

Evaluating the Effectiveness of an eHealth EBI for Latino Youth in Primary Care

NCT03009539

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1) **Protocol Title**

Evaluating the Effectiveness of an eHealth EBI for Latino Youth in Primary Care

2) **IRB Review History**

A prior protocol was approved. The approved protocol was recently modified to incorporate a pilot study. The current amendment is to incorporate the changes that were made in the pilot to the main study.

3) **Objectives**

Hispanic adolescents in the U.S. experience significant health disparities, particularly as it relates to drug use and STIs, including HIV/AIDS. Familias Unidas, the proposed prevention intervention for this study, is a Hispanic-specific, parent-centered intervention found to be efficacious in preventing and reducing drug use and HIV sexual risk behaviors (Prado et al., 2007; 2011; Pantin et al., 2009). To date, it has been exclusively delivered face-to-face in school settings. The proposed study is an Internet adaptation of Familias Unidas, “eHealth Familias Unidas”, in which the intervention is delivered via a website and Internet communication technology and the families are recruited in the pediatric primary care setting. Pediatric staff and research team members, including nurse assistants and mental health professionals, will implement eHealth Familias Unidas in pediatric primary care clinics. The purpose of the study is to test the relative effectiveness of a Hispanic-specific eHealth intervention in preventing and reducing drug use, sexual risk behaviors, and STIs among Hispanic youth in primary care.

The hypotheses of the proposed study are:

**H1a:** eHealth Familias Unidas Primary Care will be effective, relative to prevention as usual, in reducing the frequency of (past 90-day) drug use in Hispanic adolescents over time.

**H1b:** eHealth Familias Unidas Primary Care will be effective, relative to prevention as usual, in reducing the frequency of (past 90-day) unprotected sex in Hispanic adolescents over time.

**H1c:** eHealth Familias Unidas Primary Care will be effective, relative to prevention as usual, in reducing STI incidence (specifically, the incidence of gonorrhea and chlamydia).

**H2a:** Intervention effects on frequency of drug use will be partially mediated by improvements in family functioning over time.

**H2b:** Intervention effects on frequency of unprotected sex will be partially mediated by improvements in family functioning over time.

**H2c:** Intervention effects on STI incidence will be partially mediated by improvements in family functioning and decreases in unprotected sex over time.

#### 4) **Background**

##### (a) Significance and Gaps in Current Knowledge

Hispanic youth are disproportionately affected by certain health behaviors and conditions, such as drug use, sexual risk behaviors, and STIs, compared to their African American and non-Hispanic White counterparts. Fortunately, in multiple reviews of the literature specifically examining efficacious preventive interventions for Hispanic youth, family-based interventions have been found among the most efficacious. In fact, approximately three quarters of evidence-based preventive interventions for Hispanic youth are family-based interventions, highlighting the importance of targeting the family as the change agent. Familias Unidas is an example of an evidence-based family-based preventive intervention found to be efficacious in preventing/reducing drug use, unprotected sexual behavior, and self-reported STIs. An Internet adaptation of Familias Unidas, “eHealth Familias Unidas”, was recently developed and tested for use in the school setting, but also for use in pediatric primary care settings. Identifying novel contexts, such as primary care settings, to implement cost effective evidence-based drug use and sexual risk behavior preventive interventions, such as eHealth interventions, for Hispanic adolescents is an urgent public health issue (Bustamante et al., 2010).

Currently there are no efficacious or effective, Hispanic-specific, Internet-based drug use and sexual risk behavior preventive interventions in primary or pediatric settings despite the fact that: (1) EHealth interventions have been found to impact a number of outcomes, including family functioning, drug use, and unsafe sexual behavior; (2) more than three in four Hispanics report using the Internet (Lopez, Gonzalez-Barrera & Patten, 2013); (3) preventive interventions in primary care settings have shown promising results for alcohol, smoking cessation, and drug use among youth and adults; and, (4) The Patient Protection and Affordable Care Act contains several strategic initiatives aimed at increasing Hispanics’ use of primary care services, including pediatric services, and has expanded access to health insurance for 4.2 million uninsured children (10-19 years old), 35% of whom were Hispanic (Pilkey et al., 2013; Russell & Davenport, 2010).

Thus, the proposed research is significant in that the study has the potential to capitalize on Hispanics’ projected increased use of pediatric care, an under used context and novel approach to drug use and sexual risk behavior preventive interventions. We have chosen diverse primary care pediatric settings (academic practice, public health clinic, mobile clinic, private practice) likely to see expanded services for Hispanics, so that our findings can be immediately disseminated to a broader range of settings. Notably, the 2009 IOM report on Preventing Mental, Emotional, and Behavioral Disorders among Young People, stated that although there are a wide range of preventive intervention programs with evidence of efficacy, there is a need to disseminate these programs more widely in innovative

settings and to increase the understanding of the effective dissemination of these prevention programs.

(b) Relevant Prior Experience and Preliminary Results

Below we describe the main findings of three published face-to-face Familias Unidas efficacy trials in school settings, a completed face-to-face Familias Unidas effectiveness trial in a school setting, an efficacy eHealth Familias Unidas trial in a school setting, and a feasibility/acceptability study of eHealth Familias Unidas in a primary care setting. Because the completed efficacy trials have been published, the description of these studies is brief.

First Efficacy Study of Familias Unidas in a School Setting. Prado and colleagues evaluated the efficacy of Familias Unidas in preventing adolescent drug use, cigarette use, alcohol use, and unprotected sexual behavior, relative to (1) an HIV preventive intervention and (2) a cardiovascular preventive intervention. Participants ( $n = 266$ , mean age = 13.4,  $SD = .68$ ) were assessed at baseline, randomized, and reassessed at 6, 12, 24, and 36 months post baseline. Familias Unidas was efficacious, relative to the cardiovascular intervention in reducing past 90-day illicit drug use ( $z = 2.02$ ,  $p < .05$ ), efficacious relative to both the HIV intervention ( $z = 3.25$ ,  $p < .002$ ) and the cardiovascular intervention ( $z = 2.66$ ,  $p < .008$ ) in reducing past 90-day cigarette use, and in reducing unprotected sexual behavior at last sexual intercourse ( $X^2(1) = 3.87$ ,  $p < .05$ ). The effects of Familias Unidas were partially mediated by improvements in family functioning. Finally, post-hoc analyses also showed that the incidence of (self-reported) STIs in Familias Unidas was significantly lower than for adolescents in either of the two control conditions (Fisher's Exact  $p$ -value = .05).

Second efficacy study of Familias Unidas in a School Setting. Pantin and colleagues evaluated the efficacy of Familias Unidas in preventing adolescent substance use as well as unprotected sexual behavior, relative to prevention as usual in a sample of behavior problem youth. 213 participants (mean age =14.3,  $SD =0.7$ ) and their primary caregivers were enrolled. Participants were assessed at baseline, randomized, and reassessed at 6, 18, and 30 months post baseline. Analyses showed a significant difference in past 30-day substance use ( $b=0.53$ ,  $z =2.42$ ,  $p < .02$ ;  $d =0.25$ ) and in the frequency of condom use ( $b= -0.306$ ,  $z = -2.214$ ,  $p<.03$ ;  $d =0.30$ ) between Familias Unidas and prevention as usual.

Third efficacy study of Face-to-Face Familias Unidas in a School Setting. Prado and colleagues evaluated the efficacy of Familias Unidas in reducing past-90 day illicit drug use and unprotected sexual behavior, relative to prevention as usual, among adjudicated Hispanic youth. 212 (mean age = 14.6,  $SD = 1.36$ ) juveniles and their primary caregivers were assessed at baseline and reassessed at 6 and 12 months post baseline. The results showed that Familias Unidas was efficacious, relative to

prevention as usual, in improving family functioning ( $b=.28$ ,  $p=0.02$ ), increasing past 90-day condom use ( $b=0.68$ ,  $OR = 1.97$ ,  $p=0.015$ ), and in reducing past 90-day illicit drug use ( $b=-0.72$ ,  $p=0.04$ ).

