NCT05175170

Fertility Decision-Making in Youth and Young Adults

Study Protocol

Date: 02/25/2019

Submission Type: Modification Date: 11-17-2022

IRB #: IRB 2018-2263

Title: Project AFFRMED

Creation Date: 2-25-2019

Status: Review Complete

Principal Investigator: Diane Chen

M1 Modification Information

*required

A What type of submission is this?

✓ Modification *required

A Has the Lurie Children's IRB accepted the review of an external IRB for this study?

Yes

✓ No

Report of modification(s) implemented for immediate patient safety without prior IRB approval

Five day follow-up report after emergency use of a test article (drug, biologic or device)

M2 Modification Details

*required

Modification Description and Justification

Please refer to IRB Policies & Procedures Manual Section 9.2D.iv for details regarding Modification submissions.

A

Mark all items below being changed/updated/added/removed with this modification and thoroughly complete all follow-up questions.

Please remove tracked changes versions of documents that are not being revised with this modification from the application.

A.1 Study Title

A.2 Funding source(s)

A.3 Northwestern University or its affiliates involvement/engagement

A.4 Principal Investigator (PI)

A.5 Study personnel

✓ A.6 Study design and/or procedures and/or updated study protocol *required

A.6a Does this modification include the submission of an updated study protocol?

Yes

✓ No

*required

Provide the details of the change(s) in study design and/or procedures.

A.6b We are adding a Delphi method expert panel to our study. We plan to recruit up to 200 experts in the areas of reproductive health, fertility preservation, adolescent medicine, pediatric endocrinology, transgender healthcare, and psychology to provide feedback on our learning objectives that will be part of the decision aid website. The experts will complete a survey to provide feedback on the learning objectives, and then investigators will analyze their responses. Depending on the responses, a follow-up survey may be sent.

*required

Provide justification for the change(s) in study design and/or procedures.

A.6c

Receiving expert feedback from international experts in these areas will allow us to improve the learning objective language to ensure accuracy and clarity.

Please ensure that this change is made in Section 3 and applicable study documents (consent forms, recruitment materials, etc).

A.7 Number of study participants

A.8 Study population or inclusion/exclusion criteria

✓ A.9 Waivers of Consent and/or HIPAA Authorization *required

A.9a Provide details for the change in consent and/or HIPAA waiver(s).

We are requesting a waiver of documentation for the expert panel phase of this study.

*required

Provide justification for the change in consent and/or HIPAA waiver(s).

A.9b Since expert panel members' participation will be limited to completing surveys online using REDCap, we are requesting a waiver of consent. Although we are unable to separate participants' responses from their email addresses in REDCap, the data set downloaded from REDCap will not contain identifiers. The survey responses will be used for data analysis and, once complete, the original REDCap survey will be closed out and participant email addresses will be deleted along with the survey from the REDCap server.

Please ensure that this is updated in Section 7 (or research plan and HIPAA Waiver Request Form if applicable).

A.10 Addition of foreign language translation of consent/assent or other documents

A.11 Recruitment materials, verbal scripts, survey instruments, web-based instruments,

✓

questionnaires, etc.

*required

Provide details of the change in recruitment materials and/or other study documents.

A.11a

In order to invite potential expert panel members to participate, we are including an email draft to invite experts to participate. The email draft will provide information on what the panel members' participation will entail, along with the anticipated timeline.

*required

Provide justification of the change in recruitment materials and/or other study documents.

A.11b

The expert panel recruitment email will outline what the expert panel members will be asked to complete along with the projected timeline for their participation.

Please ensure that these new documents are provided in Sections 3, 4 and/or 9.

A.12 New information about the investigational agent (i.e., updated Investigational Brochure)

A.13 Updated safety information or change in study status (i.e., DSMB/C or monitor report, or opening or closing of the study)

A.14 Planned protocol deviation

A.15 Expanded recruitment/enrollment to include persons from an European Economic Area (EEA)

A.16 Other

*required

Modifications Requiring Re-Consent of Active or Past Participants

Please see IRB Policies & Procedures Manual Section 11.1K for guidance regarding the B requirement for re-consent of previously enrolled subjects.

Have any participants been enrolled in this study at Lurie Children's?

Yes

✓ No

N/A - study does not enroll active participants.

1 General Information

Study Identification

Throughout the Cayuse application, links to applicable sections of theIRB Policies & Procedures Manualare included for reference. The manual outlines for investigators and study personnel the policies and procedures that ensure the ethical conduct of research A with human participants at Lurie Children's.

For more information about the IRB submission Process, IRB Tracking, and Cayuse IRB Tasks, please refer to the Cayuse IRB Submission Process.

Guidance for specific questions is included to the right of the question in the Helper Text (Question Mark Icon).

*required

What type of submission is this?

A.1 ---

For details regarding the types of submission, please refer to IRB Policies & Procedures Manual Section 9.

✓ Research Study Involving Human Subjects (Expedited or Full Board Review)

Research Study Involving Human Subjects (Exempt Determination Request)

Research Study involving External IRB Review

Non-Research Use of Drug or Device (Emergency/Compassionate/Treatment/Single Patient/Humanitarian Use)

Use of PHI (Protected Health Information) Preparatory to Research

Case Report / Case Series

Quality Improvement / Quality Assurance Project

Use of Decedents' PHI (Protected Health Information)

Human Subjects Research Determination

*required

Select the type of review appropriate for this study:

A.2

For details regarding the types of review, please refer to IRB Policies & Procedures Manual Section 9.2.

✓ Expedited Review - Study involves procedures that are no more than minimal risk

*required

Provide justification for why this study presents no more than minimal risk.

This study falls under Category 7 for Expedited Review. The research is on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication,

A.2a cultural beliefs or practices, and social behavior) or research employing survey,interview, oral history, focus group, program evaluation, human factors

evaluation, or quality assurance methodologies.

This study employs focus groups, interviews, and survey methodology; therefore, it presents no more than minimal risk. Appropriate measures will be taken to ensure that all data is kept on an encrypted, password-protected and web-authenticated, secure NU REDCap database. Access to the data will be

restricted to the study staff. There will be no change to patient treatment or other impact on the patient other than risk of loss of confidentiality.

Full Board Review - Study involves procedures that are greater than minimal risk

Exempt from IRB Review - (e.g., publicly available data sets, de-identified chart reviews, de-identified data receipt from another institution, surveys/questionnaires/interviews of adults, etc)

B Study Personnel

For guidance regarding PI Responsibilities and who to list in Study Personnel, refer to IRB Policies & Procedures Section 5.

*required

Select the Principal Investigator (PI).

B.1 Any study conducted by a PI who is not on staff at Lurie Children's must have at least one Lurie faculty member within the division/department where the research will be conducted, serve as a sub-investigator.

Name: Diane Chen
Organization: Adolescent Medicine
Address:
Phone: 312-227-2939
Email: dichen@luriechildrens.org

*required

Select only the Research Coordinator(s)/Primary Study Contact(s).

Name: Victoria Kolbuck
Organization: Department of Pediatrics

Address: , Chicago, IL 60611-2605

Phone: 76336

Email: vkolbuck@luriechildrens.org

B.2 Name: Afiya Sajwani

Organization: Department of Pediatrics

Address: , Chicago, IL 60611-2605

Phone: 312-227-8372

Email: ASajwani@luriechildrens.org

Name: Abigail Muldoon

Organization: Adolescent Medicine

Address:

Phone:

Email: amuldoon@luriechildrens.org

Select all Sub-Investigators.

B.3 Name: Courtney Finlayson

Organization: Endocrinology

Address: 155 E. Superior , Chicago, IL 60611-2605

Phone: 312-227-9403

Email: cfinlayson@luriechildrens.org

Select other study staff.

