PARTNERS HUMAN RESEARCH COMMITTEE
PROTOCOL SUMMARY

Answer all questions accurately and completely in order to provide the PHRC with the relevant information to assess the risk-benefit ratio for the study. Do not leave sections blank.

PRINCIPAL/OVERALL INVESTIGATOR
BRIAN G. SKOTKO, M.D., M.P.P.

PROTOCOL TITLE
Down Syndrome Clinic to You (DSC2U)

FUNDING
PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

VERSION DATE
February 28, 2017

SPECIFIC AIMS

Concisely state the objectives of the study and the hypothesis being tested.

Our core objective is to leverage an innovative technology from Massachusetts General Hospital (MGH), which engages parents/caregivers, so that we can begin to reduce specific health care disparities experienced by those underserved patients with Down syndrome (DS). Specifically, through a randomized control trial (RCT), we will test whether patient/caregiver-initiated online reports with personalized recommendations versus usual care will increase caregiver-reported, provider-driven health actions consistent with national DS guidelines. While all patients with DS have a disparity as defined by their disability, we also intend to mitigate the compounding disparities of geographic location, race/ethnicity, and socioeconomic factors for the majority of families and overcome the limited reach of DS specialty care by taking advantage of the broader reach of the Internet.

BACKGROUND AND SIGNIFICANCE

Provide a brief paragraph summarizing prior experience important for understanding the proposed study and procedures.

Down syndrome (DS) is a rare, chronically debilitating genetic condition caused by extra genetic material from chromosome 21. Patients with DS are prone to multiple chronic conditions over their lifetime, including congenital heart disease, thyroid conditions, gastrointestinal disorders, leukemia, obstructive sleep apnea, and accelerated aging, among others. Most patients with DS have their medical care managed by their primary care providers (PCPs), but a recent study showed that <10% of children and adolescents with DS are up-to-date on even the basic recommendations, such as thyroid screens, celiac testing, audiograms, eye exams, and sleep apnea testing.

Recognizing the challenge that PCPs have in staying current on all of the complexities of this condition, 58 Down syndrome specialty clinics have been formed in 32 U.S. states since 1967. Yet, despite their documented impact, the 58 DS-specialty clinics, combined, only serve about 12,000 patients with DS, which is <5% of the estimated population of people with DS living in the U.S.

In 2014, the NIH published a revised research plan for DS research stating, "For individuals living with Down syndrome and their families, there is an ongoing need to study clinical and behavioral treatments and interventions". In 2008, the Centers for Disease Control and Prevention published a "Public Health Research Agenda for Down Syndrome" stating that "more research is needed to identify optimal methods of monitoring for [the comorbid] conditions. In addition, prevention strategies need to be developed for those conditions amenable to prevention". In 2011, the American Academy of Pediatrics (AAP) created DS Health Supervision Guidelines, including age-specific screening tests and procedures. For adults, consensus-based guidelines exist.

Our preliminary studies on our rules-based online intake from, which was collaboratively developed by MGH Down Syndrome Program (DSP) and MGH Laboratory of Computer Science (LCS) has shown potential for a sizeable benefit to our users, parents/caregivers and specialists. Our research will be both novel and innovative. We will offer our already created and tested online intake platform, rebranded as "Down Syndrome Clinic to You (DSC2U)," as a direct-to-public, always-available, online service yielding comprehensive, yet personalized recommendations for patients with DS who have limited access to specialty care. We want to provide game-changing care to the overwhelming majority of patients with DS who are underserved.

RESEARCH DESIGN AND METHODS

Briefly describe study design and anticipated enrollment, i.e., number of subjects to be enrolled by researchers study-wide and by Partners researchers. Provide a brief summary of the eligibility criteria (for example, age range, gender, medical condition). Include any local site restrictions, for example, "Enrollment at Partners will be limited to adults although the sponsor's protocol is open to both children and adults."