Face-to-Face Effectiveness Study of Familias Unidas in a School Setting. Prado and colleagues (under review) evaluated the effectiveness of face-to-face Familias Unidas in reducing the frequency of drug use, alcohol use, and unprotected sexual behavior, relative to prevention as usual, among 746 Hispanic youth (mean age = 13.9,  $SD = 0.67$ ) recruited from 18 middle schools. School counselors were trained to deliver Familias Unidas. Participants were assessed at baseline and reassessed at 6, 18 and 30 months post baseline. The results showed that there was, a significant intervention effect on drug use frequency ( $b = -0.201$ ,  $p < 0.001$ ,  $d = 0.265$ ). Among participants who reported being sexually active ( $n = 130$ ) in the 90 days prior to any of the assessments, the analyses showed significant differences between Familias Unidas and Prevention as Usual in past 90 day condom use frequency ( $b = 0.093$ ,  $p = .008$ ,  $d = 0.98$ ). At 6 months post-baseline, parents of youth randomized to Familias Unidas reported significantly higher levels of family functioning relative to parents of youth randomized to Prevention as Usual ( $b = 0.148$ ,  $p = 0.014$ ,  $d = 0.47$ )

Efficacy Study of eHealth Familias Unidas in School Settings. In an ongoing randomized trial, Estrada, Prado and colleagues are investigating the efficacy of an eHealth adaptation of Familias Unidas in reducing drug use and unprotected sex relative to prevention as usual among 256 Hispanic youth (CDC Grant # U01PS003316; Estrada, PI; Prado, Mentor). eHealth Familias Unidas was developed utilizing the intervention manual from the face-to-face Familias Unidas intervention, and an independent rater determined that 91% of the components of face-to-face Familias Unidas were present in the eHealth adaptation. Details on eHealth Familias Unidas and its components are described under “eHealth Familias Unidas Primary Care.”

The 6 month follow up has been completed for this study and preliminary results indicate that eHealth Familias Unidas in schools has high family engagement (mean number of sessions = 8.4 out of 12;  $SD = 4.6$ ) and is having a significant effect on parent-adolescent communication ( $b = -5.11$ ;  $p = .05$ ; see Figure below), the intervention’s mediator. Results on drug use and unsafe sexual behavior are in the expected direction and of similar effect size as in previous Familias Unidas trials (effect sizes = 0.79 and 0.40 for drug use and unsafe sex, respectively) at 6 month follow up. It is worth noting that in all of our intervention trials, changes in parent-adolescent communication were observed between the baseline and 6-month follow up assessment, and those changes in turn significantly impacted the distal outcomes, drug use and unsafe sex, at subsequent time points.

Pilot Study of eHealth Familias Unidas in Primary Care. Prado and colleagues evaluated the feasibility and acceptability of delivering eHealth Familias Unidas

Primary Care in a universal sample of Hispanic youth. Study staff recruited 48 Hispanic youth and their primary caregivers from four sites: a mobile clinic, an academic pediatric clinic, a public health clinic (Jackson Memorial Hospital), and a private practice clinic (Kidstown Pediatrics, LLC). The pilot study's aim was not to assess efficacy or effectiveness but rather to assess the: 1) feasibility of recruiting families from pediatric care clinics, 2) feasibility of having pediatric clinic personnel deliver eHealth Familias Unidas, and 3) acceptability of the intervention from both the participants' and clinic staff's perspective.

To recruit study participants, our study team interfaced with pediatric care staff. Clinic staff let the study team know when (date and time) Hispanic youth between the ages of 12 - 16 (the target age range for the proposed study) and their caregivers were scheduled. During those times, a recruiter/assessor was present to recruit, consent and screen the family. Parent-child dyads were eligible to participate if they self-identified as Hispanic, the youth was between the ages of 12 - 16, both youth and parent were willing to participate, the parent had Internet access, and the family did not have plans of moving from South Florida within the next year.

Individual in-depth qualitative interviews with clinic personnel and intervention facilitators. In-depth qualitative interviews with pediatric clinic personnel and e-Health Familias Unidas Primary Care facilitators were conducted. These interviews had two aims: 1) Receive feedback with regard to clinic personnel and facilitator experience in delivering eHealth Familias Unidas Primary Care and 2) to explore possible implementation and dissemination barriers. Clinic personnel (i.e., clinic managers, physicians) and facilitators were invited to participate in one-on-one interviews. Participants were recruited via email and interviewed for 30-60 minutes.

## 5) **Inclusion and Exclusion Criteria**

### (a) Participants

The baseline sample will consist of 456 Hispanic female and male adolescents and their primary caregivers recruited from one of the pediatric care clinics.

### (b) Inclusion criteria

- i) Female and male adolescents of Hispanic immigrant origin, defined by at least one parent born in a Spanish speaking country of the Americas. Parent must understand Spanish given that parent sessions are delivered in this language. In past studies, over 99% of all Hispanic parents understood Spanish.
- ii) Adolescent between the ages of 12 – 16 years
- iii) Adolescent living with an adult primary caregiver who is willing to participate
- iv) Families must have broadband Internet access on a device, including (but not limited to) a smartphone, iPad, tablet, computer at their home or other location (e.g., school, library, etc.)

(c) Exclusion Criteria

- i) Families reporting plans to move out of the South Florida area during the study.
- ii) Families reporting that adolescent has been diagnosed with a developmental delay.

(d) Screening for Eligibility

Clinic staff will let the research team know between a day and two weeks before whether they have Hispanic youth ages 12 - 16 scheduled to come into the clinic and if so at what time. When the potentially eligible family checks in, the family will be moved to a small office space where the assessor and/or facilitator will be. The assessor and/or facilitator will screen parent and youth (separately) by asking parents pre-defined screening questions (i.e. the inclusion criteria). If the participant declines at any moment, verbal consent or assent will be asked for the participant to complete a brief questionnaire.

Additionally, we will do the following:

a) UM/Jackson patients (parents only) will receive a letter (hand delivered, e-mail and/or mail) from their physicians informing them about the study. This letter will inform participants that they will be receiving a call from research study personnel to see if they are interested in participating. Additionally, a phone number will be provided for the potential parent participant to contact research personnel.

b) Research study staff will request permission from each clinic to have access to their scheduling system. On a daily basis, research study personnel will access data on which individuals have a scheduled appointment. No health information will be available to research study staff, only whether there is an appointment scheduled. Study staff will screen these individuals, at the clinic, to see which meet criteria. Study staff will then go to waiting room to recruit those that meet criteria.

**6) Number of Subjects**

456 adolescents, 456 caregivers

**7) Study-Wide Recruitment Methods**

(a) Methods

There will be a pilot of the study's procedures prior to the start of this main trial. This pilot study will take place in January of 2017. There will be approximately a total of 12 families asked to participate from four different sites: UHealth Pediatrics at the

Professional Arts Center, University of Miami Pediatric Mobile Clinic, Ambulatory Care Center West Pediatrics at Jackson Memorial Hospital, S. Florida Pediatrics, Kidstown Pediatrics, LLC, UHealth at Kendall, Nicklaus Children's Hospital, Borinquen Medical Centers, and Primecare Family Centers. Participants will be asked to test out different components of the intervention such as the electronic consent/assent forms, surveys, and the website. They will be asked to attend one online meeting with their family and a facilitator as well as watch the first group session online. Finally, adolescents will be asked to pilot test the procedures for the STI test sample. Parents will be compensated \$30 cash for their time, and adolescents will be compensated \$20 cash for the completion of both the survey and urine sample.

