)
- Obesity
- Lupus or other autoimmune diseases
- Diabetes or gestational diabetes

Sub-group questionnaires will be submitted to the IRB for approval prior to being launched.

4.4.2.4. Future Modules

PregSource℠ is intended to evolve over time with the investigators reviewing, revising, and adding questions, questionnaires, and interactions based on new topic areas and feedback received as well as results collected.

For example, we envision a future module on mental health issues in pregnant and post-partum women. Such a component needs to be carefully planned and implemented to be sensitive to participants' perceptions and to provide meaningful sources of intervention, as needed, for participants whose answers indicate they may be in need of immediate clinical assistance. We would first analyze the results obtained from the Mood Tracker to see how many women require notifications about negative affect. We would, then, consult with experts on post-partum depression and other relevant mental health issues to develop questionnaires and follow-up procedures. As part of that plan, we anticipate conducting beta-testing of any new questionnaires and the follow-up procedures that assure participant safety.

We will submit plans for any future modules to the IRB for review prior to beta testing and module implementation.

4.4.3. End of Participation

Unless she withdraws from the study, a participant ends her participation in the study when her pregnancy ends due to termination, miscarriage, or stillbirth, or at 36-months post-partum. She may, however, choose to continue entering data through subsequent pregnancies.

4.4.4. Follow-up

A participant will not be required to undergo any follow-up medical examinations or doctor's visits. To prompt her to enter information throughout her pregnancy, including pregnancy and newborn outcomes, PregSource℠ will send each participant regular email, text, and/or app push notification reminders, asking her to update her information.

4.4.5. Other Clinical Trials and Studies

No participant will be required to take part in any other research protocol(s), and may continue to participate in PregSource℠ whether she does or does not participate in any other protocol(s).

As part of her account profile, each participant will indicate whether she would like to be contacted to participate in other clinical trials and studies. She will be able to change her Contact and Sharing Preferences at any time in her online Account Profile.

Research investigators for other clinical studies and trials can submit an IRB-approved protocol request to the PregSource℠ Coordinator to recruit participants for their studies. The Operations Committee or its designees will review each proposal. If approved, the Database Administrator will develop an automated search for each protocol to regularly search the data of each registered and interested participant and compare it to the eligibility criteria for the protocol.

Positive search results will be sent to the Coordinators, who will verify the eligibility and send each interested and eligible participant information on how to contact the protocol investigator, if she chooses to do so.

Researchers and physicians will not have access to personally identifiable information (PII) for any participants, nor will they be able to contact participants directly. Studies external to the registry would consent participants separately, based on each study's IRB requirements.

4.4.6. Beta Testing

PregSource℠ will not implement a pilot project. Prior to launching the main PregSource℠ website, app, questionnaires, and trackers, however, we will conduct beta-testing of the website and app, in which beta testers will enter data into PregSource℠ and, in addition, answer questions about the surveys and trackers, their usability, and the process and flow of the tool. We anticipate at least 30 beta testers identified from our Partner organizations will participate.

At the request of the IRB, during the beta test, and after obtaining appropriate informed consent, all pregnant or recently pregnant beta-testers (N=10-20) will be asked to provide us with a copy of their antepartum medical records, so that we can compare their data responses in PregSource℠ to key variables in their medical record for verification. Variables for validation may include:

- Age
- Current pregnancy status
- Pre-pregnancy weight
- Pregnancy weight gain (for women who have delivered)
- Number of previous pregnancies
- History of diabetes
- History of chronic hypertension
- History of prior preterm pregnancies
- Estimated due date for the current pregnancy

These variables are chosen because of their general importance to obstetric care and outcomes and because they are very likely to be recorded in an obstetric medical record. Because many of our beta testers will be pregnant at the time of the test, to validate items from all of them we will need to limit most of the variables to those available early in gestation – excluding outcome variables or variables such as diagnosis of gestational diabetes that are identified at later gestational ages. For those who have delivered, we will also evaluate pregnancy weight gain, an objective measure that can be validated using medical records.

In consultation with biostatisticians in the NICHD Division of Intramural Population Health Research (DIPHR), we will calculate kappa (κ) statistics to quantify agreement between the baseline questionnaire data and the obstetric record. A $\kappa >= 0.61$ will be considered substantial to excellent agreement (Landis JR and Koch GG 1977).