We plan to enroll 200 parents/caregivers from around the country in a two-arm randomized controlled trial (RCT) over 21 months.

Eligibility screening questions include:

1. Do you have a child or dependent with Down syndrome?
2. What is your child or dependent's date of birth?
3. When is your child or dependent's next annual well visit ("PCP visit") scheduled with his or her primary care provider?

4. What is the PCP's contact information (first name, last name, city, and state)?
5. Does your child or dependent currently receive care at a DS specialty clinic? (If the child is actively followed in a DS specialty clinic, he or she would be ineligible.)
6. What is the name and e-mail address of the caregiver or legal guardian who will be participating in this research?
    a. Will this person be attending the PCP visit with the child or dependent? Yes/No
    b. If "No", will this person be committed to seeing that the letters of recommendation generated from this study get delivered to the PCP during this visit? Yes/No
7. What is your child or dependent's race?
8. What is your child or dependent's ethnicity?
9. What is your child or dependent's sex?
10. If I am eligible to participate in this study, I prefer to receive study materials, such as forms to fill out and my caregiver checklist, in: 1) English or 2) Spanish

In order to be eligible, the parent/caregiver need to respond "Yes" to questions #1, "No" to question #5, and must provide information to #2, #3, #4, #6, #7, #8, #9, and #10 as well as a valid e-mail address for all study communication purpose. In addition, we can only allow one patient's caregiver for each participating PCP since multiple patients seen by the same PCP would not be independent events.

Down syndrome occurs naturally and proportionally in all races and ethnicities, so our estimates are proportional to the racial/ethnic distribution of the U.S., as reported in the 2010 U.S. Census.

We would like to achieve this diversity in our enrolled participants. To this extent, we will then use a quota system in offering enrollment. Based on our idealized Enrollment Table (below), we will enroll no more than 144 whites and no fewer than 32 Hispanics (Latinos/Latinas) and 26 Blacks/African Americans. We will also enroll no more than 102 participants of either sex.

Recruitment Plan

Total number of study participants expected to be screened:	1500
Total number of study participants expected to be eligible of those screened:	300
Target sample size (use same number stated in milestones):	200

Estimated Final Racial/Ethnic and Gender Enrollment Table

Race	Male (N)	Female (N)	Total (N)
American Indian/Alaska Native	1	1	2
Asian	5	5	10
Black/African-American	13	13	26
Hawaiian/Pacific Islander	1	0	1
White	73	71	144
Multirace	3	3	6
Other race	6	5	11
Ethnicity	**Male (N)**	**Female (N)**	**Total (N)**
Hispanic (Latino/Latina)	16	16	32
Non-Hispanic	83	85	168

Briefly describe study procedures. Include any local site restrictions, for example, "Subjects enrolled at Partners will not participate in the pharmacokinetic portion of the study." Describe study endpoints.

Potential eligible participants will be directed to our study recruitment website (www.downsyndromeclinictoyou.com) to complete the eligibility screening questionnaire (Appendix A). Information of frequently asked questions and answers will also be provided on our study recruitment website (Appendix B). After a questionnaire is submitted and a parent/caregiver is deemed eligible, our study personnel will send an email notification containing a unique link to our online consent form in REDCap (Appendix C). Once they have provided consent, the parent/caregiver will continue on to complete the baseline assessment. Our study personnel will then be notified by e-mail, after which we will randomize the participant 1:1 to either the Intervention or Control arm (Appendix D).