All recruitment, assessment, and intervention activities will be conducted exclusively by approved study staff.

To recruit participants, our research staff will interface with the clinic staff from each of the pediatric clinics. Prior to recruitment (e.g. a week or day before), clinic staff will let the research team know whether they have Hispanic youth ages 12 - 16 scheduled for a clinic appointment and, if so, at what time. If so, the assessor or facilitator will arrive to the clinic preceding the potential participant's appointment (in case the target youth and his/her primary caregiver arrive early).

Additionally, we will do the following:

a) UM/Jackson patients (parents only) will receive a letter (e-mail and/or mail) from their physicians informing them about the study. This letter will inform participants that they will be receiving a call from research study personnel to see if they are interested in participating. Additionally, a phone number will be provided for the potential parent participant to contact research personnel.

b) Research study staff will request permission from each clinic to have access to their scheduling system. On a daily basis, research study personnel will access data on which individuals have a scheduled appointment. No health information will be available to research study staff, only whether there is an appointment scheduled. Study staff will screen these individuals, at the clinic, to see which meet criteria. Study staff will then go to waiting room to recruit those that meet criteria.

When the potential participating family checks in, clinic staff will briefly introduce the study and ask if the family would like more information. If so, the family will be moved to a small office space or clinical exam room where the assessor and/or facilitator will be at. In the office space or exam room, participants will be asked whether they are interested in learning more about a study to prevent HIV and substance use among Hispanic youth. Parents and adolescents will be screened for eligibility, and if the individual states that he/she meets the criteria and would like to learn more information, the recruitment process will continue. If the family declines, they will be asked to complete a brief questionnaire (detailed below). If the family



would like more information, Familias Unidas facilitators will explain the study in detail to parents and youth and have interested participants sign the informed consent (parents) and informed assent (adolescents). To avoid coercion of the youth by the parent, adolescent and parents will each be in different rooms when they sign consent and assent to ensure that the adolescent has total privacy. In case the adolescent does not want to sign, the family will be told they did not meet one or more of the inclusion/exclusion criteria but the facilitator will not reveal to the parent that the child did not sign (to avoid any consequences to the child). Participants who are not interested in participating in the study will still be asked to provide the following information:

Adolescents: age, gender, lifetime drug use, lifetime sexual activity, grade, nationality and time in the US

Parents: age, gender, income, level of education, nationality and time in the US

This collected information from non-participants will not contain any names, therefore, it will be de-identified. We will attempt to collect this information from participants who say no at initial contact and from participants who go through the screening and then refuse to participate. To collect this information, we will request verbal consent and assent. We are requesting permission to only utilize a verbal consent and assent because it is unlikely that participants who do not wish to participate in the study will answer these questions if they have to identify themselves by signing a consent form.

For participating families, once the family completes the consent/assent, they complete the baseline assessment. Once the baseline assessment is complete, adolescent will take an STI test, and the family is blindly randomized to one of the two study conditions, they, the primary caregiver and adolescent, will be compensated for their time.

Families that are interested in participating in the study, but do not have time to complete consent/assent and baseline assessment in the clinic will be offered the option to be visited at home. If the family agrees, a research team member will visit the family during an arranged time to complete the consent/assent, baseline assessment and urine test with the adolescent.

Total time to recruit, including baseline assessment, randomization and compensation, will be approximately 45 minutes, but it may vary from family to family depending on whether or not the family needs more or less time to comprehend the study procedures. At each of the five assessment time points, baseline, 6, 12, 24, 36 months, the parent will be compensated, \$40, \$45, \$50, \$55 and \$60, respectively. At each of the assessment time points, baseline, 6, 12, 24, 36

months, the adolescent will be compensated with \$20 cash for completing both the survey and the STI test.

(b) **Materials**

Posters will be hung at each of the primary care offices. The poster will be an enlarged version of the flyer.

8) **Study Timelines**

(a) The duration of an individual subject's participation in the study

4 years

(b) The duration anticipated to enroll all study subjects

2 years

(c) The estimated date for the investigators to complete this study

February 2022

9) **Study Endpoints**

(a) Study endpoints

i) Primary:

- Frequency of (past 90-day) drug use in Hispanic adolescents over time.
- Frequency of (past 90-day) unprotected sex in Hispanic adolescents over time.
- STI incidence (specifically, the incidence of gonorrhea and chlamydia).

ii) Secondary:

- Improvements in family functioning over time (e.g. parent-adolescent communication, parental monitoring of peers).
- Frequency of unprotected sex will be partially mediated by improvements in family functioning over time.
- Reduction of STI incidence will be partially mediated by improvements in family functioning and decreases in unprotected sex over time.

(b) Safety endpoints

Not applicable.

10) **Procedures Involved**

(a) Study Design

This study tests the effectiveness of eHealth Familias Unidas Primary Care in preventing drug use, unprotected sexual behavior, and STIs in a universal sample of Hispanic youth, this study will use a randomized trial design with two levels of intervention (eHealth Familias Unidas Primary Care and prevention as usual) as the between subjects factor with five repeated measures assessments at baseline, 6, 12, 24, and 36 months post baseline as the within subject factor.

Once both primary care giver and adolescent have completed the consent/assent, they will complete the baseline assessment electronically. Once the baseline assessment is complete, they will be randomized to one of the two conditions: eHealth Familias Unidas Primary Care (experimental prevention as usual (control) Condition. Please see attached for consent/assent forms (in English and Spanish). All consent forms will be completed electronically. All confidential study participant information will be stored electronically in secure University of Miami systems.

i) eHealth Familias Unidas Primary Care

eHealth Familias Unidas Primary Care is an adaptation of the face-to-face version of Familias Unidas. As with face-to-face Familias Unidas, eHealth Familias Unidas Primary Care aims to prevent drug use, sexual risk behaviors, and STIs by improving family functioning (including communication between parents and youth). eHealth Familias Unidas Primary Care consists of 12 sessions total (8 mock group sessions and 4 virtual family sessions). The mock group sessions are approximately 30 minutes in duration and were designed to recreate the content and process of the eight parent groups of the evidence-based face-to-face Familias Unidas intervention. The content was recreated under the context of a daytime talk show, a culturally centric device, in which real-life Hispanic parents were cast as the guests on the talk show and led discussions about the same topics that would be seen by a parent in the face-to-face intervention. As in the face-to-face intervention, the parent actors processed situations commonly experienced by parents of adolescent children by sharing personal anecdotes and role-playing new skills. A telenovela series was also incorporated into the mock group sessions to facilitate processing around the common topics, e.g. parent-adolescent communication, adolescent risk behavior, and behavior management. Each mock group session features one 10-15 minute telenovela, whose theme corresponds with the session topic. The sessions also include interactive exercises which are used to reinforce session content and to adapt the participatory learning strategy used in the face-to-face intervention. The type of interactive exercise varies from session to session and includes true/false questions, multiple-choice questions, and point-and-click responses. Parents are provided with

instant feedback regarding their responses and all on-screen text (e.g. instructions, response choices, answer summaries) is paired with audio to reduce literacy-related barriers. The intervention facilitators are able to review parents' responses and use this information to facilitate discussion between parents and adolescents during the online family sessions.