If you are working with REDCap at Northwestern, please list "REDCap User" in

B.4 this role so that REDCap staff may access to approval status and letters.

Name: REDCap User

Organization: Non-Medicine

Address: , Chicago, IL 60611-2605

Phone:

Email: redcap@northwestern.edu

Select non-Lurie Children's personnel engaged in the study conduct at Lurie

B.5

Children's site(s).

*required

B.6 To whom has the PI delegated responsibility to obtain informed consent?

✓ All Primary Research Coordinator(s)/Study Contact(s) listed in B.2

All Sub-Investigators listed in B.3

All other study staff listed in B.4

All non-Lurie Children's personnel engaged in the study conduct at Lurie Children's site(s) listed in B.5

Limited to the following personnel:

Not applicable (waiver of informed consent being requested or informed consent not required)

2 Study Settings

A Multi-Institutional Research

*required

A.1 Is this a multi-center protocol?

- Yes
- ✓ No

*required

A.2 Mark any activity, personnel or funding involving Northwestern University (NU) or an NU Affiliate.

- Participants have study visits/activity at an NU site
- Identified data and/or samples are being sent to investigators at NU
- Non-Lurie Children's NU faculty or staff are engaged in the research
- Some or all of the funding is coming through the NU Office of Sponsored Research
- ✓ Data being collected or stored using Northwestern's REDCap access
- ✓ Sharing de-identified data/specimens
- Providing standard of care services only (e.g.radiation therapy that is only being done for standard of care)
- Performing commercial service (e.g. statistical analysis, lab analysis, etc.)
- Other:
- No, NU or an NU Affiliate is not involved in this research study

B Study Setting

*required

B.1 At which site(s) will the study be conducted by Lurie Children's investigator(s)?

- ✓ Ann & Robert H. Lurie Children's Hospital of Chicago and/or remote/satellite sites.
- School
- Community Settings
- PPRG (Pediatric Practice Research Group)
- Participant's Home
- Other

*required

C Research Support Services

*required

C.1 Does this study require any ancillary research support services?

- Yes
- ✓ No

*required

Safety Review D

For more information, refer to IRB Policies and Procedures Manual Section 9.

*required

D.1 Does this study require any safety review (Biosafety Committee or Radiation Safety)?

Yes

✓ No

3 Study Design

Study Design

A

The description of the protocol as outlined in this section must present an interpretable enough description of the study design and reflect the conduct of the study at this institution to allow for a valuable IRB review . While information included in this section may be based on the protocol, it must be summarized and condensed by the PI/study team to ensure it is comprehensible enough to a general audience to allow for the IRB to review the ethical and safety considerations of the study while having the background design for reference. This should not involve directly copying and pasting from the study protocol. Before certifying this submission, the PI should review this section to ensure that it is written for a general audience and does not rely on terminology specific to this field of study with all acronyms and complex terms defined at their first use.

*required

A.1 Select all categories that apply to the main study design.

- Clinical Trial
- ✓ Prospective Collection of Data or Specimens
- Retrospective Collection or Review of Data

*required

A.2 Is there more than one cohort (i.e., treatment group vs control group) to be enrolled into this study?

- ✓ Yes

*required

List the groups to be enrolled and ensure that all answers below outline the study details for each group.

GnRHa Cohort

Potential participants will be screened for eligibility based on the following criteria: (1) youth is between the ages of 8-14 years, (2) youth self-asserts a transgender identity, and (3) youth has expressed interest in GnRHa or is currently on GnRHa treatment.

A.2a GnRHa Parent Cohort

Parents of eligible youth in GnRHa cohort will be eligible.

GAH Cohort

Potential participants will be screened for eligibility based on the following criteria: (1) Adolescent/young adult (AYA) is between the ages of 13-24 years, (2) AYA self-asserts a transgender identity, and (3) AYA has expressed interest in GAH or is currently on GAH treatment.

GAH Parent Cohort

Parents of eligible youth in GAH cohort will be eligible.

No

B Study Background and Objectives

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*required

Provide the background and rationale of the study including appropriate references if not included in a study protocol.

The goal of this study is to develop and evaluate the feasibility, acceptability and efficacy of a patient-centered, mobile-first website Aid For Fertility-Related Medical Decisions (AFFRMED).

The AFFRMED is targeted for transgender youth facing fertility preservation (FP) decisions due to gender-affirming treatments that impair long-term fertility. The AFFRMED will positively impact care for transgender youth by: (1) fostering patient-centered communication about sensitive issues related to future fertility, (2) aiding transgender youth in making difficult decisions about medical care that may impact future fertility, and (3) facilitating informed decision-making about FP.

A.1. Fertility is an understudied issue in transgender care. Gender-affirming hormones (GAH; i.e., estrogen for transgender women; testosterone for transgender men) are medically indicated to treat gender dysphoria (i.e., distress due to a mismatch between birth-assigned sex and gender identity). However, long-term GAH use leads to impairments in gonadal histology that cause infertility or biological sterility. However, clinical thresholds have not been established for amount and duration of exogenous GAH exposure leading to permanent negative effects on fertility. Thus, the Endocrine Society clinical practice guidelines, the World Professional Association of Transgender Health standards of care, and the ethics committee of the American Society of Reproductive Medicine all recommend counseling regarding fertility and reproductive options for transgender individuals before initiating GAH treatment.

A.2. FP options have expanded significantly in recent years, offering transgender youth theopportunity to preserve their reproductive autonomy. Until recently, many transgender people regarded the loss of fertility as the “price to pay” for gender transition. However, there are now non-experimental FP options available to post-pubertal transgender individuals. Options include cryopreserving mature gametes (i.e., eggs and sperm) that would otherwise be adversely affected by transitioning with GAH. Transgender adults are increasingly referred for FP as there is growing recognition that they desire biological children at similar rates as their cisgender counterparts. One study found that over a third of transgender adults surveyed would have cryopreserved gametes had FP technology been available. However, two recent studies show that less than 5% of transgender youth pursue FP, despite routine counseling and referral to fertility clinics. Reasons youth cited for not pursuing FP included cost, invasiveness of procedures, desire not to delay medical transition, and intent to adopt children or no intent to parent in the future. Yet, our community survey of 156 transgender youth found that a third (36%) were interested in having biological children and a quarter (26%) were unsure about their parenting intentions. Almost half the transgender adolescents sampled in another study recognized that their desires for biological parenthood might change over time. Moreover, our preliminary data suggest that transgender youth lack specific knowledge of GAH effects on fertility and FP options. Thus, transgender youth may be making decisions

that have long-term implications on their reproductive health and autonomy based on incomplete knowledge and understanding of reproductive biology and FP options. Taken together, findings suggest that current protocols for fertility counseling may not be meeting youths' needs for informed decision-making.

A.3. Evolving standards of transgender healthcare emphasize the need to address fertilityearlier in the care continuum. As public awareness of gender diversity has increased over the last decade, transgender youth are seeking transition-related medical care at younger ages. Providing medical care to transgender youth in early puberty complicates fertility-related counseling. Clinical practice guidelines recommend pubertal suppression with gonadotropin-releasing hormone analogues (GnRHa) for youth in early puberty (i.e., Tanner stages 2-3). GnRHa represent a reversible intervention that suppresses sex hormone production, which prevents pubertal changes that may be emotionally distressing to transgender youth. However, GnRHa not only prevents the development of unwanted secondary sex characteristics, but also suspends germ cell maturation. Puberty appears to progress normally after discontinuing GnRHa treatment. But transgender youth typically initiate GAH concurrently with GnRHa or before discontinuing GnRHa. Thus, germ cells never fully mature, limiting non-experimental FP options. This emphasizes the need for fertility-related counseling before initiating GnRHa treatment, when youth may be as young as 8-9 years old. As such, parents of peripubertal transgender youth are often tasked with making medical decisions that can impair their child's reproductive functioning and interfere with reproductive autonomy.

