

STU#: STU00216874

**PROTOCOL TITLE:** Randomized Controlled Trial of Home Semen Testing in Men Beginning Attempts to Conceive

**PRINCIPAL INVESTIGATOR:**

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**VERSION DATE:**

2.21.22

**STUDY SUMMARY:**

Investigational Agent(s) (Drugs or Devices)	
IND / IDE / HDE #	
Indicate Special Population(s)	<input type="checkbox"/> Children <input type="checkbox"/> Children who are wards of the state <input type="checkbox"/> Adults Unable to Consent <input type="checkbox"/> Cognitively Impaired Adults <input type="checkbox"/> Neonates of Uncertain Viability <input type="checkbox"/> Pregnant Women <input type="checkbox"/> Prisoners (or other detained/paroled individuals) <input type="checkbox"/> Students/Employees
Sample Size	200
Funding Source	Department of Urology
Indicate the type of consent to be obtained	<input checked="" type="checkbox"/> Written <input type="checkbox"/> Verbal/Waiver of Documentation of Informed Consent <input type="checkbox"/> Waiver of HIPAA Authorization <input type="checkbox"/> Waiver/Alteration of Consent Process
Site	<input type="checkbox"/> Lead Site (For A Multiple Site Research Study) <input type="checkbox"/> Data Coordinating Center (DCC)
Research Related Radiation Exposure	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
DSMB / DMC / IDMC	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

**OBJECTIVES:**

The overall objective of the proposed study is to enhance early detection of male factor infertility and reduce cost and morbidity associated with delayed diagnosis through development of a universal screening model based on home semen testing. The advent of inexpensive and accurate home semen testing has enabled a potential paradigm shift in the approach to male fertility evaluation. Our central hypothesis is that universal home semen testing prior to attempts to conceive is easy for patients and can lead to reduced fertility-related anxiety and early detection of male factor infertility, thereby expediting evaluation and treatment for the couple while minimizing unnecessary cost and morbidity.

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This study is specifically designed to assess the feasibility and utility of home semen testing for couples who are beginning attempts to conceive. First, we will assess patients' ability to complete the home semen testing, ease of use, and obstacles encountered in doing so. Second, we will examine the impact of home semen testing in fertility-related quality of life among couples beginning attempts to conceive, as well as ability of home semen testing to increase the diagnosis and treatment of male infertility in these couples.

#### **BACKGROUND:**

Infertility affects 15% of all couples in the United States, and successful diagnosis and treatment costs an average of up to \$50,000 per couple. Approximately half of all infertile couples have a male factor etiology, yet male partner evaluation is disproportionately bypassed with an estimated 860,000 male partners not evaluated at the time of fertility consultation. While American Society for Reproductive Medicine (ASRM) guidelines recommend that couples do not seek evaluation until attempting to conceive for 12 months, most couples attempt to conceive for 22.3 months before presentation for male fertility evaluation, almost a year in delayed diagnosis. This delay in diagnosis and treatment can impair quality of life, impact treatment outcomes, and increase overall healthcare costs. Infertile couples are at greater risk of marital stress, sexual dysfunction, and decreased quality of life, which may extend even to this initial 12-month period. Furthermore, morbidity and costs associated with extensive female partner evaluation could be reduced or altogether avoided with earlier male factor detection. There is a critical need to develop practical interventions which can easily be implemented into practice in order to increase access to care for male infertility evaluation and treatment.

Our prior work has shown that accessibility of male infertility providers and semen testing are key barriers to care access. We surveyed men (N=634) without children to understand attitudes towards fertility and home semen testing. Among men concerned about infertility, only 29% were likely to discuss these concerns with a health care provider. Moreover, men were more likely to pursue home semen testing versus laboratory based semen testing ( $p=0.04$ ). These data indicate a critical role for home screening to detect subfertility in men who might otherwise not pursue evaluation in a timely fashion.