The four virtual family sessions will be conducted by a trained study team member or pediatric staff member (elsewhere, "Facilitator") according to the same protocol used in the face-to-face Familias Unidas intervention. However, eHealth Familias Unidas will use online video conferencing technologies to virtually recreate the therapeutic environment of the family session. The sessions are delivered via the Internet utilizing webcams and a videoconferencing software called VSee. eHealth Familias Unidas Primary Care facilitators will be responsible for scheduling and delivering the four online family sessions with each of their families. The online family sessions will provide parents the opportunity to practice with their adolescent the skills that they learned in the mock parent group sessions. The content of each of these four family sessions is identical to that of face-to-face Familias Unidas. Virtual family sessions will be conducted in Spanish and/or English so to accommodate the language preferences of the parent and adolescent participants of each family session. Pending parent and adolescent consent and assent, all virtual family sessions will be video-recorded via VSee. All recorded sessions will be stored in secure University of Miami servers and will be labeled with the family's case ID. The recordings will only be used for purposes of clinical supervision, research and training—provided participant consent/assent.

A log-in procedure accessed through the Familias Unidas website will serve as the mechanism by which to ensure secure access and confidentiality for participants. Each participant will be assigned a unique log-in name and password, which will provide them access to the eHealth Familias Unidas Primary Care session. The log-in procedure will also facilitate the close monitoring of participants, particularly as it relates to session participation rates. Specifically, the log-in procedure will be utilized to record who (i.e., which participant), when (i.e., day/time), how long (e.g., time of session attendance), and for what purpose (e.g., which session) the intervention website was accessed.

Our information technology team employs the latest technology to ensure security and confidentiality of participants, including but not limited to data error checking through forms, filtering output, and the use of encryption. Server Port Hardening will be implemented to keep

the web server safe from intrusion. Additionally, a Secure Socket Layer Encryption certificate will be issued to help prevent Internet fraud. The implementation of SSLs (i.e., cryptographic protocols) aims to enhance security over the Internet. IT will conduct stringent testing of web applications prior to the implementation of eHealth Familias Unidas Primary Care to prevent any exploits from occurring and to ensure the confidentiality of participants.

ii) Control Condition

Participants randomized to the control condition continue prevention as usual. These participants will not be receiving any services from our staff. These participants will only be asked to complete a survey at each of the 5 time points: when they first enroll, and at 6, 12, 24, and 36 months. The adolescent will also be asked to provide a sample for an STI test during each of these time points.

(b) Assessments

After the intervention is complete, assessors will call the families to return to complete follow up assessments. The follow up assessments will occur on the University of Miami Miller School of Medicine Campus, at the clinic sites or at the homes of the participants. The follow up assessments collect the same data as the baseline assessment. All measures will be self-report and completed using survey software provided by the study team

(c) Data Collection

Demographics. A demographics form developed by the creators of Familias Unidas will be administered to caregivers and youth in order to collect information on contact information, age, date/place of birth, number of years residing in the U.S., parents' marital status, and family income.

Family functioning (reported by both youth and parents) consists of parental investment in the adolescent and parent-adolescent communication. Parental investment in the adolescent will be assessed using 1) the Parenting Practices (Loeber et al., 1999), and 2) the Family Relations Scale (Tolan et al., 1997). Two subscales of the Parenting Practices: (a) extent of parental involvement (20 items) and (b) positive parenting (9 items) will be used to assess parental investment. Cronbach's alpha for the two (parent reported) subscales were .83 and .78, respectively. Cronbach's alpha for the two (adolescent reported) subscales were .86 and .85, respectively. The Family Relations Scale assesses the amount of social support the adolescent receives from the parent (6 items) (Tolan et al., 1997). Cronbach's alpha for this subscale is .73 (parents) and .70 (youth).

Communication will be assessed via the Parent-Adolescent Communication Scale (Barnes & Olson, 1985), which assesses the quality and content of communication between parents and youth. Youth report on the quality and content of communication they perceive with their parent. In the parent version, parents report on their perception of the quality and content of their communication with their youth. Cronbach's alpha coefficients for this measure was .85 (parents) and .93 (youth).

Youth's own sexual risk behaviors will be assessed using a 22-item instrument from Jemmott, Jemmott, and Fong (1998). This self-report measure will be used to document the number of times youth report having sex (oral, vaginal, and anal) in their lifetime and in the past 3 months. This instrument is also used to document the number of times youth has been exposed to situations of high risk during sexual intercourse (e.g. having unprotected sex and/or being under the influence of alcohol or drugs while having sex). This measure also asks participants whether they have sex with males and/or females.

Youth's and parents' own drug use will be measured using items used as part of the Monitoring the Future survey (Johnston et al., 2010). This 47-item self-report instrument assesses lifetime drug use and the frequency of drug use (by type of drug) in the 3 months prior to assessment. Additionally, questions regarding the use of e-cigarettes and hookahs for lifetime use, the previous 90 days and previous 30 days will be asked. CRAFFT (10 items) will assess the consequences of alcohol and drug use. Finally, three questions regarding second hand smoking will be asked:

*How much do you think you are exposed to tobacco smoke at home?"  
(select one: not at all, somewhat, moderately, a lot, extremely  
How much do you think you are exposed to tobacco smoke outside of  
home?" (select one: not at all, somewhat, moderately, a lot, extremely  
How many years in total did you live in the same household with someone  
else who smoked tobacco products?"*

The Klein Sexual Orientation measure (adolescents only, 8 items) will be used to assess adolescent sexual orientation and preferences.

Vancouver Index of Acculturation (VIA; parents and adolescents, 20 items) will be used to assess acculturation and practices.

The CES-D (parents and adolescents, 20 items) will be used to assess symptoms of depression.

ACES (for parents only, 17 questions) will assess adverse events before the age of 18 for parents

The CASA (for parent and adolescent, 8 items) will assess use of community services.

Four items (adolescent only) have been incorporated to evaluate experiences with bullying.

The Revised Behavior Problem Checklist (RBPC; parent only, 55 items): the externalizing subscales of the RBPC will be used to assess adolescent problem behaviors from the parent perspective.

The externalizing subscales of the Youth Self Report (YSR; adolescent only, 32 items) will be used to evaluate adolescent problem behaviors from the adolescent perspective.

Health related quality of life (QOL; parent and adolescent, six items) will be used to examine physical, mental and emotional health.

CRAFFT (adolescent, 10 items): assesses the consequences of alcohol and drug use.

Five questions have been created to assess participant understanding of the consent form.

In addition to the self-report measures described above, we will measure gonorrhea and chlamydia by a real-time PCR assay for the direct, qualitative detection of the plasmid DNA of *Chlamydia trachomatis* and the genomic DNA of *Neisseria gonorrhoea* which is currently being used in clinical practice and clinical trials at our institution. This assay has shown high sensitivity and specificity for the detection of both organisms in asymptomatic and symptomatic patients. Youth who test positive for an STI will be referred to treatment. Youth will also be encouraged to refer sex partners for treatment. The county health department will be notified of reportable STIs. For analyses, sexually transmitted infection incidence will be defined as a positive laboratory test result for a new chlamydia or gonorrhea infection at any of the five assessment time points. Previous studies with ethnic minority youth have demonstrated feasibility and a high acceptance rate with respect to the collection of biological markers for determining STI incidence.