A.4. Experimental protocols are currently in place for storing prepubertal gonadal tissue for pediatric patients who are receiving gonadotoxic therapies. Current American Society of Clinical Oncology Guidelines recommend a discussion of investigational FP options with parents of prepubertal oncology patients. The updated Endocrine Society guidelines also specifically recommend fertility discussions with early pubertal transgender youth and their families prior to starting GnRHa. Fertility experts expect that methods for maturing precursor egg and sperm cells will be possible with advanced assisted reproductive technologies (ART) in the future. Therefore, clinicians must educate youth and families on the potential for ovarian or testicular tissue cryopreservation to protect the reproductive autonomy of transgender youth.

A.5. Discussions and decisions about FP are complicated because: (1) clinical thresholds have not been established for how much GAH exposure will lead to permanent negative effects on fertility, (2) pediatric FP options and ART are complex and rapidly evolving, (3) transgender youth must consider parenting intentions although youth may not be

developmentally ready to engage in family planning decisions, and (4) impaired fertility affects future quality of life, rather than current functioning or survival. Additionally, fertility-related decision-making is highly subjective, relying on patient values and preferences, which emphasizes the importance of implementing a shared decision-making model. The proposed decision aid will provide education on gender-affirming interventions affecting fertility and logistical considerations in weighing whether or not to pursue FP. The decision aid will include values clarification exercises and support shared decision-making. Novel decision aid formats using web-based, interactive technologies have been shown to improve patient knowledge, timely access to care, and decision satisfaction.

Use of a Delphi expert panel will contribute to information included within the decision aid. International experts will be asked to provide their thoughts on necessary content to include in the decision aid to incorporate multiple perspectives on relevant content.

A.6. Contribution of the Proposed Work. Our long-term goal is to improve quality of care for transgender youth. Developing, evaluating, and disseminating a patient-centered Aid For Fertility-Related Medical Decisions (AFFRMED) targeted for transgender youth represents a
B.1 necessary step to foster informed decision-making and protect transgender youth's reproductive autonomy.

REFERENCES

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*required

State the main hypothesis and/or objective(s).

Aim 1. Develop a patient-centered Aid For Fertility-Related Medical Decisions (AFFRMED) targeted for transgender youth.

Aim 1a. Apply user-centered design principles to develop a web-based AFFRMED prototype with input from a multidisciplinary transgender health and fertility medicine expert advisory panel.

Aim 1b. Finalize design and content of the AFFRMED prototype based on patient and parent

B.2 input through focus groups and usability testing.Aim 1c. Develop a knowledge test instrument to be used in the Aim 2 AFFRMED pilot trial.

Aim 2. Pilot test the feasibility, acceptability, and efficacy of the AFFRMED in a single arm, pre-/posttest trial.

Hypothesis1. Transgender youth and parents' fertility knowledge will significantly improve following AFFRMED use.

Hypothesis2. Transgender youth and parents will rate the AFFRMED highly on validated implementation outcome measures: Acceptability of Intervention Measure, Intervention Appropriateness Measure, and Feasibility of Intervention Measure.

*required

State the main study outcome measures/endpoints.

The primary study outcome is change in fertility-related knowledge from same-day pre-AFFRMED to post-AFFRMED exposure. Participants will complete a fertility-related knowledge test instrument immediately prior to AFFRMED exposure. Participants will be given 1 hour to freely navigate the web-based AFFRMED prototype. Thereafter, participants will get a 5-minute break before completing a post-AFFRMED fertility knowledge test.

B.3 The appropriateness of the AFFRMED. Participants will also be asked to rate the acceptability,other study outcomes are related to participant-reported feasibility, acceptability, and appropriateness, and feasibility of the AFFRMED using the validated Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM). The AIM (4-items; Cronbach's α=.85) measures the perception among participants that the AFFRMED is agreeable, palatable, or satisfactory. The IAM (4-items; Cronbach's α=.91) measures the perceived fit, relevance, or compatibility of the AFFRMED to address fertility-related decision-making. The FIM (4-items; Cronbach's α=.89) measures the extent to which participants feel the AFFRMED can be successfully used in the clinical setting. Items are rated on a 5-point Likert scale from completely disagree (1) to completely agree (5), with higher scores indicating greater acceptability, appropriateness, and feasibility.

*required

List the inclusion criteria.

Delphi Expert Panel Members

1. At least 2-years of postgraduate training expertise in one of the following areas: A) fertility/infertility medicine; B) pediatric transgender healthcare
2. For individuals with expertise in pediatric transgender healthcare, experts must meet the following additional criteria: A) cared for at least 50 transgender/gender-expansive adolescents and young adults OR B) published at least 1 peer-reviewed paper related to fertility or reproductive health in transgender populations
3. For individuals with expertise in reproductive endocrinology, infertility, obstetrics and gynecology, reproductive biology, experts must meet the following additional criteria: A) cared for at least 2 transgender patient clinically within the last year OR 2) published at least 10 relevant peer-reviewed papers

B.4

GnRHa Cohort

Potential participants will be screened for eligibility based on the following criteria: (1) youth is between the ages of 8-14 years, (2) youth self-asserts a transgender identity, and (3) youth has expressed interest in GnRHa or is currently on GnRHa treatment.

GnRHa Parent Cohort

Parents of eligible youth in GnRHa cohort will be eligible.

GAH Cohort

Potential participants will be screened for eligibility based on the following criteria: (1) Adolescent/young adult (AYA) is between the ages of 13-24 years, (2) AYA self-asserts a transgender identity, and (3) AYA has expressed interest in GAH or is currently on GAH treatment.

GAH Parent Cohort

Parents of eligible youth in GAH cohort will be eligible.

*required

List the exclusion criteria with justification for any related to age, gender, race, ethnicity, language, or social status.

Exclusion criteria are: (1) youth/parents are unable to read, speak or understand English, and (2) youth/parents are unable or unwilling to provide consent/assent/parental permission for study participation. None of the study investigators are fluent in other languages, and thus B.5 would not be able to conduct required study visits to non-English speakers.

Exclusion criteria ONLY FOR COGNITIVE INTERVIEW OR MEASURE VALIDATION PHASES: Participants who participated in focus groups and/or usability testing can participate in either the cognitive interview phase or the measure validation phase, but cannot participate in both phases.

Exclusion criteria ONLY FOR PILOT TEST PHASE: Participants who participated in any other phase of the study, including focus groups, usability testing, cognitive interviews, and/or measure validation are ineligible to participate in the pilot test phase.

C Population

*required

C.1 Check all targeted age ranges of participants to be enrolled in this study.

✓ Children

*required

C.1a Age range:

Neonates (birth to less than 1 month)

✓ Infants and Young Children (older than 1 month up to age 12)

✓ Children (between 12 and 18 years of age)

*required

Provide justification for the inclusion of children in this study.

C.1b This study intends to develop a decision-aid tool to be used by youth eitherinterested in or on pubertal suppression treatment, or youth interested in or on gender-affirming hormone treatment. To determine if the decision-aid prototype is understandable and relatively easy to use by youth in either of these groups, we are asking youth to participate to provide feedback and to validate the knowledge test.

✓ Adults (18 years and older)

✓ Parents of children treated at Lurie Children's

*required

Indicate all other targeted populations in this study.