To limit chance confounding between variables that might influence guideline compliance, we will stratify randomization based on two variables (six strata) collected prior to randomization during the Baseline assessment when data are gathered only from parents (PCPs are first surveyed after their appointment with the patient who has Down syndrome):

- Travel time to primary care physician: < 30 minutes; 30–60 minutes; > 60 minutes
- Primary insurance: public (e.g., Medicaid, Medicare) or private

Given the sequence of study procedures, we will not stratify on any variables reported by the PCP. With 200 participants randomized, we expect to

achieve effective mixing of PCP characteristics that might be associated with differential guideline compliance. Moreover, by not conditioning on PCP characteristics, findings from our primary analysis will be most broadly generalizable. However, we do want to increase precision in our secondary analyses by accounting for relevant sources of variation among PCP practices. To this extent, we will collect the following variables for inclusion as covariates:

- PCP practice size: < 5 MDs; 5–9 MDs; 10+ MDs (collected in PCP Experience Survey during Post-visit Assessment 1)
- PCP practicing in a federally qualified community health center: yes or no (collected in PCP Experience Survey during Post-visit Assessment 1)
- Years of PCP practice (collected in PCP Experience Survey during Post-visit Assessment 1)
- Number of patients with Down syndrome cared for by PCP (collected in PCP Experience Survey during Post-visit Assessment 1)

Baseline Assessment (Intervention & Control Arms)
The intervention and control groups will both complete a Baseline Assessment; up to 3 e-mail reminders will be sent to the parent/caregiver every 1 week. The Baseline Assessment, implemented using REDCap (Research Electronic Data Capture), a secure, NIH-funded, and Health Insurance Portability and Accountability Act (HIPAA) compliant web-based application hosted by Partners HealthCare Research Computing, will request the following information:

- *Caregiver information*: first name, last name, gender, date of birth, relationship to patient, phone number, address, and email address
- *Child or dependent's information*: first name, last name, gender, date of birth, race/ethnicity (NIH standardized format)
- *PCP information*: first name, last name, gender, office phone, office address and e-mail (if available)
- Travel time to primary care physician: < 30 minutes; 30–60 minutes; > 60 minutes
- Primary insurance: public (e.g., Medicaid, Medicare) or private
- *Date of annual well visit ("PCP visit") appointment*
- *Symptoms indicating need for celiac disease testing or sleep study.* We plan to assess these symptoms among other symptoms not related to these conditions so as to minimize any priming effects. For example, "Does your child snore at night?" might be asked next to "Does your child have any rashes?" (A sleep study might be warranted for snoring, but not for rashes.) (Appendix E)
- *Health Care Outcome Survey* (Metrics measuring adherence to national health care guidelines): thyroid screening, celiac disease screening, sleep apnea testing, ophthalmology exams, and audiograms (Appendix F)

- *Secondary outcome measures:* PedsQL 2.0 Family Impact Module and PedsQL 4.0 parent-proxy, standard Short Form 15 Generic Core Scales (Appendix G)

Intervention Arm
After submission of the Baseline Assessment, the parents/caregivers will be e-mailed a unique link to their DSC2U intervention form. The parent/caregiver will need to enter the month and day of birth of the person with Down syndrome to access their form. Using that information and their unique link, they can return to and complete the DSC2U form (Appendix H) at their convenience. Reminder e-mails to complete the DSC2U form will be sent at 4, 3, and 2 weeks prior to their son's/daughter's scheduled PCP annual well visit appointment. After they have completed DSC2U form, the system will send the parent/caregiver a link to their Caregiver Checklist (Appendix I) and Primary Care Provider Plan (Appendix J), which they will access by entering the month and day of birth of the person with Down syndrome. The DSC2U Caregiver Checklist and Primary Care Provider Plan will be accessible online until the end of the study period and may be downloaded and printed at the user's discretion.

Control Arm
After submission of the Baseline Assessment, parents/caregivers in the Control arm will be sent an e-mail message thanking them for their participation in the study. Included will be a reminder to let study personnel know if their son's/daughter's scheduled appointment with the PCP changes. Control arm participants will be receiving usual care—that is, the natural advice and recommendations that would be offered by their PCPs. (Upon conclusion of the RCT, control group participants will be offered the same Caregiver Checklist and Primary Care Provider Plan intervention.)