We would also like to collect data from clinic facilitators, clinic leaders, and physicians to assess organizational level factors and attitudes towards evidence-based interventions. To do this, we will use the below measures:

*Attitudes Towards Evidence-Based Practice Scale (EBP; facilitator; 15 items): this measure will be administered to facilitators to assess their views on evidence-based practices.*

*Multifactor Leadership Questionnaire (clinic leaders/physician, 21 items): this measure will be administered to clinic leaders/physicians to assess transformational and transactional leadership behavior.*

*Implementation Leadership Scale (ILS; Clinic leaders/physicians, 11 items): this measure assesses the degree to which organizational leaders support their staff in the implementation of evidence-based interventions*

*Implementation Climate Scale (clinic leaders/physician, 18 items): assesses the level of a strategic organizational climate within an organization.*

#### **11) Data and Specimen Banking\***

For STI measurement, a urine sample will be collected from the adolescent at each time point. Both the adolescent and the research assessor shall be present (at the same time) during the procedures outlined in this section. The procedures for the data to be stored or associated with each specimen are described below:

- (a) Both the adolescent and the research assessor shall keep the adolescent's urine specimen in view at all times before the specimen is sealed and labeled. If any of the specimen is transferred to another container, the research assessor shall ask the adolescent to observe the transfer and sealing of the container with a tamper-evident seal.
- (b) The research assessor shall place an identification label securely on each container. The label must contain the date, the adolescent's specimen number, and the adolescent's code number as the identifying information. The research assessor shall apply a tamper-evident seal on each container if it is separate from the label. The specimen bottle must be securely sealed to prevent undetected tampering.
- (c) The adolescent shall initial the identification label(s) on the specimen bottle(s) with his or her case ID in order to certify that the specimen was collected from him or her.
- (d) The specimen and chain-of-custody forms must be packaged for transfer to Quest laboratories. If the specimens are not immediately prepared for transfer, they must be appropriately safeguarded during temporary storage. The collected urine will be picked up by Quest laboratories a minimum of once per week.
- (e) While any part of the chain-of-custody procedures is being performed, the specimens and custody documents must be under the control of the involved research assessor. The assessor may not leave the collection site during the interval between presentation of the specimen by the adolescent and securing of the specimens with identifying labels bearing



the adolescent's specimen identification numbers and Case ID. If the involved assessor momentarily leaves his or her workstation, the sealed specimens must be secured or taken with him or her. If the assessor is leaving for an extended period of time, the specimens must be packaged for transfer to Quest laboratories and secured before the assessor leaves the collection site.

- (f) The specimen(s) sealed in a shipping container must be immediately transferred, appropriately safeguarded during temporary storage, or kept under the personal control of an authorized individual until transferred.
- (g) The research assessor shall ensure that a custody-and-control form is packaged with its associated urine specimen bottle.
- (h)

## 12) Data Management\*

### (a) Data Analysis Plan and Power Analysis

**H1a:** *eHealth Familias Unidas Primary Care will be effective, relative to Care as Usual, in reducing the frequency of (past 90-day) drug use in Hispanic adolescents over time.*

This hypothesis will be analyzed using Latent Growth Modeling (LGM). Growth models can be expressed in terms that are identical to models using random coefficients regression, mixed models or multi-level models, where the first level fits each response in time to an individual-level growth model. The second level represents the condition effect on the slope of drug use. LGM analyses will test for differences in trajectories of drug use over the 5 assessment time points among the 2 conditions. As recommended by Raudenbush and Bryk, we will use 2-level analysis to determine whether the mean trajectories of drug use for eHealth Familias Unidas Primary Care and prevention as usual differ significantly over time. Data analysis for this hypothesis and all others will be conducted using Mplus (v 7.2).

Power. Mplus Monte Carlo simulation with 10000 replications was used to calculate the power for this hypothesis using a latent growth curve model framework with one covariate (i.e., condition assignment) and missing data. With 5 time points (0, 6, 12, 24 and 36 months) and assuming a 5% attrition rate at each assessment (also assuming equal sample size across both conditions), with 228 cases in each condition at baseline (or 185 at the final assessment timepoint in each condition), we have 80% power to detect a regression coefficient equal to 0.09 (effect size = 0.3) in the regression of the slope growth factor on intervention condition. This is considered slightly over a small (0.2) effect size.

**H1b:** *eHealth Familias Unidas Primary Care will be effective, relative to prevention as usual, in reducing the frequency of (past 90-day) unprotected sex in Hispanic adolescents over time.*

The analytic plan and power analysis for this hypothesis are similar to that of H1a.

**H1c:** *eHealth Familias Unidas Primary Care will be effective, relative to prevention as usual, in reducing STI incidence (specifically, the incidence of gonorrhea and chlamydia).*

This hypothesis will be analyzed using a univariate logistic regression for the binary outcome, new diagnoses of STIs (Yes/No). STI incidence will be defined as a positive laboratory test result for a new chlamydia or gonorrhea infection at any of the four follow up assessment timepoints. In the analysis for this hypothesis, condition will predict STI diagnosis. The test of the hypothesis will be based on a Wald test comparing the intervention regression coefficient to its standard error. Additionally, the time of STI diagnosis will be included as a covariate in the logistic regression to test the robustness of the intervention's effect.

**Power.** According to CDC national statistics, the annual STI incidence rate is 3.16% for Hispanic adolescents aged 15 to 19. Thus, we expect the 3-year STI incidence rate in the control group to be approximately 9.2%. Using a one-sided Z test with pooled variance to test the difference between two independent proportions (assuming the same 5% attrition rate at each assessment timepoint), the study has over 80% power to detect a difference of 6.1% in STI incidence between the two conditions. This difference in proportions translates to an effect size of Cohen's  $h = 0.26$ , considered a small ( $h = 0.2$ ) to medium ( $h = 0.5$ ) effect size, according to Cohen (1988).

**H2a:** *Intervention effects on frequency of drug use will be partially mediated by improvements in family functioning over time.*

To test for mediation, we will use the "product of coefficients" test described by MacKinnon and colleagues, which is based on the distribution of the indirect effect of the intervention through the mediator (Cohen, 1988). This procedure tests whether the product of the coefficients from the intervention to the mediator (a) and from the mediator to the outcome (b) is significantly different from zero. Specifically, we will estimate paths between intervention and family functioning (a), and between family functioning and drug use (b). Because we have five time points, our first mediation analyses will fit bivariate growth curves for both family functioning and drug use and examine the role of the (latent) slope of family functioning on the slope of

drug use. The product of the two pathways  $(a) \times (b)$  is the indirect effect of eHealth Familias Unidas Primary Care to drug use through the family functioning trajectory. As noted above, we will be testing whether the product  $(a) \times (b)$  is statistically significantly different from zero, by comparing the observed value of  $(a) \times (b)$  to the empirical distribution calculated using the bias-corrected bootstrap. In addition to this long-term developmental mediation model, we will also test if the initial changes in family functioning from baseline to the 6 month follow-up mediate the effect of intervention on drug use trajectory. Our team has expertise in conducting mediational analyses in multilevel models.

Power. Mplus Monte Carlo simulation with 10000 replications was used to calculate the power for this hypothesis using a mediation model framework. With a final sample size of 370 (assuming 5% attrition rate at each assessment timepoint), we have 80% power to uncover a significant mediating effect when the regression coefficient of pathways 'a' is approximately -0.36 and 'b' is approximately -0.18 (i.e.,  $R^2$  effect size were 0.033 for the relationship between X and M (i.e., path 'a;') and M and Y (i.e., path 'b'), which is considered a small effect (Cohen, 1988).

***H2b: Intervention effects on frequency of unprotected sex will be partially mediated by improvements in family functioning over time.***

The analytic plan and power analysis for this hypothesis are similar to that of H1b.

***H2c: Intervention effects on STI incidence will be partially mediated by improvements in family functioning and decreases in unprotected sex over time.***

We will use MacKinnon's method<sup>103</sup> described in H1b with the exception that the outcome for this hypothesis is binary. The Weighted Least Squares Means and Variance adjusted (WLSMV) estimator in Mplus will be used to estimate the indirect effect. With WLSMV, a continuous latent response variable ( $y^*$ ) underlying the observed dichotomous variable is used to test for the mediated or indirect effect.