C.2

For guidance regarding Vulnerable Participants, refer to IRB Policies & Procedures Manual Section 12.

Pregnant women, Fetuses

Nonviable Neonates and Neonates of uncertain viability

Research involving the placenta, the dead fetus or fetal material after delivery

Prisoners/Detainees

Minors who can consent for themselves (e.g., emancipated minors)

✓ Lurie Children's and/or Northwestern Employees/ Medical Students

*required

C.2e Provide justification for the inclusion of Lurie Children's and/or Northwestern Employees/Medical Students in this study.

Northwestern University faculty are eligible to participate as experts in this study since they demonstrate expertise in the areas we are studying.

Studies involving Northwestern University Feinberg School of Medicine students or Northwestern/McGaw residents or fellows as study subjects are to be reviewed and approved by Diane Wayne, MD, Vice-Dean, Education, Northwestern University Feinberg School of Medicine (dwayne@northwestern.edu).

Cognitively Impaired Adults

✓ Economically or socially disadvantaged populations

*required

Provide justification for the inclusion of economically or socially disadvantaged populations in this study.

C.2g The aim of this study is to develop and test a decision-aid for use with transgender youth when considering fertility options prior to initiating gender-affirming medical interventions. Further research is needed to better understand

transgender youth's needs related to decision-making around fertility and fertility preservation, thus transgender youth are included in this study.

Control/Healthy Group

N/A

*required

C.3 Does this study target any health disparity population(s)?

✓ Yes, a health disparity population is a specific focus of this research.

Yes, a health disparity population is not a specific focus of the research but the recruitment and study contact methods will be enrolled to assure inclusion of a health disparity population.

No, a health disparity population is neither a specific focus nor is the study written to assure inclusion of health disparity populations.

*required

How many participants are expected to be enrolled at Lurie Children's?

Enrollment numbers are specified by both phase of the study as well as by cohort.

1. Focus Groups
   - a.Focus Group 1 (GAH Cohort): 6-9 AYA
   - b.Focus Group 2 (GAH Parent Cohort): 6-9 parents

   c.Focus Group 3 (GnRHa Youth and Parent Cohorts): 6-9 youth and parents
2. Usability Testing
   - a. GnRHa Cohort: Up to 5 youth
   - b. GnRHa Parent Cohort: Up to 5 parents

   c. GAH Cohort: Up to 5 AYA

C.4
   - d. GAH Parent Cohort: Up to 5 parents
3. Cognitive Interviews
   - a. GnRHa and GAH Cohorts: Up to 10 youth/AYA

b. GnRHa and GAH Parent Cohorts: Up to 10 parents

4. Measure Validation
   - a. GnRHa and GAH Cohorts: 100 youth/AYA
   - b. GnRHa and GAH Parent Cohorts: 100 parents

5. Pilot Test
   - a. GnRHa and GAH Cohorts: 10 youth/AYA
   - b. GnRHa and GAH Parent Cohorts: 10 parents

*required

C.5 Is this a multi-center study with enrollment at other sites?

Yes

✓ No

D Research Procedures

---

*required

List and describe all procedures/interventions to be done and/or data to be collected as part of this study.

If a visit schedule/table is not provided in D.2, ensure that this narrative includes the expected location and length of each visit.

Aim 1: Develop a patient-centered Aid For Fertility-Related Medical Decisions (AFFRMED) targeted for transgender youth.

Aim 1a. Apply user-centered design principles to develop a web-based AFFRMED prototype with input from a multidisciplinary transgender health and fertility medicine expert advisory panel. The

AFFRMED prototype will be developed using the Ottawa Decision Aid Toolkit, informed by the Ottawa Decision Aid Framework, and the International Patient Decision Aids Standards. Our decisional needs assessment identified the following fertility topic domains and information needs: (1) general education about reproductive biology, (2) current information about how gender-affirming medical and surgical treatments affect fertility potential, (3) FP options, and (4) short-term and long-term considerations about pursuing FP or not. Content will be transformed into text, images, graphics, and videos that utilize gender inclusive language, are accessible (i.e., literacy levels <5th grade), visually attractive and user friendly, and convey the decisions that need to be considered. An interactive, web-based AFFRMED prototype will be created, organized by past, current, and desired future gender-affirming medical and surgical interventions that affect fertility potential.

A 5-person multidisciplinary panel will be assembled to serve as the AFFRMED Expert Advisory Board. Experts will be provided with the AFFRMED prototype and given 1 week to review. Experts will then complete a 45-60 minute audio-recorded phone interview to provide qualitative comments about content and user interface and propose improvements. Expert feedback will assure accuracy, completeness, and neutrality of content. The study team will carefully consider and incorporate the Expert Advisory Board's comments and suggestions in revising the AFFRMED prototype.

Additionally, we will use a Delphi method expert panel to gather feedback from a panel of up to 200 international experts in reproductive health, fertility preservation, psychology, pediatric endocrinology, adolescent medicine, and trans healthcare. The Delphi panel will provide feedback on the learning objectives generated by the internal study team via online survey.

Aim 1b. Finalize design and content of the AFFRMED prototype based on patient and parent input through focus groups and usability testing.

Participatory Design Focus Groups. We will conduct 3 in-person participatory design focus groups in an iterative fashion. The purpose of these user-centered design sessions is to identify optimal content and technical features, as well as solicit feedback on the user interface so that the AFFRMED prototype can be refined. Each 90-minute focus group will be conducted by the PI and a trained research coordinator using a moderator's guide to lead focus group discussions. Each group will include 6-9 participants (18-27 participants total). Separate focus groups will be held for transgender AYA ages 13-24 ("GAH cohort") and parents of transgender AYA ages 13-24 ("GAH parent cohort"). A third focus group will comprise transgender youth ages 8-14 ("GnRHa youth cohort") and parents of transgender youth ages 8-14 (GnRHa parent cohort"). We will provide participants with mock-ups of the

AFFRMED prototype and ask for structured feedback on design, layout, and content, including length and clarity. The mock-ups will be a mixture of paper mock-ups as well as web-based mock-ups. Focus groups will be audiorecorded and reviewed by the study team, who will carefully consider and incorporate comments, suggestions and proposed changes in the revised AFFRMED prototype. Focus groups will occur in a private room at Lurie Children's. Youth in the GnRHa cohort (ages 8-14) will participate in the same focus group as their parents, thus they will be in the same room with their parents.

Usability Testing. Usability testing allows for the optimization of a tool prior to its integration into a clinical workflow environment. Each study visit is expected to last 45-60 minutes and will be conducted by a trained research coordinator. We will ask participants to use the AFFRMED prototype in the laboratory setting and “think aloud” as they navigate through the decision aid. Usability testing will involve the use of a desktop or laptop computer using the AFFRMED prototype hosted by Noggin Lab, the company we are developing the AFFRMED prototype with. For example, specifying why they are clicking on a specific part of the tool and explaining why it is (or is not) helpful. We also will give participants target goals (e.g., go find X content) and observe whether they can find the most efficient pathway to identify target content. This type of usability testing identifies barriers to adoption and surface level usability issues. These research visits will be audio-recorded and reviewed by the study team, who will carefully consider and incorporate comments, suggestions, and proposed changes in revising the AFFRMED prototype.

D.1

Usability testing will follow an iterative process in rounds of 4, with 1 participant from each target subgroup (1 parent and 1 youth/AYA from each cohort) completing usability tests before revising the AFFRMED for the next set of usability testing. We will recruit up to 5 transgender youth/AYA and 5 parents of transgender youth/AYA from each cohort (GnRHa and GAH cohorts; up to 20 total participants) to complete usability testing. Participants who participated in the focus groups may participate in this phase if they are interested. Study visits will occur in a private room at Lurie Children's. Youth under the age of 12 will complete the study visit in a room separate from their parents.