SECTION 5. STORAGE OF DATA AND SAMPLES

5.1. REGISTRY DATA STORAGE

Under a contract with Lockheed Martin, PregSource℠ will use a web-based, patient opt-in registration system developed by PatientCrossroads, Inc., San Mateo, California, for DS-Connect® and other registries. PatientCrossroads will track participant enrollment, capture data, and deliver appropriate summary information based on entered data via a secure web portal, using MySQL Server as the back end relational database.

Lockheed Martin will work with PatientCrossroads to ensure that the system is compliant with the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and with the Federal Information Security Management Act of 2002 ("FISMA", 44 U.S.C. §3541). Security features target multiple levels, including the data element (e.g., restricted access to fields), user (e.g., password authentication access), application (e.g., role-based access to features, access audit trails), and hosting services (e.g., firewall, secure sockets layer). These features ensure access and audit control, data integrity, user authentication, and transmission security.

All server requests are transmitted over Secure Sockets Layer (SSL). All servers have multiple layers of data and access protection: (1) A dedicated, managed Cisco router firewall, (2) A redundant array of independent disk (RAID) Level 5 is used to ensure that data will not be lost if a hard drive fails between backups, (3) A system level backup is performed nightly, retained for 2 weeks, and stored in the data center, (4) a database level backup is performed nightly, retained for 2 months, and stored at the data center.

5.2. DATA SHARING

Researchers may request data from the registry to analyze it for research purposes, such as to determine the prevalence of clinical manifestations and/or estimate numbers of participants who may be eligible for approved clinical studies or trials. The Operations Committee or its designees will review these requests. If approved, researchers may be given access to de-identified data only via the Website's Professional Portal which will be launched in the future.

5.3. DATA DISPOSITION

On a regular schedule (not less often than once every 5 years) and when the registry stops accepting new participants and new data from existing participants, PregSource℠ will submit de-identified data to a NICHD data repository such as DASH (Data and Specimen Hub) for future researchers to access and analyze.

Once a participant has completed the registration and consent process, she will be able to view summaries of the de-identified data from all participants. This access will allow her to see how she compares with other similar participants.

5.4. REGISTRY SAMPLES STORAGE AND DISPOSITION

PregSource℠ does not plan on collecting biological samples at this time.

5.5. ADDITIONAL CONSIDERATIONS

5.5.1. Research with Investigational Drugs or Devices

PregSource℠ will not be conducting research with any investigational drugs or devices.

5.5.2. Gene Therapy

PregSource℠ will not be using any gene therapy.

SECTION 6. POTENTIAL RISKS AND BENEFITS

6.1. KNOWN AND ANTICIPATED RISKS AND DISCOMFORTS

There are no known or anticipated physical, psychological, social, legal, or economic risks from taking part in this study.

Psychologically, if a participant is not comfortable answering or does not want to answer a question in the study, she does not have to answer it. When looking at summaries of de-identified data and comparing it to her own situation, it is possible that a participant may learn information that is upsetting to her.

One potential risk is a loss of private or confidential information, such as from a security breach. In the event of a breach, we will let participants know about it as soon as possible.

6.2. STEPS TAKEN TO MINIMIZE RISK

6.2.1. Data Security

While we cannot guarantee security for information stored on each participant's computer or mobile device(s), or while it is being transmitted via cell phone towers, Wi-Fi, or the Internet, once received, our database has a FISMA-moderate level of security, including multiple security safeguards and protections. To minimize the risk of a security breach, we will:

- Use up-to-date, compliant, and proven database and security software and data transmission protections (See Section 5.1 for details)
- Monitor the Website and database system continually
- Maintain updated anti-viral protections
- Conduct regular evaluations of the database and security features by an independent, outside security expert
- Maintain multiple levels of restricted access for user access (e.g., a password is needed to enter), application access (e.g., role-based access to features, access audit trails), and hosting services (e.g., firewall, secure sockets layer)
- Store direct participant identifiers (i.e., subject names and other personally identifiable information) in tables separate from medical information
- Limit access to participant identifier tables to the Coordinators only
- Anonymize any shared data following current HIPAA standards

These safety features help ensure that participant information is protected. In the event of a breach, we will notify participants about it as soon as possible.