Power. We aimed to identify the minimal detectable regression coefficient for the mediator based on Vittinghoff and colleagues' methodology. The results show that we have 80% power to detect a mediating effect if the logistic regression coefficient for the mediator is 0.63, which is equal to an OR of 1.88, corresponding to an effect size of  $d = 0.35$ . According to Cohen, this is considered a small ( $d = 0.2$ ) to medium ( $d = 0.5$ ) effect size.

(b) Secure Data and Quality Control

All adolescent and parent self-report measures will be administered electronically through a tablet.

Data will be uploaded weekly in a database housed on a server maintained and secured by the University of Miami Department of Public Health Sciences. The server is password protected as well as protected by a firewall. The Principal Investigator will have access to the data electronically on his password protected laptop. His designees (i.e. Project Coordinator and Statistician) will also have access to electronically stored data. Principal Investigator and his team are on the tenth floor of the Clinical Research Center at 1120 N.W. 14th Street, Miami, FL 33136.

We will also collect identifying data (e.g. participant name and contact information). This data will be collected electronically and stored in secure University of Miami systems. We will use a record system in which all participant records are filed numerically by case number, with no identifying information attached to the outcome data. A master sheet, with individual names and their respective code numbers will be kept electronically and accessed only under the supervision of the Principal Investigator. No one other than the Principal Investigator, the Project Coordinator, and approved study staff will have access to records identifying subjects' names at any time. Only the Principal Investigator and the Project Coordinator (under the supervision of the Principal Investigator) will have access to both the participants' identifying information and their assessment data.

(c) Data and Specimen

If both the parent and adolescent have agreed to these tests, urine will be collected from adolescent participants to test for gonorrhea and chlamydia. The research assessor will be responsible for properly implementing urine collection procedures, storing and labeling (without identifiers) the collected urine. Urine will be collected from the adolescent in a completely private manner; at no moment will the assessor watch the adolescent collect the urine specimen. The urine will be analyzed by Quest Diagnostics. Detailed procedures are outlined in section 11) Data and Specimen Banking.

**13) Provisions to Monitor the Data to Ensure the Safety of Subjects\***

We do not expect for this study to create more than minimal risk for the participating families. Yet, the study will be monitored by the study investigators and/or sponsors. In addition, a formally constituted Scientific Advisory Board will help monitor the study if additional advice is needed.

#### 14) **Withdrawal of Subjects\***

Participants will be told that this study is completely voluntary and that they have the right not to participate in any intervention procedure. They also can completely withdraw from the study at any time without any negative consequences.

In past studies, we have not had to withdraw subjects. There is potential for withdrawal of subjects if the adolescent is arrested, reports suicidal ideation, or some other extreme adverse event. If a subject is arrested, reports suicidal ideation, or some other extreme adverse event, a qualified study personnel, i.e., the clinical supervisor, may ask them to please withdraw from the study, and if appropriate, refer them to the correct treatment.

According to IRB, if a subject becomes incarcerated while enrolled in a study, all research interactions and interventions with that subject, and the obtaining of identifiable private information about the subject must cease.

#### 15) **Risks to Subjects\***

We do not expect that there will be any negative consequences from participating in this study. However, the sensitive nature of some intervention topics (e.g. sexual behaviors and drug use) may be embarrassing and/or distressing to some participants. It is also possible that they may feel tired or fatigued after answering the questionnaires, or made uncomfortable by the questions that are asked. In addition, STI testing may involve minimal physical discomfort for the adolescent. Being tested for STIs may also cause anxiety for the adolescent and/or parent regardless of the adolescent's test results. Receiving positive results may make the adolescent and/or parent very upset. If the test is negative, there is still the possibility that the adolescent could be infected with an STI and test positive at some time in the future. Also, it is always possible that the test results could be invalid. Should an adolescent test positive for gonorrhea and/or chlamydia, the facilitator, with guidance from the clinical supervisor, a licensed clinical social worker, and principal investigator, will work with the adolescent on how to process disclosure of the positive test result to the parent or legal guardian. If after discussions with the facilitator and clinical supervisor, the adolescent still refuses to disclose (the law in FL does not require parents to be notified of STI infection) because s/he fears negative consequences such as being thrown out of the house or severe family discord, the facilitator and clinical supervisor will work with the adolescent to connect her/him to proper treatment. If an adolescent tests positive for an STI, we are required, by Florida law, to report the result to the Florida Department of Health.

If a parent or adolescent reports elevated levels of depression, or if an adolescent reports incidence of bullying, he or she will be directed to speak with a facilitator for further assessment. If necessary, a referral will be made for additional services.

**16) Potential Benefits to Subjects\***

There may be direct benefits to participating in this study. Depending on which intervention participants are assigned to, adolescents may be less likely to use drugs and engage in risky behaviors such as having sex without a condom. Additionally, depending on the intervention, families may communicate more effectively.

**17) Vulnerable Populations\***

The research involves children under the age of 18. To avoid coercion or undue influence, the adolescents will assent and complete assessments separate from their primary care giver. In case the adolescent does not want to assent, the family will be told they did not meet one or more of the inclusion/exclusion criteria but the facilitator will not reveal to the parent that the child did not assent (to avoid any consequences to the child).

**18) Multi-Site Research\***

Participants will be recruited from South Florida Pediatric Partners, Nicklaus Children's Hospital, Borinquen Medical Centers, Primecare Family Centers, and from Kidstown, which are both located outside the University of Miami.

**19) Community-Based Participatory Research\***

Not applicable.

**20) Sharing of Results with Subjects\***

Youth will be encouraged to refer sex partners for treatment. The county health department will be notified of reportable STIs. The subjects, county health department will be notified via phone call or in-person by a study personnel team member.

**21) Setting**

The research team will identify and recruit potential subjects in nine pediatric clinics. The first site is an academic pediatric clinic within the University of Miami's Health District. This practice serves mostly insured individuals. The second pediatric clinic we have partnered with is a mobile clinic that provides medical care at no charge to uninsured youth. Both of these clinics participated in our pilot feasibility and acceptability study. The third and fourth sites are private pediatric care clinic. These sites serve mostly insured youth. The fifth clinic is Jackson Memorial Medical Center, a general community clinic in Miami. The sixth clinic is UHealth Kendall which is a part of the UM system. The seventh clinic is Nicklaus Children's Hospital, a private

hospital located in Miami-Dade. The eighth and ninth clinics are pediatric centers serving the S. Florida community, Borinquen Medical Centers and Prime Care Family Centers. All recruitment, consent/assent, baseline assessment, and randomization will occur in one of the clinics. The intervention will be delivered via the Internet, thus subjects will most likely be in their homes or a place with Internet capabilities (e.g. school, library) to receive the intervention. The follow up assessments and STI testing will take place on the University of Miami Miller School of Medicine Campus, one of the clinic sites, or the participant's homes.

## 22) Resources Available

### (a) Investigative team Qualifications

Dr. Prado, a first-generation Mexican researcher, is Miller Professor of Public Health Sciences, Director of the Division of Prevention Science and Community Health, and Dean of the Graduate School at the University of Miami. Prado has been conducting research with Hispanic youth for 15 years and has published extensively in this area with over 100 peer-reviewed publications. Prado's research on drug use and sexual risk behavior prevention has been recognized by numerous organizations, including the Society for Prevention Research, the National Hispanic Science Network, and the Society for Research on Adolescence. Throughout his career, Prado has received over \$75 million dollars of extramural funding as either PI, Co-I, or mentor. Prado has presented on his program of research at the National Institutes of Health, the Centers for Disease Control and Prevention, and the Institute of Medicine. Prado has substantial experience coordinating and managing the research activities of major longitudinal randomized clinical trials including recruitment, data collection, quality control, data analysis, and dissemination of study findings. He will be dedicating 30% of his effort to the proposed study.