Aim 1c. Develop a knowledge test instrument to be used in the Aim 2 pilot test of the AFFRMED.

Measure Development. We will follow the recommended steps for scale development proposed by Robert DeVellis: (1) determine clearly what is to be measured; (2) generate an item pool; (3) determine the format for measurement; (4) have the initial item pool reviewed by

experts; (5) administer items to a development sample; (6) evaluate the items; and (7) optimize the scale length.

Cognitive Interviews. We will recruit up to 10 transgender youth/AYA and up to 10 parents of transgender youth/AYA to complete cognitive interviews of the knowledge test instrument to refine wording and item order. The purpose of cognitive interviews is to understand whether subjects understand the question, both consistently across subjects and in the way intended by the researcher. Participants will be asked to “think aloud” and provide their interpretation of each scale item’s meaning and provide suggestions for revisions. These interviews will last 30-45 minutes and will be audio-recorded and reviewed by the study team to refine the measure. Cognitive interviews will be conducted in an iterative manner until no additional measurement concerns arise. Study visits will occur in a private room at Lurie Children's. Youth under the age of 12 will complete the study visit in a room separate from their parents.

Measure Validation. We will recruit a sample of 100 transgender youth and AYA and 100 parents of transgender youth and AYA for measure validation. Content validity will be assessed by the 5-person Advisory Board using the Lynn index. Construct validity will be established using Principal Component Analysis (PCA) to extract factors. Reliability will be assessed with Cronbach’s alpha. The study visit will last 10-15 minutes, and the participant will be asked to take the knowledge test described earlier which was refined during the cognitive interview phase. The test will ask questions related to knowledge of fertility and fertility preservation. Study visits will occur in a private room at Lurie Children's. Youth under the age of 12 will complete the study visit in a room separate from their parents.

Aim 2: Pilot test the feasibility, acceptability, and efficacy of the AFFRMED on knowledge in a pre-/post-test design.

We will evaluate the AFFRMED in a single-arm pilot feasibility, acceptability, and efficacy trial among transgender patients who are considering GnRHa and GAH and their parents. We will recruit 10 youth/AYA and 10 parents as described in Section C.4. Subjects will participate in a 2-hour, in-person visit. During this visit they will complete the pre-AFFRMED 15-20 minute demographics survey (e.g., age, fertility history), the validated Transgender Youth Fertility Attitudes Questionnaire (TYFAQ), and the fertility knowledge test instrument developed in Aim 1c. Each participant will receive the corresponding version of the demographics survey. Then, they will freely navigate the web-based AFFRMED prototype for 1-hour. Thereafter, participants will get a 5-minute break before completing a post-AFFRMED fertility knowledge test. Participants will also be asked to rate the acceptability, appropriateness, and feasibility of

the AFFRMED using validated implementation outcome measures: Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM). The AIM (4-items; Cronbach's α=.85) measures the perception among participants that the AFFRMED is agreeable, palatable, or satisfactory. The IAM (4-items; Cronbach's α=.91) measures the perceived fit, relevance, or compatibility of the AFFRMED to address fertility-related decision-making. The FIM (4-items; Cronbach's α=.89) measures the extent to which participants feel the AFFRMED can be successfully used in the clinical setting. Items are rated on a 5-point Likert scale from completely disagree (1) to completely agree (5), with higher scores indicating greater acceptability, appropriateness, and feasibility. Study visits will occur in a private room at Lurie Children's. Youth under the age of 12 will complete the study visit in a room separate from their parents.

Development of AFFRMED will occur simultaneously with the development of the knowledge test. The development of the AFFRMED will involve three sequential steps:
AFFRMED Development
(1) expert panel (Aim 1A)
(2) participatory design focus groups (Aim 1B)
(3) usability testing (Aim 1B)
Development of the knowledge test will occur simultaneously, and will also involve three sequential steps:
(1) measure development (Aim 1C)
(2) cognitive interviews (Aim 1C)
(3) measure validation (Aim 1C)

If a visit schedule/table is being used to outline these procedures/interventions, upload it here.

D.2 _____

This table should include the expected location and length of each visit.

*required

D.3 Aside from chart review, are any of the procedures listed in Item D.1 being done for research purposes only or being done more frequently than for usual clinical care?

_____

✓ Yes

*required

List which of the above procedures are being done for research purposes only, including procedures done more frequently than usual clinical care.

D.3a

All study procedures are being done for research purposes only.

*required

Provide the expected duration of study participation including any long term follow-up.

D.3b

All five phases of this study involve the use of a discrete, one-time study visit. There will be no follow-up visits for any phase of this study.

*required

Is the sponsor or investigator funds paying for all of the research only procedures?

D.3c

✓ Yes

No

*required

D.3d Are any portion(s)/procedure(s) of this study optional for participants?

Yes

✓ No

No

*required

Provide the approximate timetable for study completion.

We anticipate study activities will be completed within a 2-year funding period. The tentative research timeline by month is outlined below:

Table 1.

Research Timeline by Month	1-3	4-6	7-9	10-12	13-15	16-18	19-21	22-24
Project Start-Up Tasks								
Planning meeting with investigative team	X							
IRB preparation and approval	X							
Specific Aim #1: Develop a Aid for Fertility-Related Medical Decisions (AFFRMED)								
Web-based development of AFFRMED prototype	X	X	X	X	X			
Advisory panel								

	feedback on AFFRMED prototype		X		
	Focus groups to refine design of AFFRMED prototype			X	
	Usability testing to refine content of AFFRMED			X	X
D.4	prototype				
	Develop a knowledge test instrument to be used in the Aim 2 AFFRMED pilot test	X	X		
	Advisory panel feedback on knowledge test instrument		X		

Cognitive
interviewing
to refine
X X knowledge
test
instrument

Validation of
knowledge
X X X

test instrument

Specific Aim #2: Pilot test the feasibility and effects of the AFFRMED on knowledge in a pre-post design

Feasibility
X X

testing

Data
X
Analyses

Next Steps

Prepare
manuscripts
X
for dissemination Preliminary
data for X future grant submission

*required

D.5 Does this study include genetic testing?

Yes

✓ No

*required

D.6 Is it likely that clinically important incidental findings will be discovered during the study?

Yes

✓ No

E Statistical Analysis

*required

Describe the statistical plan for the study, including appropriate references to the protocol.

E.1 We will test the significance of fertility knowledge change between same-day pre-AFFRMED and post-AFFRMED scores using a paired t-test. Pre-AFFRMED knowledge scores will also be compared by t-test by participants' demographic characteristics (e.g., birth-assigned sex; fertility history). We will also explore bivariate correlations between pre-AFFRMED knowledge scores and (1) age and (2) fertility attitudes as measured by the TYFAQ. Descriptive statistics will be used to characterize participant ratings of AFFRMED acceptability, appropriateness, and feasibility using the AIM, IAM, and FIM. Specifically, we will calculate the percentage of participants who "agree" or "completely agree" that the AFFRMED is acceptable, appropriate, and feasible.

F Survey, Questionnaire, or Interview

*required

F.1 Does the study utilize surveys, questionnaires, or interviews/focus groups?

✓ Yes

*required

Attach all copies of surveys, questionnaires, or scripts for interviews/focus groups.