PCP Visit
Prior to each patient's scheduled PCP visit, the parent/caregiver will receive 2 reminders for their upcoming appointment, including a request to let our study personnel know if the date of the appointment has changed. Because the timing between study enrollment and scheduled PCP visit will vary among participants, we will plan to send these appointment reminders at approximately 4 weeks, then 1 week prior to the scheduled appointment.

Post-Visit Assessments (Both Intervention and Control Arms)
- Secondary outcome measures: PedsQL 2.0 Family Impact Module; PedsQL 4.0 parent-proxy, standard Short Form 15 Generic Core Scales (Appendix G)

In addition, with direct input from our Patient/Caregiver working group (WG) and PCP WG, we will be designing three novel surveys:

- Health Care Outcome Survey (for parents/caregivers) (for Primary Outcomes) (Appendix F)
- Parent/Caregiver Experience Survey (for Secondary Outcomes) (Appendix K)
- Primary Care Provider Experience Survey (for Secondary Outcomes) (Appendix L)

Survey Implementation

The Experience Surveys (for both the parents/caregivers and PCPs) will be administered approximately 2 weeks after the PCP visit at Post-visit Assessment 1 (T1) (Figure 1). Parents/Caregivers will be invited by e-mail to complete their experience survey through REDCap. PCPs will receive their experience survey by mail, with an option to complete the survey electronically on REDCap. PCPs whose e-mails were provided by the parents/caregivers will also receive a direct invitation by e-mail to complete their survey. In order to minimize loss to follow-up, reminder e-mails will be sent 3 times about 2 weeks apart, concluding with a phone call in the eighth week by our study personnel. We certainly hope to maximize the PCP response rate, but our primary outcomes are not dependent on their responses.

Parents/Caregivers will be asked by e-mail to complete the Health Care Outcomes Survey through REDCap approximately seven months after the PCP visit at Post-visit Assessment 2 (T2) (Figure 1). In order to minimize loss to follow-up, reminder e-mails will be sent 3 times about every 2 weeks apart, concluding with a phone call in the 8th week by our study personnel.

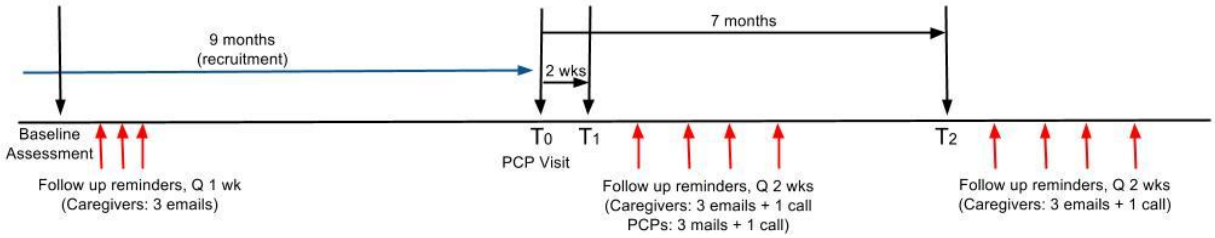

Figure 1. Survey implementation at various points.

- *Baseline*: Health Care Outcome Survey, PedsQL 2.0 Family Impact Module and PedsQL 4.0 parent-proxy, standard Short Form 15 Generic Core Scales
- *T_0 (PCP Visit)*
- *T_1 (Post-visit Assessment 1)*: PedsQL 2.0 Family Impact Module and PedsQL 4.0 parent-proxy, standard Short Form 15 Generic Core Scales, Parent/Caregiver Experience Survey, and PCP Experience Survey
- *T_2 (Post-visit Assessment 2)*: Health Care Outcome Survey, PedsQL 2.0 Family Impact Module and PedsQL 4.0 parent-proxy, standard Short Form 15 Generic Core Scales

Validation Assessment

Ten percent of the respondents across both groups will be asked to validate their self-report by providing documentation of laboratory and procedural results. For example, if parents attest to thyroid checks being done for their

sons/daughters, they will be asked to send documentation of the primary outcomes (e.g. study report or physician sign off). These participants will also receive 3 reminder e-mails and a phone call every 2 weeks.