Other study personnel includes pediatricians. Three of the pediatricians (Drs. Gwyn, Forster, and Ofir) have an academic faculty appointment at the University of Miami and have collaborated on extramurally funded studies and have published. All of the pediatricians have experience working with Hispanic families in their practice.

Other study personnel includes, Dr. Yannine Estrada who has a doctoral degree in Counseling Psychology. She is currently the principal investigator of a mentored cooperative agreement funded by the Centers for Disease Control and Prevention. Estrada has led, in conjunction with senior mentors Prado and Pantin, the Internet adaptation of Familias Unidas. Estrada will be responsible for coordinating the research and research-clinical interface

aspects of the study. She will be responsible for developing the procedures manual for the study; establishing and maintaining project files; maintaining collaborative relationships with the IRB (along with Prado); and developing and implementing quality control assurance procedures. In addition, Estrada will be responsible for making all necessary preparations for the assessments, as well as overseeing the assessors with the data collection across all five years. These tasks include but are not limited to, preparing all equipment, re-training of the assessors, and overseeing the assessments of both youth and parent study participants. Estrada will be responsible for overseeing the assessors in the recruitment and retention of study participants and overseeing the screening of potential study participants. Of important note, is that Estrada is the Research Coordinator/Project Director for a study which has achieved over 95% retention (over 18 months). Estrada will also collaborate with the senior investigative team in planning the outcome analyses and in preparing manuscripts for publication.

Ms. Maria Tapia, Clinical Trainer and Supervisor is a Licensed Clinical Social Worker with over 20 years of experience working with Hispanic families. She is trained in delivering family-based interventions, including Familias Unidas, to Hispanic parents and their youth. Tapia has engaged over 85% of Hispanic parents into the Familias Unidas intervention over the past 10 years. She also has extensive experience training and supervising on the Familias Unidas model. In fact, Tapia has trained over 50 individuals in the Familias Unidas intervention over the past three years. For the proposed study, Tapia will be responsible for training and supervising the pediatric care facilitators in the delivery of the intervention. She will conduct the supervision meetings with the pediatric care facilitators and will help them problem solve potential barriers of intervention engagement and retention. Additionally, Tapia will handle any adverse or serious adverse events that may come up during the assessments.

Assessors will be assigned to each of the pediatric care clinics. Each of the pediatric care clinics will have one pediatric care facilitator (nurse assistant, licensed clinical social worker, mental health counselor). Assessor and/or facilitators will be responsible for screening potential study participants. Assessors are responsible for conducting the parent and youth assessments over the five years. The assessor will also be responsible for scheduling these assessments. Finally, the assessor will also be responsible for maintaining cordial contact in between assessment time points, in order to maximize retention rates at assessments. They will also be responsible for tracking family completion of online sessions and progression through the intervention.



Other study personnel, such as student and research assistants will be trained in study operating procedures, including consent/assent. All study personnel members are CITI trained and are adequately informed about the protocol, research procedures, and their duties and functions. Trainings will be held for study personnel members before the beginning of the study in: protocol, research procedures, and assessments. Study personnel will be asked to role play procedures at the training. If more training is needed, they will be trained again throughout the study. All of the study personnel have been involved in NIH funded studies and are all familiar with the recruitment/study procedures as those being proposed. Regardless of experience, trainings will still be held by the lead clinical supervisor and principal investigator to assure all study personnel members are adherent to the study procedures. Weekly meetings will also be held to discuss study updates, issues or concerns.

(b) Resources Available

The physicians and trained mental health professionals from the clinics are the medical and/or psychological resources for the subjects. We only anticipate that the subjects are in need of these resources, outside of their usual use, if they test positive for an STI. The clinic sites are: UHealth Pediatrics at the Professional Arts Center, University of Miami Pediatric Mobile Clinic, UHealth at Kendal, Ambulatory Care Center West Pediatrics at Jackson Memorial Hospital, Kidstown Pediatrics, LLC, Nicklaus Children's Hospital, South Florida Pediatric Partners, Borinquen Medical Centers, and Primecare Family Centers.

**UHealth Pediatrics at the Professional Arts Center.** The Department of Pediatrics at UHealth is nationally and internationally acclaimed for education, research, patient care, and biomedical innovation. Offering a variety of services from routine healthcare and immunizations to the treatment of severe and chronic illnesses, UHealth Pediatrics is integrated into a dynamic research environment where innovative and effective preventive and treatments services are delivered and under development. UHealth Pediatrics is affiliated with Holtz Children's Hospital, one of the largest children's hospitals in the southeast United States. With over 150 child health specialists honored as Best Doctors®, UHealth Pediatrics has more Best Doctors than any institution in South Florida. UHealth Pediatrics at the Professional Arts Center is one of 9 UHealth sites. The pediatrics offices at UHealth have 10 exam rooms, a small conference/meeting area, and a reception/waiting area. UHealth Pediatrics at the Professional Arts Center is directed by Dr. Lourdes Forster, a co-investigator on the proposed application.

**University of Miami Pediatric Mobile Clinic.** The University of Miami Pediatric Mobile Clinic (UMPMC) has provided medical care to uninsured children since 1992. Services provided include well-visits, sports physicals, immunizations, management of chronic conditions, urgent care, mental health, and social work. UMPMC provides direct primary medical care for nearly 3,000 children a year who are without health insurance, access to medical providers and linking to specialists. UMPMC is a bus with medical supplies and three medical exam rooms. UMPMC's staff members travel with the bus across a 50 mile radius to serve communities with the highest percentage of children living in poverty and/or likely to be uninsured. Specific communities that will continue to be served through this program include: Little Havana, Homestead, Florida City, Little Haiti/North Miami, Westchester, and North Dade. Most of the visited areas have a community center or school rooms that can be utilized for extra medical exam room space. Typically, each site can offer three rooms. Dr. Lisa Gwynn, a co-investigator on the proposed study, is the Medical Director for the University of Miami Pediatric Mobile Clinic.

**UHealth at Kendall.** We will recruit participants from UHealth at Kendall which is a part of the University of Miami health system. UHealth at Kendall has more than 60 physicians and serves children in the S. Florida area, including general pediatrics.

**Ambulatory Care Center West Pediatrics at Jackson Memorial Hospital.** Ambulatory Care Center West Pediatrics at Jackson Memorial Hospital is located within the Jackson Memorial Health System. The Jackson Memorial Health System is governed by the Public Health Trust, a dedicated team of citizen volunteers acting on behalf of the Miami-Dade Board of County Commissioners. Jackson Health System consists of Jackson Memorial Hospital; multiple primary care and specialty care centers; a variety of school-based clinics serving elementary, middle and high schools; two long-term care nursing facilities; six Corrections Health Services clinics; a network of mental health facilities; Holtz Children's Hospital; Jackson Rehabilitation Hospital; Jackson Behavioral Health Hospital; Jackson North Medical Center, and; Jackson South Community Hospital. Jackson Memorial Hospital is an accredited, non-profit, tertiary care hospital and the major teaching facility for the University of Miami Leonard M. Miller School of Medicine. With more than 1,550 licensed beds, Jackson Memorial Hospital is a referral center, a magnet for medical research, and home to Ryder Trauma Center - the only adult and pediatric Level 1 trauma center in Miami-Dade County. Ambulatory Care Center West Pediatrics at Jackson Memorial Hospital provides patients with comprehensive care in a variety of services including pediatric primary care, gynecology and obstetrics. The pediatric practice serves over 7,000 children and youth a year. The Ambulatory Care Center West has more than

a dozen exam rooms for the pediatricians. Dr. Audrey Ofir, co-investigator on the proposed application, is the Director of Ambulatory Pediatrics.