6.2.2. Contacting Subjects about Other Clinical Studies

As mentioned in Section 4.4.5, approved researchers will not have access to personally identifiable information for any participants that would allow them to contact participants directly. Once approved, potentially eligible and interested participants would be sent the

contact information for the researchers by the Coordinators; it would be each participant's choice whether to contact those investigators.

Studies external to PregSource℠ would consent participants separately, based on each study's IRB requirements.

6.2.3. Sharing De-identified Data with Other Researchers and/or Data Repositories

Researchers may request de-identified data from the study to analyze for research purposes, such as to estimate the prevalence of clinical manifestations or numbers of participants who may be eligible for approved clinical studies or trials. The Operations Committee or its designees will review these requests. If approved, researchers may be given access to the data via the Website's Professional Portal and/or sent a file of the de-identified data.

De-identified data may also be deposited in data repositories, such as the DASH.

6.3. CLASSIFICATION OF RISK

Per 45 CFR 46, PregSource℠ falls under Subpart B, Additional Protections for Pregnant Women, Human Fetuses, and Neonates Involved in Research.

For adults, including those without consent capacity, PregSource℠ will involve only minimal risk.

For infants/children, PregSource℠ falls under 45 CFR 46.404, "Research that does not involve greater than minimal risk to children," as we will be collecting developmental data on the infants born to the mothers and reported by them.

Overall, given the known and anticipated risks and discomforts, PregSource℠ will not involve more than minimal risk to any participant, and we believe the risks are reasonable in relation to anticipated benefits.

6.4. ANTICIPATED BENEFITS

6.4.1. Direct Benefits

A participant will not benefit directly from participating in PregSource℠.

6.4.2. Indirect Benefits

Because PregSource℠ provides a means for each participant to track her personal health information, and it may suggest that she contact her healthcare team based on her answers to particular questions, it may help her better inform her healthcare team about her health. For example, if a woman indicates that she is gaining weight beyond recommended levels, the database may send her a message telling her that she may want to discuss this with her prenatal care provider. Both the tracking capabilities and the prompts may help her healthcare team better monitor and address her healthcare needs.

Each participant will also get evidence-based information about pregnancy. For example, if a woman indicates that she has morning sickness, she will be able to see how many other women in the database also have this symptom. She will also get links to information and websites about morning sickness from PregSource℠ partner organizations and other trusted sources.

Finally, being able to see how she compares to others similar to her may give a participant some peace of mind about her concerns (i.e., “I’m not the only one”) and/or prompt her to contact her healthcare team for issues that are of concern (i.e., “This doesn’t seem normal – I should see my doctor”).

SECTION 7. SUBJECT SAFETY MONITORING

7.1. STUDY MONITORING PLAN

7.1.1. Data and Safety Monitoring Plan and Stopping Rules

7.1.1.1. Safety

Because we do not anticipate any health risks to participants for taking part in PregSource℠, we will not have a Data and Safety Monitoring Committee. The lead principal investigator, in conjunction with the Management Team, will monitor study data and safety.

PregSource℠, its Website, and app content are not intended to be a substitute for independent, professional medical judgment, advice, diagnosis, or treatment. Participants should always seek the advice of their physicians or other qualified health providers with any questions or concerns they may have regarding their health, their pregnancy, or their baby's health.

If a participant reports a health- or safety-related concern, the Coordinator will report it to the lead principal investigator and the Management Team for review.

If a participant enters data indicating a health or safety concern, the database will send an automated notice to her that she may want to contact her doctor for advice. The database may also refer her to related factsheets and websites with further information.

7.1.1.2. Futility and Stopping Rules

The Operations Committee will review study recruitment numbers and study data completion rates annually. If recruitment targets and/or study questionnaire completion rates are not within the expected target, the Committee may recommend options to the Director of NICHD to alter the design, halt, or terminate the study.

If a particular study question or questionnaire is being completed by less than 67% of relevant participants, the Committee will review it and may recommend revisions and/or deletions.