The rapid proliferation and wide accessibility of inexpensive and accurate home semen tests has the potential to overcome the aforementioned barriers towards initial male fertility evaluation. In our prior survey, we found that men were more likely to pursue home semen testing versus laboratory based semen testing ( $p=0.04$ ). These data indicate a critical role for home screening to detect subfertility in men who might otherwise not pursue evaluation in a timely fashion. As such, we conducted a cost-effectiveness analysis to evaluate the theoretical benefits of universal home screening for men pursuing fertility. We found that a policy of universal home screening would result in significant decreases in time to diagnosis at a very limited cost. These data provide the basis for the current study, which aims to examine home semen testing as a screening tool for all couples planning to conceive.

#### **STUDY ENDPOINTS:**

Primary:

1. Completion of home semen testing (Arm A: treatment group only)
2. Change in fertility-related World Health organization-5 Well-Being Index (WHO-5) and Fertility Problem Inventory (FPI).

Secondary:

1. Subsequent pursuit of formal male infertility evaluation
2. Pregnancy

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### **STUDY INTERVENTION(S) / INVESTIGATIONAL AGENT(S):**

We will be conducting this study in partnership with the home semen testing YoSperm® device, a commercially available FDA-approved device to assess semen parameters via smart device, a mobile medical application (MMA) designed by Medical Electronic Systems. We plan to work with the YoSperm® device to complete at home semen testing. Eligible patients will be randomized to one of two arms: standard of care office-based pathway or the at home semen testing pathway utilizing the FDA, commercially approved YoSperm® device.

YoSperm® details:

Purpose of the app:

The purpose of the app is for at-home semen analysis including sperm motility concentration and sperm quality (YO Score) and compares the results to laboratory standards. We will be utilizing the YoSperm® technology in order for patients to send their semen analysis results directly from their device to their provider via secure email.

The app is appropriately suited for adults 18 and older and is aesthetically easy to read/navigate and easy to understand.

App functionality:

YO 2.0 can be accessed via URL link (<https://yospermtest.com/download-yo-home-sperm-test-app>) to their website using any computer with Internet capability. It can also be accessed in app format and can be downloaded onto iOS or Android devices via Google Play and Apple App Store. The app is free and there is no cost to the participant. Participants will use their own devices for the study. Participants without mobile phone/computer capability to utilize YoSperm® app will be excluded from the study. YoSperm® has technical support available on their website with Frequently Asked Questions as well as on demand technical support via a Customer Support Ticket (<https://yospermtest.com/support/>) or email [support@yospermtest.com](mailto:support@yospermtest.com) for any participants with app related technical issues. When a device's operating system is updated, the app's functionality will not be impacted. However, YoSperm® mobile app does require iOS 11 or later or Android 6.0+. The PC operating system must be Windows 7 or above or MAC OS version 10.14 and above.

Participant/user support:

Participants will be trained to use the app and device during their initial in person visit if they choose to sign up for the study and are randomized to the YoSperm® device. In addition, the app provides a tutorial for usage when first downloaded. Participants have access YoSperm® has technical support available on their website with Frequently Asked Questions as well as on demand technical support via a Customer Support Ticket (<https://yospermtest.com/support/>) or email [support@yospermtest.com](mailto:support@yospermtest.com) for any participants with app related technical issues. Participants will be able to message providers with questions regarding the app or regarding their care through via Epic myChart.

Obtaining consent and the app's Terms of Service:

We will obtain written consent during a patient's initial appointment. Participants will not be consented via the app. YoSperm® Terms of Service, which are located on their website. Data ownership is outlined in the Data Privacy Policy, which is also available on YoSperm®'s website. All data collected and provided by participants is owned by Medical Electronic Systems Limited. The Terms of Service will be summarized in the IRB consent form in a participant friendly manner. The Terms of Service are compliant with research regulations and local/state/federal law. We will plan to monitor for changes or updates to the Terms of Services

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by visiting the Website for updates.