**Kidstown Pediatrics, LLC.** Kidstown Pediatrics, LLC, is located in a residential area 10 minutes outside of downtown Miami. It is housed in a multistory office building and has 2,000 square feet available for office space. Kidstown is a private practice that provides comprehensive primary care services for children of all ages. Specific treatments offered include HPV vaccination, medical care for asthma, treatment for ADD/ADHD, and other vaccinations. Emergency services are available 24 hours a day, 7 days a week, but it is generally open from 8:30am to evening, Monday through Friday. Dr. Margaret Okonkwo, a practicing and board certified pediatrician, is President of KidTown, LLC. Dr. Okonkwo has been in practice for more than 10 years and serves approximately 6,000 children and adolescents per year.

**South Florida Pediatric Partners.** South Florida Pediatric Partners is a private pediatric practice located in Kendall, Florida. It is directed by Dr. Carol Da Costa, a solo practitioner who has been part of the community for the last 15 years. She provides comprehensive pediatric primary care services for children of all ages. Dr. Da Costa serves over 100 Hispanic families per week and provides routine well-child care (e.g., vaccinations) as well as treatment for a range of childhood illnesses and symptoms. The clinic is open Monday-Friday 9am-5:30pm and two Saturdays per month. Patients also have access to an after-hours emergency line.

Nicklaus Children's Hospital. Nicklaus Children's hospital is a pediatric healthcare center that serves children from birth through adolescence. This hospital has over 740 physicians and more than 3,500 employees.

Borinquen Medical Centers was established in 1972 as a grass-roots effort to provide medical care in Miami-Dade County. It offers comprehensive Primary Health Care, dental and behavioral health care.

Primecare Family Care provides pediatric to children and adolescents in the Hialeah area.

## 23) **Prior Approvals**

N/A

**24) Local Number of Subjects**

Approximately 2500 subjects will be screened, and 912 will be enrolled. Additionally approximately 12 parents and 12 adolescents will participate in the pilot study.

**25) Confidentiality**

The issues surrounding confidentiality are of supreme importance and sensitivity because personal information will be obtained from the adolescent and their family members. Participants sign a statement attesting to their understanding that the information they provide will be held as personal and confidential. Consent forms clearly state the right to refuse participation at any time. In addition, because this project involves the collection of drug use and sexual behavior information, to strengthen the security of our records in relation to local and state courts, a Confidentiality Certificate under section 502C of Part E, Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970, Public Law 91-513, has been obtained. This Certificate has been utilized in previous prevention studies and has been instrumental in maintaining the privacy/confidentiality of sensitive client information.

To assure confidentiality at STI testing during each time point, only the adolescent and the research assessor will be present (at the same time) during the procedure. Urine will be collected from the adolescent in a completely private manner; at no moment will the assessor watch the adolescent collect the urine specimen. Both the adolescent and the research assessor shall keep the adolescent's urine specimen in view at all times before the specimen is sealed and labeled. The research assessor will place an identification label securely on each container. The label will contain the adolescent's code number as the only source of identifying information. The assessor will drop off to study research offices the collected urine sample on the same day that it is collected.

In addition, we will do everything we can to keep others from learning about the participants in this study. As mentioned above, to help further protect their privacy, the study researchers have been granted a Federal Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced, even by a court order, to share research information that may identify the participants in any civil, criminal, administrative, legislative, or other proceedings in any court. The researchers will use the Certificate to resist any demands for information that would identify the participants, except to prevent serious harm to them or others, and as explained below.

The participants should understand that a Certificate of Confidentiality does not prevent them, or a member of their family, from voluntarily releasing information

about themselves, or their involvement in this study. If an insurer or employer learns about their participation, and obtains participant's consent to receive research information, then we may not use the Certificate of Confidentiality to withhold this information. This means that the participants and their family must also actively protect their own privacy. Disclosure will be necessary, however, upon request for the purpose of audit or evaluation, and is limited only to Department of Health and Human Services employees involved in the review. The participant should understand that we will in all cases, take the necessary action, which may include reporting to authorities, to prevent serious harm to themselves or others.

**26) Provisions to Protect the Privacy Interests of Subjects**

During the recruitment and electronic consent/assent process, and prior to the assessments, the subjects are told that information is private, confidential and only accessed by specific study personnel. The subject is given a case ID to further protect their identity. The subject is free to ask any questions, and the consent form has the contact information of the Principal Investigator should they have further questions and the phone number to the University of Miami's Human Subjects office.

Please refer to Section 12(b) Secure Data and Quality Control.

As described before, each follow-up visit will include screening for Neisseria gonorrhoeae (GC) and Chlamydia trachomatis (CT) as indicated by reported sexual risk behaviors and per local site clinical and public health standards. Adolescents will be encouraged to refer sexual partners for treatment.

**27) Compensation for Research-Related Injury**

Not applicable.

**28) Economic Burden to Subjects**

Not applicable.

**29) Consent Process**

**(a) Obtaining Consent**

University of Miami research study personnel will screen families in the clinics that are interested in participating. They will present and read the electronic consent forms to the caregivers who are eligible to participate based on the inclusion and exclusion criteria. The consent form will be an electronic document, and each page will bear the HSRO approval stamp/watermark. If a participant prefers the consent or assent process to be non-electronic, a paper consent or assent form will be provided. After the caregivers understand the study and after all questions have been answered

to their satisfaction, individuals who elect to participate in the study will be asked to sign the consent form. The consent process will last approximately 30 minutes, but it may take caregivers a little less or a little more depending on how clearly they comprehend the study procedures.

If a parent is not available to complete consent, a legal guardian is allowed to provide permission for the adolescent to assent. A legal guardian is a step mother or step father, or another person who has obtained legal rights to the child. During the recruitment screening process, study personnel will determine if the primary caregiver is a legal guardian if they demonstrate the correct paperwork.

Since recruitment will take place at different clinics, it is a possibility that potentially eligible families will visit the clinic when the research team is not present. If the clinic personnel identifies such a family, they will be able to provide them with a flyer about the study and information on how to contact the research team. If the family is interested and contacts the research team, they will be provided with the next date that the research team will be at the clinic so that the family can be informed about the study and conduct the consent, assent and baseline assessment, if the family is interested in being in the study.

(b) Non-English Speaking Subjects

The consent forms will also be available in Spanish. The consent forms have been translated, back-translated and pilot tested for understanding in past pilot studies.

(c) Waiver or Alteration of Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception)

We would like to request information from parents and adolescents that decide not to participate in the study. We are collecting this information because in at least two manuscripts where we report main outcomes for Familias Unidas, reviewers have requested information regarding participants who decide not to engage in the trial. This information will be completely de-identified. We would like to collect this information through the use of a verbal consent and verbal assent. We are requesting permission to only utilize a verbal consent and assent (not signed) because it is unlikely that participants who do not want to participate in the study will answer these questions if they have to identify themselves by signing a consent or assent form.

(d) Subjects who are not yet adults (infants, children, teenagers)

Adolescents, ages 12-16, will go through a similar process as their parents. Their age is confirmed with the pediatric clinic administrator, nurses, and/or physician. After the parent has consented, the facilitators will present the assent forms to the adolescent. This will occur in a different room without the caregivers present to prevent the adolescents from being coerced to participate. Only the adolescent present for the clinic appointment will complete the assent form. The assent process will last approximately 30 minutes, but it may take the adolescent a little more or a little less depending on how clear they comprehend study procedures.

(e) Cognitively Impaired Adults  
Not applicable.

(f) Adults Unable to Consent  
Not applicable.

**30) Process to Document Consent in Writing**

Consents will be stored electronically in secure University of Miami servers. Information for de-identified participants who do not wish to participate in the study and provided verbal consent/assent to answer the questions for non-participating families will be kept in secure University of Miami servers.

**31) Drugs or Devices**

Not applicable.