TYFAQ Youth Report and Parent Report V2 8.29.18.pdf

Focus Group Facilitator Guide V2 9..6.18 CLEAN.docx

Demographics Survey_ Parents_GAH Cohort_V1_9 6 18.doc

F.1a

Demographics Survey_ Parents_GnRHa Cohort_V1_9.6.18.doc

Demographics Survey_GAH Youth & Young Adults_V1_9.6.18.doc

Demographics Survey_GnRHa Youth_V1_9.6.18.doc

Project AFFRMED Delphi Survey V5 4.22.19_CLEAN.docx

Project AFFRMED Delphi Survey V5 4.22.19_TRACKED.docx

No

*required

F.2 Does any portion of the survey, questionnaire, or interview have the potential to make the participants upset or uncomfortable?

✓ Yes

Please ensure that the risks associated with these questions is reflected in Section 8 of the Cayuse IRB application as well as the Informed Consent Document(s) and/or Information Sheet(s).

No

*required

F.3 Does the survey, questionnaire, or interview record any information that can identify the participants?

Yes

✓ No

*required

F.4 Will questionnaires/surveys/interviews be completed by a parent/guardian not represented in Section C Population above?

Yes

✓ No

K Lurie Children's and/or Northwestern Employees/ Medical Students

*required

K.1 Indicate how the investigator will minimize coercion to participate, share data (if applicable), and ensure participation will not affect employment status at the Institution.

Northwestern University faculty members would be approached (not students). Experts who are contacted to participate will be informed it is an optional survey that they can participate in if they would like to. If they would like to participate, they will be offered authorship on a future

manuscript but they can choose to participate without receiving authorship if they would like.

Recruitment

A

For guidance regarding Participant Selection and Recruitment, refer to IRB Policies & Procedures Manual Section 10.

*required

A.1 Select all recruitment tools and approaches that will be used.

- ✓ Verbal (Direct participant contact)
- ✓ Referral from colleagues
- Direct recruitment by study staff in departments/divisions/clinics not represented by the study personnel
- ✓ Email
- Flyers
- Letter from investigator
- Letter from personal physician
- Newspaper/Magazine Advertisements
- ✓ Telephone interview (recruitment script)
- Public Website(s)
- ✓ Medical Records
- Investigator's Records (study records, databases, or registries)
- Social Media (e.g., Facebook, Twitter, Instagram, Snapchat, etc)
- Other

*required

How will this/these recruitment tool(s)/approach(es) will be used?

Using active and passive recruitment strategies, we will recruit transgender youth and adolescents/young adults and their parents in decision aid development and design via the following methods: (1) eligible youth will be recruited during routine appointments in our multidisciplinary Gender & Sex Development Program (GSDP), (2) patient lists of youth seen previously within GSDP will be used to identify potentially eligible participants who will be contacted by telephone and email, and (3) our community partner, the Chicago chapter of

A.2 Parents of Transgender Individuals (PTI), a local support group for parents of transgender individuals, will assist with recruitment by forwarding recruitment emails to their support group listserv.

For the Delphi expert panel, we will send a recruitment email containing a survey link to experts who have been determined by our internal team to potentially meet criteria for this study. Potential participants will be asked to complete the screening questionnaire as part of the survey link to determine eligibility. Participants who meet eligibility (determined by programming in REDCap based on our inclusion criteria) will then receive the expert panel survey. Participants who do not meet eligibility criteria will see a message informing them they are not eligible and thanking them for their time.

*required

Who will be responsible for approaching potential participants?

A.3 The Research Coordinator and study staff will approach potential participants.

The research coordinator, Principal Investigator, and co-Investigator will contact potential participants via email for the Delphi expert panel.

*required

When and where will potential participants be approached?

A.4 Potential participants will be approached before or after a medical or mental health appointment. Potential participants and their parents will also be approached via telephone and/or email.

Delphi expert panel participants will be contacted via email for recruitment.

*required

Attach all recruitment materials.

All publicly posted recruitment materials must include the following required language: “This study is Lurie Children’s IRB #, TITLE, Principal Investigator Name. The content of this flier/brochure/e-mail/etc. has been approved by the Lurie Children’s IRB.”

Phone Script Usability Testing V1 8.7.18.docx

Phone Script Cognitive Interview V1 8.7.18.docx

Phone Script Measure Validation V1 8.7.18.docx

A.5 Phone Script Pilot Testing V1 8.7.18.docx

Email Script Usability Testing V2 8.31.18_CLEAN.docx

Email Script Cognitive Interview V2 8.31.18_CLEAN.docx

Email Script Measure Validation V2 8.31.18_CLEAN.docx

Email Script Pilot Testing V2 8.31.18_CLEAN.docx

Email Script Focus Group V3 9.7.18 CLEAN.docx

Phone Script Focus Group V3 9.7.18 CLEAN.docx

Delphi email draft 4.11.19.pdf

*required

A.14 Will children be recruited via social media?

Yes

✓ No

Payment/Compensation/Reimbursement to Participants and Families

B

For guidance on Compensation and Reimbursement, refer to IRB Policies & Procedures Manual Section 10.1.D.

*required

B.1 Will there be payment/compensation/reimbursement to participants and/or their families?

- ✓ Yes
- No

*required

B.2 Select all types of payment(s) to participants and/or families.

- Reimbursement for expenses.
- ✓ Compensation for time and effort.

*required

B.2b Specify the dollar amount method/form and timing of compensation for expenses to participants/families. f this will be provided in the form of a gift card, please provide the details of the gift card.

Each participant will receive incentives for the following phases:

1. Focus groups: $50 gift card
2. Usability testing: $50 gift card
3. Cognitive interview: $25 gift card
4. Measure validation: $5 gift card
5. Pilot testing: $50 gift card

Participants will receive their incentive immediately after completing the study visit.

Delphi expert panel members will be offered authorship on the manuscript that will eventually be developed from this project for their participation.

Gifts (such as presents or toys)

6 Confidentiality, Privacy, and Release

Participant Confidentiality

A

Confidentiality refers to the protection of a participant's identity, their protected health information, and the information/documents collected as a part of a research study.

*required

A.1 Select the precaution(s) that will be used to maintain the confidentiality of participant identity and/or protected health information

Study data will be stored in password protected computers in locked offices and/or in locked cabinets to which only members of the study team have access.

✓

Study data will be stored in an online database/repository with provisions to ensure data cannot be accessed by unauthorized individuals/entities.

✓

Study data will be stored with identifiers and only study personnel will have access to identifiers.

✓ Participant identifiers will be stored separately from the coded study data.

*required

A.1b List those who will have access to the link and/or identifiers.

Only the PI, Research Coordinator, and study staff will have access to the link to coded study data.

Study data will be completely de-identified as it is collected.

A Certificate of Confidentiality will be used.

Other

*required

A.2 Will data from medical records be recorded as part of this study?

✓ Yes

*required

A.2a Mark the personal identifiers to be recorded.

✓ Names/Initials

Medical Record Number

Health plan identification number

Street address, city, county, precinct, zip code, or equivalent geographical codes

Account number

All elements of dates directly related to an individual (e.g., date of birth,

✓

admission date, discharge date, date of death)

Certificate/License Number

Elements of date, including year, for persons 90 or older

Vehicle identifiers and serial number, including license plate number

✓ Telephone number

Device Identifiers and serial numbers

Fax number

Web addresses; Internet IP addresses

✓ E-mail address

Biometric identifiers, including finger and voice print

Social security number

Full face photographic images and any comparable images

Any other unique identifying number, characteristic or code that may identify individual participants (e.g., student or employee ID number)

No

*required

A.3 Will participant specimens (blood, urine, tissue, etc) be collected and maintained as part of this study?

Yes

✓ No

*required

A.4 Will data or specimens be stored for other future research study purposes?