Privacy and confidentiality protections:

Medical Electronic Systems Limited collects and processes the following data. Optional Profile Data, Contact Data, and Communications Data. Your data and information is stored securely in Firebase, Bigquery and Mongo DB. The data stored is on secure cloud services and running in the United States. Firebase and Bigquery are part of Google. Google and MongoDB are organizations committed to privacy and have stated that the model clause relating to transfer of data between the European Union and the United States are compliant with GDPR. Data is also compiled and maintained in an encrypted REDCap database through our institution. Data will be accessible only to authorized members of the study team. YoSperm® does require a username and password for each individual. Usernames are generated by the user. If a participant forgets their username and/or password, there are links in which participants can receive a username/password reset sent to their email.

Risks related to app use:

YoSperm® Data Privacy Policy is available on their website and attached with this protocol. All efforts will be made to protect data; however, no method of transmission over the internet or electronic storage is 100% secure. If the app does not work as intended or malfunctions, participants can contact the Customer Support urgently (support@yospermtest.com). Patients will also have the option to ask care-related concerns through Epic MyChart. All information in this study is kept confidential between the study team and the participants.

## **PROCEDURES INVOLVED:**

### **Visit 1 – Screening (Day -45 – Day 0)**

1. Patients will complete:
  - a. Patient Informed Consent Form
  - b. HIPAA Form
  - c. Intake questionnaire
  - d. WHO-5
  - e. FPI
2. Investigative team will complete:
  - a. Patient demographics, medical history, inclusion / exclusion criteria
  - b. Randomization
    - i. :At Home Semen Testing
      1. Provision of home semen testing kit to men selected for the testing group
      2. Instructions in the use of home semen testing kit
    - ii. Standard of Care

### **Visit 2 – Home semen testing (Day 0)**

1. Only patients randomized to at home semen testing will complete:
  - a. Home semen testing (testing group only)
  - b. Patient will send home semen test results to the study team via the application
  - c. Patient will complete the post-test survey via REDCap
2. Investigative team will complete:
  - a. Recording of home semen test results
  - b. Confirm completion of post-test survey

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**Visit 3 – Three-month follow-up (Day 90)**

1. Patients randomized to either at home semen testing or standard of care will complete:
  - a. WHO-5
  - b. FPI
  - c. Follow-up fertility questionnaire
2. Investigative team will complete:
  - a. Confirm completion of questionnaires

**Visit 4 – Six-month follow-up (Day 180)**

1. Patients randomized to either at home semen testing or standard of care will complete:
  - a. WHO-5
  - b. FPI
  - c. Follow-up fertility questionnaire
2. Investigative team will complete:
  - a. Confirm completion of questionnaires

**Visit 5 – Twelve-month follow-up (Day 365)**

1. Patients randomized to either at home semen testing or standard of care will complete:
  - a. WHO-5
  - b. FPI
  - c. Follow-up fertility questionnaire
2. Investigative team will complete:
  - a. Confirm completion of questionnaires

Home semen testing will be performed via the YoSperm® device, a commercially available FDA-approved device to assess semen parameters via smart device (<https://yospermtest.com/>). The YoSperm® technology enables patients to send results directly from their device to their provider via secure email.

Randomization will be performed in 1:1 fashion to the home testing or control groups using REDCap.

All surveys will be administered via REDCap

**DATA AND SPECIMEN BANKING**

Data will be collected and stored electronically in REDCap. Quality assurance steps will include testing of database including any potential data calculated by command functions within REDCap by the study team prior to moving to production mode. The following quality control methods will be used: 1) single entry of data with random checks of accuracy, and 2) extraction and cleaning of data on a monthly basis that will be used for analysis every 3 months until completion of enrollment.

Clinical variables from the medical record may be abstracted if additional data is needed to evaluate the survey responses. These variables may include lab tests and results, medical history, family history, and clinical examinations. Dr. Halpern will have access to the codebook with patient identifiers, which will be stored on the FSM server and only accessible to authorized members of the study team listed on this protocol.

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Data will be accessible to only authorized members of the study team. Any presentations on the study or published findings will use only de-identified data.

Data will be stored for 7 years after the end of the study. After this period, electronic data will be deleted.