7.1.2. Procedures for Suspending or Stopping Enrollment

PregSource℠ will suspend registration and data entry if there is a security breach that compromises the ability to collect information in a secure, confidential manner. Participants will be notified in a timely manner about the breach. Registration/data entry will be restarted only if/when the Management Team, including the independent security experts, are confident that the system is secure, and the IRB has approved continuation.

If the study end is planned for a set future date (e.g., at the end of the contract), new participants will be warned of the end date before they join, so that they may make an informed decision about whether to enroll.

When PregSource℠ ends, current participants will be notified of the end date and given a reasonable opportunity (e.g., 3 months) to download and/or print their own data before the Website and database are shut down.

7.2. QUALITY ASSURANCE

7.2.1. Data Curation

PregSource℠ Coordinators will be trained in curation methods to review and investigate participant responses, reports, or registration details that are inconsistent with each other and/or the expected clinical course or status of the participant. Coordinators will follow up with the participant, as needed, to correct and/ or explain the inconsistencies.

7.2.2. Monitoring the Participant Registration Process

PregSource℠'s curation and quality monitoring program will assess the appropriateness of the participant through a review of contact, demographic, and consent details. If the participant appears valid, the PregSource℠ Coordinators may review a selection of Health History questionnaire responses. Accounts are assessed and assigned a status with regard to the completeness and reliability of the participant-provided information. Monitoring is ongoing as the participant contributes future information.

7.2.3. Monitoring Participant Burden

PregSource℠ will implement a curation and quality monitoring program to monitor participant burden of use and adherence/attrition over time. This will include monitoring:

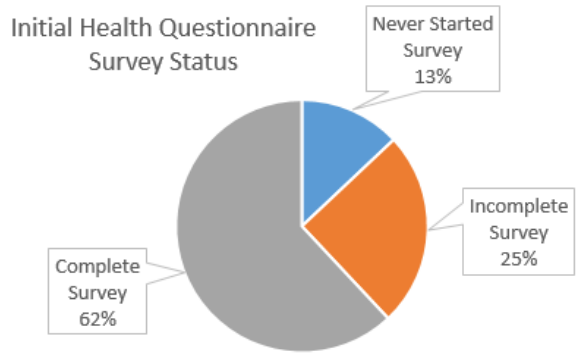
- Number of participants who complete monthly questionnaires
- Number of participants who complete weekly trackers at least once per week
- Number of participants who have turned off/adjusted reminder frequencies in their Profiles
- Number of participants who dropout (do not enter data for more than 3 months) and/or withdraw from the study, the timing in their pregnancy of dropout/withdrawal, and their demographic characteristics
- Number of participants continuing to enter data through the end of their pregnancy
- Number of participants continuing to enter data for neonatal outcomes
- If participants enroll at earlier gestational ages, are they more or less likely to continue entering data throughout their pregnancy?
- Are participants more likely to enter certain types of data than others (morning sickness, sleep, mood)?

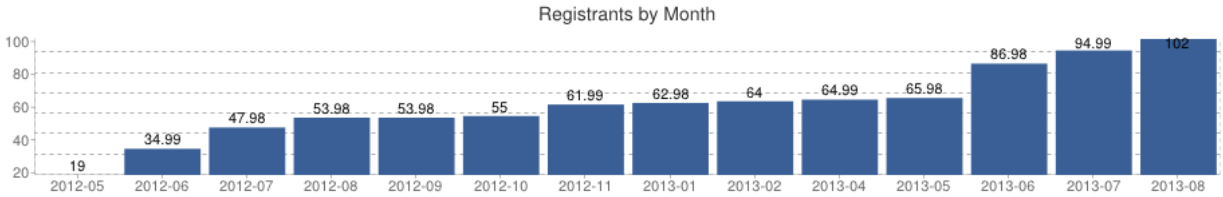
The database will also use statistical tracking and Google Analytics to report on participants':

- Date of registration
- Date of last login
- Date of last update (demographics and complete audit of questionnaire responses)
- Registrants by country
- Registrants by date

- Website visitors by date
- Website visitors by country
- Most frequently accessed content
- Average length of time spent on the site
- Number of app downloads

For example, the system can report on completion of health history questionnaires similar to the pie chart or bar chart below. Additional sample reports can be viewed at http://www.nltechno.com/awstats/awstats.pl?config=destailleur.fr.