Yes

✓ No

*required

B Participant Privacy

Privacy refers to the way potential participants are identified/contacted, the setting in which they'll be approached/seen, and who is present during participant interaction.

*required

B.1 Will there be direct participant contact or interaction?

✓ Yes

*required

B.1 Select the precaution(s) that will be used a to maintain participants' privacy.

- ✓ The consent process will be done privately.
- ✓ All study procedures will be conducted in a private room/space.
- ✓ Participant information and study conduct will only be discussed with individuals listed in the study personnel.
- Other

No

*required

C Release of Participant Data/Specimens

Release refers to the transfer of Lurie Children's study participant data and/or specimens to authorized individuals/entities outside of the institution.

*required

C.1 Will participant data be released outside of Lurie Children's?

- Yes
- ✓ No

*required

C.3 Will participant specimens be released outside of Lurie Children's?

Yes

✓ No

*required

General Data Protections Regulation (GDPR) for International Participants

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D The General Data Protection Regulation (GDPR) is a European Union law that protects the privacy and security of personal data of individuals (data subjects) are who are in the European Economic Area (EEA). The GDPR applies to individuals physically present in the EEA, which includes: *EEA citizens, EEA residents, anyone visiting an EEA country while enrolled on a study.*

*required

D.1 Will persons in a European Economic Area (EEA) be recruited and/or enrolled for participation in this study?

Yes

✓ No

If during the course of this study, the investigator/study team becomes aware that a participant will be in an EEA country, extra consent provisions may apply. Please contact ORIC Staff for guidance.

---

7 Informed Consent

Informed Consent and Waivers

A

For guidance regarding Informed Consent and Waivers, refer to IRB Policies & Procedures Manual Section 11.

*required

A.1 From the list below indicate how consent will be obtained for this study. (Check all that apply).

- ✓ Written/signed permission for a minor by a Parent or Legal Guardian
- ✓ Written/signed consent by the adult or minor who can consent for themselves
- Written/signed consent by a Legally Authorized Representative (for adults incapable of consenting)
- ✓ Written/signed assent (patients 12-17)
- ✓ Verbal assent (children under the age of 12 included in the study population)
- ✓ Waiver or Alteration of the informed consent process (including waivers of parental permission or adolescent assent, waiver of documentation, or alteration of informed consent)

*required

A.2 Indicate the type of waiver of informed consent that applies to this study.

For guidance regarding waivers of informed consent, refer to IRB Policies & Procedures Manual Section 11.5. Waiver of Informed Consent

- Alteration of Informed Consent
- Waiver of Parental Permission

Waiver of Adolescent Assent

✓ Waiver of the Requirement of Obtaining a Signed Consent Form *required

A.3 Indicate if you are obtaining HIPAA authorization from the participant or requesting a waiver of HIPAA authorization.

✓ Obtaining HIPAA authorization in consent form

Full or partial waiver of HIPAA authorization

HIPAA does not apply as no identifiers are being maintained with this study.

B Consent Process

For guidance regarding the Informed Consent process, refer to IRB Policies & Procedures Manual Section 11.

*required

Describe the expected method of obtaining consent from potential participants including where and how it will take place and measures to ensure that potential participants understand the study procedures.

The Research Coordinator will recruit participants for the study by speaking with patients and their parents/legal guardians face-to-face or by telephone. Once it is determined that the individual may qualify for the study, details will be discussed and all questions answered during the informed consent process. Research participants will be asked to review and sign an informed consent/assent form. The informed consent/assent form covers information about

B.1 the overall purpose of the study, what the study entails, potential risks, potential benefits to participating individuals and society, the confidentiality of data, and contact information for the Principal Investigator and the IRB.

For participants aged 8 to 11 years old, the participant will be asked for their verbal assent, and the parent/legal guardian will sign a consent form. For participants aged 12 to 17 years old, the participant will sign an age-appropriate assent form, and the parent/legal guardian will sign a consent form. For participants aged 18 years or older, the participant will sign a consent form. Once informed consent/assent has been obtained, the research staff will have the form reviewed by a fellow research team member, who will confirm that it is fully completed before it is filed in a secure location under double-lock when not in use and with restricted access during work hours and/or when unattended.

*required

Describe the timing of the informed consent process prior to study procedures occurring. Include a discussion of the adequacy of the allotted time for potential participants/their families to make a decision.

B.2

The Research Coordinator will recruit participants for the study by speaking with patients and their parents/legal guardians face-to-face after regularly scheduled medical or mental health appointments are completed or by telephone or email. Information regarding the study will be provided and interest in participation will be assessed. Those interested in participation and meet inclusion criteria, will be scheduled for a study visit. Formal written informed consent/assent/parental permission will be obtained at the start of the first study visit, giving patients and parents adequate time to consider study participation.

*required

Describe the measures that will be taken during the recruitment and consent process to safeguard against potential coercion or the appearance of coercion.

B.3

Participants will review the consent/assent forms privately and be provided with as much time as requested for this review. Research staff will be nearby to answer any questions. Participants will be informed that they may opt out of any measure which they do not wish to complete. Participants may withdrawal from the study at any time without consequences.

*required

Does the PI anticipate obtaining consent from non-English speaking patients?

B.4

For guidance regarding obtaining consent from non-English speaking patients, refer to IRB Policies & Procedures Manual Section 11.3. Yes

✓ No

B.4b Confirm that if non-English speaking participants are found to be eligible and offered consent, the IRB short form and an interpreter will be used to obtain consent.

✓ Yes

Waiver of the Requirement of Obtaining a Signed Consent Form

F

For guidance, refer to IRB Policies & Procedures Manual Section 11.6.B.

*required

F.1 Select which criterion applies to this study.

(1) That the only record linking the participant and the research would be the consentdocument and the principal risk would be potential harm resulting from a breach of confidentiality. The participant must be offered an opportunity to sign a consent form and be told this document will link them with the research.

✓ (2) That the research presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context.

Please ensure the information sheet(s) is attached in Section 9 Supporting Documents.

H Re-Consent Process

For guidance regarding the re-consent process, refer to IRB Policies & Procedures Manual Section 11.1.

*required

H.1 Please check all that apply:

Study enrolls participants who will turn 12 during their participation on the study.

Study enrolls participants who will turn 18 during their participation on the study.

Enrolled participants may turn the age of 12 and/or 18 while identifiable/coded data and/or specimens are being maintained.

✓ This study does not enroll participants who may/will turn 12 and/or 18 during their participation on the study and/or while identifiable/coded data and/or specimens are being maintained.

8 Risks and Benefits

A Study Risks

*required

A.1 Are there risks associated with study participation aside from those related to confidentiality/privacy as outlined in Section 6?

✓ Yes

*required

Summarize and provide an overall assessment of the physical/psychological/emotional risks and discomforts of the study interventions and procedures.

A.1a The risks of participation in this study are minimal. Potential risks consist of discomfort with interview questions and potential breaches of confidentiality. It is possible that certain questions may make participants feel uncomfortable. Procedures for youth who do experience discomfort are detailed below. Additionally, a number of precautions and safeguards have been developed in order to protect the confidentiality of study participants. No personal identifying information will be used on study measures. Consent forms will be filed and stored separate from the raw data in a secured location under double-lock when not in use with restricted access during work hours and/or when unattended.

*required

Describe steps that will be taken to minimize the risks listed above.

Protection against Risk

Discomfort or distress during the research. Because there is potential for psychological discomfort due to the research topic, we will make every effort to create a secure and trustworthy environment. Participants will be informed that they do not have to answer any question they do not wish, and they can take breaks while completing the survey. Moreover, the participant can ask study staff to provide referrals to counselors or other means of support if they become emotionally upset.