## SHARING RESULTS WITH PARTICIPANTS

Study results will not be shared with participants.

## INCLUSION AND EXCLUSION CRITERIA

### Inclusion Criteria

- Natal males over the age of 18 with no prior children who are interested in future fertility
- Current female partner
- Not attempting to conceive for more than 3 months
- Willing to sign the Informed Consent Form
- Able to read, understand, and complete patient questionnaires, pain texts, and medication diary.
- Ownership or accessibility of a smart phone or electronic device that is compatible with the YoSperm® device

### Exclusion Criteria

- Prior semen testing
- History of male infertility, Klinefelter syndrome, undescended testis, or chemotherapy
- Female partner with history of infertility
- Female partner with irregular menstrual periods

## PARTICIPANT POPULATION(S)

Accrual Number:	Category/Group: (Adults/Children Special/Vulnerable Populations)	Consented: Maximum Number to be Consented or Reviewed/Collected/Screened	Enrolled: Number to Complete the Study or Needed to Address the Research Question
Local	0	200	200
Study-wide	0	200	200
Total:	0	200	200

## RECRUITMENT METHODS

Recruitment will be accomplished through institutional outreach using a combination of institutional advertising (flyers) and partnership with primary care providers throughout Northwestern Medicine. Patients will be offered compensation for study enrollment and at study completion.

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A research coordinator will work closely with the primary care, OBGYN, and Urology teams to screen, recruit and enroll patients in this trial; the Department of Urology at Northwestern University employs multiple full-time research coordinators for assistance with clinical trials recruitment and coordination.

Enrollment into the study will be performed by a qualified research coordinator or member of the authorized study team. Patients expressing interest in the study will reach out to the study coordinator directly and undergo an initial screening assessment and completion of the intake questionnaires and consent. Patients enrolled will then schedule a separate appointment with the research coordinator, at which point they will undergo randomization and receive instruction and teaching in use of home semen testing if they are randomized to the testing group.

#### **COMPENSATION FOR PARTICIPATION IN RESEARCH ACTIVITIES**

Patients will be compensated \$20 for participating at the time of enrollment. An additional \$20 will be compensated at the time of study completion.

#### **WITHDRAWAL OF PARTICIPANTS**

If a subject wishes to withdraw from the study, he may do so by verbal request to the research team. A subject may be withdrawn from the study by a physician-investigator if determined to be in the subject's best interest for medical reasons.

#### **RISKS TO PARTICIPANTS**

There is no risk to participants in this study from the testing or questionnaires. There is a small potential for adverse mental health consequences (anxiety) of an abnormal semen test, if this is detected among men in the study group.

#### **POTENTIAL BENEFITS TO PARTICIPANTS**

Participants may have substantial benefit through early detection of semen parameter abnormalities, which can lead to early diagnosis and treatment of male infertility.

#### **DATA MANAGEMENT AND CONFIDENTIALITY**

Data will be collected and stored electronically in REDCap. Quality assurance steps will include testing of database including any potential data calculated by command functions within REDCap (ex: age of patient at time of surgery calculated by using patient's date of birth and date of surgery) by study team prior to moving to production mode. The following quality control methods will be used: 1) single entry of data with random checks of accuracy, and 2) extraction and cleaning of data on a monthly basis that will be used for analysis every 3 months until completion of enrollment.

#### **PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF PARTICIPANTS**

Data will be collected and stored electronically in REDCap and will only be accessible to members of the study team.

Data resulting from this study will not be linked to subjects. Subjects will not be referred to by name or initial in any publications.

#### **CONSENT PROCESS**

Enrollment into the study will be performed by a qualified research coordinator. Patients expressing interest in the study will reach out to the study coordinator directly and undergo consent.

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**PROTECTED HEALTH INFORMATION (PHI AND HIPAA)**

HIPAA authorization will be obtained as part of the consent. PHI from medical records and information collected from research and tumor samples will be protected by using coded subject numbers. The coded identifiers will be stored on a password protected spreadsheet stored on the FSM Urology server.