We will also be monitoring site/app usage statistics and analyzing user behaviors so we can refine questions and site/app function as PregSource℠ continues. For instance, if the majority of users drop out of the pre-conception survey before completing it, we can break up the survey into segments to make it easier for people to complete.

7.2.4. Monitoring Recruitment and Demographic Distribution

PregSource℠ coordinators will monitor recruitment every quarter – and more often if necessary – paying particular attention to the demographics (race, ethnicity, income) of U.S. participants in the study population. If minority enrollment is more than ~10% below the demographics of the U.S. population, based on the most recent U.S. Census for which data are publicly available, the Operations Committee will initiate additional recruitment efforts to enroll participants from under-represented sub-groups.

7.2.5. Lost to Follow-up

Because the pregnant woman will be the person entering data, and given the possibility of maternal deaths, we will give the participant the option of providing the name and email address for an alternate contact (e.g., a family member or friend). If the participant has not entered final maternal and neonatal outcome data after repeated reminders, at 6 months after her expected due date, the Coordinators will email the alternate contact to try to gather this information if permission is granted under Contact and Sharing Preferences.

7.3. REPORTING OF UNANTICIPATED PROBLEMS, ADVERSE EVENTS AND PROTOCOL DEVIATIONS

There is a small risk that confidential information may be lost, or there may be a breach in the computer database storing personally identifiable information (PII).

The Lead Principal Investigator is responsible for detecting, documenting, and reporting unanticipated problems, adverse events (AEs), including serious adverse events (SAEs), and protocol deviations in accordance with NIH policy, IRB requirements, and federal regulations. Relatedness to the research of all serious adverse events will be determined by the PI.

Serious unanticipated problems and serious protocol deviations will be reported to the IRB as soon as possible and in writing not more than 7 days after the PI first learns of the event. Adverse events that are deemed not to be serious will be reported to the IRB as soon as possible and in writing not more than 14 days after the PI first learns of the event.

All adverse events, deviations, and unanticipated problems will be summarized and reported at the time of Continuing Review.

7.4. CRITERIA FOR INDIVIDUAL SUBJECT WITHDRAWAL FROM THE STUDY

A participant may be removed from the study at any time if the Management Team believes that it is not in the participant's best interest to continue, or if the participant is unable to comply with the requirements or Terms and Conditions.

Participation is entirely voluntary. If a participant changes her mind and wishes to withdraw her information from the study, she is free to do so without having to provide any explanation and without loss of benefits or privileges to which she is otherwise entitled. If a participant no longer wants to take part, she can change her profile preferences so that she stops receiving reminders. If she wants to withdraw her data from the database, she can contact the Coordinators to start that process; however, data that has already been de-identified and provided to outside researchers and/or data repositories before the request was received and processed cannot be retrieved.

SECTION 8. STATISTICAL ANALYSIS PLAN

8.1. ANALYSIS OF DATA/STUDY OUTCOMES

PregSource℠ will be a research registry for investigators to use. As such, we do not have any pre-planned statistical analysis. Power calculations would vary depending on the proposals investigators submit for approval.

8.2. SAMPLE SIZE, POWER ANALYSIS, AND AVAILABLE POPULATION

Given PregSource℠'s online, self-consenting process, there is no set limit to the number of participants who can enroll, and it is difficult to estimate accurately how many women will find the study, choose to enroll, and enter their data consistently.

For 2009 (the latest year for which data is currently available), the CDC reported an estimated 6,369,000 pregnancies, resulting in 4,131,000 live births (Curtin 2013). According to the Pew Research Center's Internet & American Life Project, in 2012, 72% of U.S. adults in the survey said that they had gone online in the past year to look up health information; and women were more likely than men to look up information about specific medical conditions for themselves or someone else (Fox 2013).

Conservatively, with falling birth rates reported (Curtin 2013), if only 1% of these pregnant women locate the study and 50% choose to join, the study could enroll more than 30,000 women per year. This could lead to an anticipated enrollment of 120,000 women over 4 years.