If discrepancies are identified between parental report and source verification in more than 10% of these samples, then our team will perform a full verification of all 200 participants. Verification will be made by source documentation (e.g., sleep study reports) or verbal confirmation through telephone calls to primary care physicians.

Primary Outcomes:
We will be measuring adherence to detect improvement in: thyroid screening, celiac disease screening, sleep apnea testing, ophthalmology exams, and audiograms

- *Thyroid*: TSH should be checked annually beginning at age 1
- *Celiac disease*: if symptoms present, obtain tTG-IgA and total IgA annually
- *Sleep study*: performed by 4 years of age and, again, if symptomatic
- *Ophthalmology exam*: annually, ages 1-5; every 2 years, ages 5-13; every 3 years, ages 13-21; every 2 years, ages 21 and older
- *Audiograms*: annually up to age 21, every 2 years thereafter

The indication for 1, 2, 3, 4, or 5 evaluations for a given participant at the time of their PCP visit based on age, history, and symptoms will be collected prior to randomization as described in the "Baseline Assessment" section.

Secondary Outcomes:
We also want to determine whether the intervention improves quality of life as measured by the nationally validated PedsQL survey instruments.

Six summary scores will be derived from the two PedsQL instruments: measures of (1) psychosocial health, (2) physical health, and (3) an overall total score from the PedsQL 4.0 parent-proxy, standard Short Form 15 Generic Core Scales; and measures of (4) parental health-related quality of life, (5) family functioning, and an (6) overall total score from the PedsQL 2.0 Family Impact Module.

We will also measure the quality of experience with the intervention from parents and PCPs and identify ways that the *Caregiver Checklist* and *Primary Care Provider Plan* could best serve the needs of underserved patients with DS. For this assessment, rather than assuming we know which questions to ask to best assess their experience, we will engage our Parent/Caregiver and PCP WGs to help us pose relevant questions. Our expectation is that the assessments will ask for their level of satisfaction with the content and

guidance offered by the *Caregiver Checklist* and *Primary Care Provider Plan*, similar to the voluntary questionnaire used in our preliminary study described above. We also anticipate including open-text responses solicited from caregivers and providers about their experience using the system.

Data Analysis Plan

Our primary analysis will compare the mean number of caregiver-reported evaluations completed within 7 months of the index PCP visit between the intervention and usual care arms. We will analyze the data using a generalized linear model assuming beta-binomial distributed counts of evaluations among those indicated with parameters estimated by maximum likelihood. We will confirm our inference using a permutation test by direct randomization of assigned treatment labels. Significant benefit will be declared if the mean number of recommended tests is greater among participants randomized to the intervention and a two-tailed p-value for the treatment comparison is less than 0.05. A significant effect of the intervention will be declared only if the permutation test concurs with inference from the beta-binomial regression as the permutation test makes no assumptions concerning the true distribution of the data. We will analyze longitudinal changes in our secondary outcome measures using a shared-baseline repeated-measures ANOVA for each of 6 quality of life outcomes derived from the two PedsQL instruments. Linear contrasts will be used to test for treatment-specific improvements over time. As a sensitivity analysis, we will also use simple two-group Wilcoxon ranksum tests to compare changes from baseline in each follow-up assessment individually. With 6 secondary outcomes, we will test each secondary outcome at alpha = 0.008 two-tailed to control for multiple comparisons.

For studies involving treatment or diagnosis, provide information about standard of care at Partners (e.g., BWH, MGH) and indicate how the study procedures differ from standard care. Provide information on available alternative treatments, procedures, or methods of diagnosis.

Not applicable

Describe how risks to subjects are minimized, for example, by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk or by using procedures already being performed on the subject for diagnostic or treatment purposes.