A.1b Participants will have access to a licensed clinician (Dr. Chen) who can help address any feelings and/or questions which arise in the course of their participation.

Confidentiality of study data. We have developed systematic protocols for data handling and storage over multiple studies. Computer files consist of de-identified survey responses. Tracking files are maintained in password-protected electronic systems on a secure, password-protected institutional server. The database contains all contact information, and is used to recruit eligible patients. Contact information will be deleted once a participant completes the survey. Contact information for parents who were unable to be reached in the recruitment process will be deleted at the end of the study's data collection.

*required

Describe the patient safety monitoring plan for the study.

Data and Safety Monitoring Plan

Procedures for Monitoring Data Management and Integrity

To protect the integrity of participants' data, the Project Coordinator will assign an ID number to all participants. The participant ID number will be used to identify data collected. Since the study has repeated follow-up visits, we will maintain a list of participants which link identifying information to study ID numbers. Only a limited number of staff members will have access to this list, which will be kept in locked files and in a password protected computer file. Other study personnel will have access on an as needed basis to perform their duties.

All research personnel will complete extensive training before they are granted access to this identifying information. Study personnel will complete Human

Subjects Training which complies with federal guidelines delineated in 45 CFR Part 46.

Personnel will also sign confidentiality statements that specify that if the participants' confidentiality is breached unintentionally that personnel will follow the procedures for reporting this breach to the PI. The confidentiality statement also states that unintentional or deliberate violations of participants' confidentiality may result in demotion or termination depending upon the severity of the event.

Personnel will also participate in training with the Investigators and/or Project Coordinator regarding data safety, confidentiality of participants, limits of confidentiality, and proper administration of the study protocol.

We will store all personally identifying data in locked cabinets. All forms containing personally identifying information, including participant locator forms (i.e., containing contact information) will be maintained in a password-protected

A.1c computer file.

Data that are entered into computer files will be de-identified and maintained on a subdirectory of an institutional server with access password protected. The PI will review all requests, current and future, to use the data and any data files that are provided to other individuals will be de-identified.

Procedures for Monitoring Adverse Events

Possible adverse events that are anticipated include the need to violate participant confidentiality. Study personnel will be trained regarding the limits of confidentiality. This training will include reviewing possible scenarios and knowledge of key questions to assess risk. We will train staff to err on the side of caution and to contact a supervisor as needed. Supervisors will be available by phone 24 hours a day should staff need to consult regarding an emergency. In this situation, we will train staff members to leave participants in the company of study personnel and immediately contact supervisors before participants leave. Under the guidance of supervisors, staff will be trained either to ensure the safety of participants (i.e. call the police, or if appropriate, to escort participants to the Emergency room).

Possible adverse events that are unanticipated will be brought to the attention of the Principal Investigators and reported immediately to all relevant IRBs. The IRB

will determine whether it is appropriate to stop the study protocol temporarily or will provide suggestions/modifications to the study procedures. Possible modifications include adding these possible adverse events to the consent form and re-consenting all study participants. The PI will be responsible for monitoring participant safety on a monthly basis at regularly scheduled research meetings. She will keep a written log of all adverse events and ensure that the IRB is contacted immediately. She will also keep a log of the outcome of IRB decisions regarding adverse events and apprise the research team of any changes that need to be made as a result of IRB decisions.

No

*required

A.2 Is there a data safety monitoring board/committee (DSMB/C) for this study?

Yes

✓ No

B Potential Benefits and Alternatives

*required

B.1 Are there any anticipated direct benefits to the individual study participants?

Yes

✓ No

*required

Describe any potential indirect benefits to future persons, science, and society.

The purpose of this study is to develop a fertility-related decision aid for transgender youth and

B.2 AYA seeking gender-affirming medical interventions.While there are no potential direct benefits to the research participants, possible risks (i.e.
discomfort answering questions) are minimal and are outweighed by the anticipated societal benefits. The proposed research has the potential to prepare transgender youth and AYA for informed discussions about potential fertility risk, provide an understandable overview of fertility preservation and alternate family-building options, and support informed decision-making about whether or not to pursue fertility preservation.

*required

B.3 Does this study involve interventions?

Yes

✓ No

9 Supporting Documents

Protocol, Consent, and Assent Documents

A Refer to the IRB Consent Forms & Resources Page for all informed consent templates and guidance for writing the documents.

With subsequent submissions after approval, please remove tracked changes versions of documents that are not being modified.

A.1 Attach the main study protocol

Attach copies of all the Lurie Children's parental permission forms to be used for this study

A.2 Parent Permission Usability Testing V3 9.6.18 CLEAN.doc

Parent Permission Cognitive Interview V3 9.6.18 CLEAN.doc Parent

Permission Measure Validation V3 9.6.18 CLEAN.doc

Parent Permission Pilot Testing V3 9.6.18 CLEAN.doc

Parent Permission Focus Group V5 9.7.18 CLEAN.docx

Attach copies of all the Lurie Children's adolescent assent forms to be used for this study

Adolescent Assent Usability Testing V3 9.6.18 CLEAN.docx

A.3 Adolescent Assent Cognitive Interview V3 9.6.18 CLEAN.doc

Adolescent Assent Measure Validation V3 9.6.18 CLEAN.doc

Adolescent Assent Pilot Test V3 9.6.18 CLEAN.docx

Adolescent Assent Focus Group V5 9.7.18 CLEAN.docx

Attach copies of all the Lurie Children's adult consent forms to be used for this study

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Parent Consent Focus Group V4 9.6.18 CLEAN.docx

Adult Consent Usability Testing V3 9.6.18 CLEAN.doc

Parent Consent Usability Testing V3 9.6.18 CLEAN.doc

Adult Consent Cognitive Interview V3 9.6.18 CLEAN.doc

A.4

Parent Consent Cognitive Interview V3 9.6.18 CLEAN.doc

Adult Consent Measure Validation V3 9.6.18 CLEAN.doc

Parent Consent Measure Validation V3 9.6.18 CLEAN.doc

Adult Consent Pilot Testing V3 9.6.18 CLEAN.doc

Parent Consent Pilot Testing V3 9.6.18 CLEAN.docx

Adult Consent Focus Group V5 9.7.18 CLEAN.docx

Study Information Sheets (for use when a Waiver of the Requirement of Obtaining a Signed Consent Form is requested)

A.5

AFFRMED Delphi Information Sheet 3.26.19.doc

B Additional Supporting Documents

Attach Package Inserts or Investigator's Brochures for drugs/biologics and device label and instructions for use.

B.1

Study diaries

B.2

Miscellaneous Sponsor/FDA Documentation

B.3

Attach any other documents requiring IRB review.

B.4

*required

B.5 Is this study federally funded?

✓ Yes

*required

Is Lurie Children's, the Lurie Children's PI, or Northwestern University the prime awardee of the grant?

B.5a

✓ Yes

*required

B.5a-1 Please indicate the sponsor

As prime awardee of the grant, it is the PI responsibility to ensure this study is listed on ClinicalTrials.gov and the Consent Form(s) is/are uploaded to a public registry. For guidance in posting to ClinicalTrials.gov, please contact the site administrator.

For guidance in posting the Consent Form(s) to a public registry, please refer to the grant program officer.

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*required

2 Attach the Research Strategies, Specific Aims, and B.5a-2 Protection of Human Subjects from the grant.

Research Plan Final 2.13.18.pdf

No, Lurie Children's, the Lurie Children's PI, or NU is a sub-award of the grant

*required

B.5b Will genomic data be submitted to an NIH data repository for future research?

Yes

✓ No

No