For recruitment purposes, if a participant drops out or withdraws her information, no specific effort will be made to replace her.

8.3. PROJECTED RECRUITMENT TIME

The current contract with Lockheed Martin covering PregSource℠ is for 3 years from September 30, 2014 – September 29, 2017. NICHD is committed to continuing PregSource℠ even after the current 3-year contract period either by extending the contract or using another solicitation as needed.

SECTION 9. HUMAN SUBJECTS PROTECTION

9.1. SUBJECT SELECTION

9.1.1. Statement of Equitability

The racial and ethnic characteristics of PregSource℠ participants will reflect the demographics of the individuals who are seeking information regarding pregnancy and interested in participating in clinical trials or research studies. With appropriate consent, no individuals who meet the inclusion criteria will be excluded from participation based on race or ethnicity (see exclusion criteria). Given the nature of pregnancy, men will not be included in sample collection.

Justification for inclusion of children
Not applicable. Participation in PregSource℠ is open to adults between the ages of 18 to 70 years who are pregnant.

In addition, we will be collecting developmental data on the infants born to the mothers.

9.2. JUSTIFICATION FOR INCLUSION OF VULNERABLE SUBJECTS

Pregnant women who have access to the Internet may join PregSource℠. Because this study will only be collecting data, not providing or requiring any physical examinations or procedures, inclusion of pregnant women does not pose any specific risk above minimal risk to her or her fetus.

9.3. SAFEGUARDS FOR VULNERABLE POPULATIONS

The registry is only for a pregnant woman who can provide consent herself.

9.4. QUALIFICATIONS OF INVESTIGATORS

9.4.1. Lead Study Investigator

Caroline Signore, MD MPH, NICHD. Dr. Signore is the Deputy Director of the Division of Extramural Research. She is a board-certified obstetrician-gynecologist, served as a medical officer and program scientist in the NICHD's Pregnancy and Perinatology Branch for 7 years. There, she has served as a program scientist overseeing the Prenatal Alcohol and SIDS and Stillbirth (PASS) Network, the Early Adult Reduction of weight through Lifestyle intervention clinical trial consortium, and the Lifestyle Interventions For Expectant Moms (LIFE-Moms) clinical trial consortium. Dr. Signore will provide expertise in obstetrics and gynecology for PregSource℠. She will be the lead principal investigator for PregSource℠.

9.4.2. Associate Investigators

Catherine Y. Spong, MD, NICHD. Dr. Spong is the Acting Director for NICHD, and a recognized national and international expert in maternal-fetal medicine, obstetrics, and gynecology.

Stephanie Wilson Archer, MA, NICHD. Ms. Wilson Archer is a clinical trials specialist with a master's degree in Sociology. As a member of NICHD's Pregnancy and Perinatology Branch, she is the coordinator for the Neonatal Research Network, and the Genomics and Proteomics Network for Preterm Birth. Ms. Wilson Archer will be one of the Coordinators.

Sujata Bardhan, PhD, NICHD. Dr. Bardhan is an organic chemist with experience working in the Medicinal Chemistry Division of a pharmaceutical company. She is also a member of the Trans-NIH Down Syndrome Working Group, and one of the registry coordinators for DS-Connect®. Dr. Bardhan will also be one of the Coordinators.

Lisa Kaeser, JD, NICHD. Ms Kaeser is a member of the DS-Connect® management team, and will provide legal and regulatory information for the Management Team. She is also a liaison to the partner organizations.

Melissa Parisi, MD PhD, NICHD. Dr. Parisi is a board-certified medical geneticist. As the Chief of the Intellectual Development and Disabilities branch at NICHD, she is the lead investigator for DS-Connect®, and oversees the contract covering DS-Connect® and PregSource℠.

9.4.3. Coordinators

Vanessa Rangel Miller, MS, CGC, PatientCrossroads. Ms. Rangel Miller is a board-certified genetic counselor with expertise in developing and managing rare and genetic disease patient registries. She has long-standing ties to patient registries sponsored by advocacy organizations, biotechnology, and pharmaceutical companies, including registry programs such as DS-Connect® and DuchenneConnect (ParentProject Muscular Dystrophy), as well as GenomeConnect (NHGRI-funded patient registry for ClinGen). Ms. Rangel Miller will work as a project manager.

Debbie Jae, MS, PatientCrossroads. Ms. Jae is trained in genetic counseling, and has worked in a variety of settings ranging from large pediatric hospitals, to small outpatient clinics, to medical device development companies. She will work as a project coordinator.

9.4.4. Required Human Subjects Training

The Lead Principal Investigator has verified that all investigators working on this study have completed the NIH Human Research Protections Program under OHSRP SOP 25.

9.5. CONSULTANT EXPERTS

In addition to our Partners, PregSource℠ investigators will request input from key experts on relevant topics, as needed. Below we list some of these consultants.

Paul Albert, PhD, Division of Intramural Population Health Research (DIPHR). Dr. Albert is senior investigator and Branch Chief of DIPHR's Biostatistics and Bioinformatics Branch. He received his A.B degree from Oberlin College and his Ph.D. in biostatistics from the Johns Hopkins University. Dr. Albert's research interests primarily focus on the analysis of longitudinal data, diagnostic testing, and the analysis of data from biomarker studies.

Rosalind King, PhD, NICHD Population Dynamics Branch. Dr. King holds a Ph.D. in sociology and demography from the University of Pennsylvania. She is the program scientist for the Work, Family, Health, and Well-Being Initiative and oversees a grants portfolio in fertility, infertility, adoption, and new reproductive technologies. She also manages the portfolio in life course health and biopsychosocial processes. Dr. King represents the NICHD to several trans-NIH and agency projects including OppNet, the Sleep Disorders Research Advisory Board, and the National Survey of Family Growth (NSFG). Dr. King's own research has focused on adolescent social and physical development, union formation, and fertility.

Susan F. Newcomer, PhD, NICHD Population Dynamics Branch. Dr. Newcomer holds a Ph.D. in population studies from the University of North Carolina, an M.S. in educational administration from Iowa State University, and a B.A. in psychology and Chinese from Barnard College. She is responsible for managing the Branch portfolio of extramural research on reproductive health, including social and behavioral research on fertility, contraceptive use, and AIDS/HIV risk research. Her own research has focused on teen pregnancy prevention, sexual behavior, and contraceptive use.

9.6. ALTERNATIVES TO PARTICIPATION

Joining PregSource℠ is the participant's choice. Because participants will not receive or forego any treatment by participating in this study, the alternative is not to participate.

9.7. CONFIDENTIALITY

9.7.1. Confidentiality of Research Data

Upon completion of the Consent Form, the database will generate a study identification number for each participant. All study data will be stored using this ID number and personal contact information will be stored in a separate table.

Only the Management Team will have access to the data, and only the Coordinators will have access to the participants' identification data. Access will be limited by user role via password-protected accounts. All personnel with access to identifiable data must sign the IT Rules of Behavior from PatientCrossroads acknowledging appropriate use of the information.

As part of the Consent Form, each participant will be informed that her name and contact information will not be made public, and that her data will be de-identified and shared with approved research investigators.

In addition to having access to the data she has entered in PregSource℠, via her password-protected account, each participant will be able to view summaries of data on the Website. She will not have access to the identifiable or individual information of any other participant, nor will she have the ability to contact other participants.

External investigators will be given access only to summarized and/or de-identified data.

Investigators for other clinical trials and studies seeking to recruit PregSource℠ participants for those studies will not be given participant contact information. Instead, the potentially eligible and interested participant will be given the investigator's contact information. It will be her choice whether to contact the investigator about the other study or not.

9.7.2. Certificate of Confidentiality

PregSource℠ will obtain a Certificate of Confidentiality to help insure participants' privacy.

9.7.3. Privacy Policy and Terms and Conditions of Use

The PregSource℠ Privacy Policy and Terms and Conditions for using the Website will be posted on the Website. All participants will be asked to view these documents and agree to them as part of the account set-up process.

9.8. CONFLICT OF INTEREST

NIH guidelines on conflict of interest have been distributed to all investigators.

There are no conflicts of interest to report for this study.

9.9. RESEARCH AND TRAVEL COMPENSATION

Participants will not be compensated for taking part in this study.

SECTION 10. REFERENCES

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