Our study does not involve any diagnostic or treatment procedures. The risk associated with participating in this study is considered to be minimal and commensurate with everyday risks. No physical or economic harm is anticipated. A foreseeable risk and discomfort of participating in this study is the time and effort of filling out "Down Syndrome Clinic to You" and study questionnaires. It will be made clear during the recruitment and consent process that the participation is totally voluntary, and parent/caregivers may discontinue participation at any time during the study period. Deciding not be part of the study will not change participants' regular medical care in any

way. We will also implement several safety measures (storing de-identified participant data in password-protected databases and limiting access to study data to only study team) to ensure that personal data is protected. Study participants will be assured that no information will be published in any manner that would personally identify them.

Describe explicitly the methods for ensuring the safety of subjects. Provide objective criteria for removing a subject from the study, for example, objective criteria for worsening disease/lack of improvement and/or unacceptable adverse events. The inclusion of objective drop criteria is especially important in studies designed with placebo control groups.

The attribution of any adverse events to this study is categorized as Unlikely. The principal investigator will, however, evaluate any adverse events and report these to the Partners Human Research Committee (PHRC). Any serious adverse events will be reported within 24 hours of the event, followed by a complete written report within 10 working days. Adverse events considered to be mild or moderate will be summarized in the progress report for the continuing review, as specified by the PHRC adverse event reporting guidelines.

FORESEEABLE RISKS AND DISCOMFORTS

Provide a brief description of any foreseeable risks and discomforts to subjects. Include those related to drugs/devices/procedures being studied and/or administered/performed solely for research purposes. In addition, include psychosocial risks, and risks related to privacy and confidentiality. When applicable, describe risks to a developing fetus or nursing infant.

The risk associated with participating in this study is considered to be minimal and commensurate with everyday risks. Our research activities will not cause any physical, psychological, financial, or legal harm to participants. The only study-related risks that participants could be exposed to are those relating to privacy and confidentiality. We have implemented several safety measures (storing de-identified participant data in password-protected databases and limiting access to study data to only study team) to ensure that personal data is protected. The likelihood that this data will remain secure is very high. Study participants will be assured that no information will be published in any manner that would personally identify them.

EXPECTED BENEFITS

Describe both the expected benefits to individual subjects participating in the research and the importance of the knowledge that may reasonably be expected to result from the study. Provide a brief, realistic summary of potential benefits to subjects, for example, "It is hoped that the treatment will result in a partial reduction in tumor size in at least 25% of the enrolled subjects." Indicate how the results of the study will benefit future patients with the disease/condition being studied and/or society, e.g., through increased knowledge of human physiology or behavior, improved safety, or technological advances.

Study participants who are assigned to the intervention group to complete DSC2U form then receive customized "Caregiver Checklist" and "Primary Care Provider Plan" will have a greater likelihood of an improvement in adherence to the national Down syndrome guidelines. Study participants who are assigned to the control group will receive current standard of care and there will be no immediate potential benefits to this group of participants during the RCT period. However, participants in the control group will be offered the opportunity to complete the DSC2U form and receive a personalized "Caregiver Checklist" and "Primary Care Provider Plan" upon conclusion of the study. In addition, the "Primary Care Provider Plan" would potentially improve PCP's practice behaviors by providing personalized information based on evidence-based guidelines.

EQUITABLE SELECTION OF SUBJECTS

The risks and benefits of the research must be fairly distributed among the populations that stand to benefit from it. No group of persons, for example, men, women, pregnant women, children, and minorities, should be categorically excluded from the research without a good scientific or ethical reason to do so. Please provide the basis for concluding that the study population is representative of the population that stands to potentially benefit from this research.

For the RCT, parents/caregivers who have sons and/or daughters with DS, of all ages, living in the U.S. who do not have access to a DS specialty clinic are eligible for this study. To emphasize, we are enrolling the parents/caregivers and *not* their sons/daughters with DS. Both English-speaking and Spanish-speaking families will be recruited. All genders, races, and ethnicities will be given the same opportunities to participate in research activities. Participants will have equal exposure to recruitment through our recruitment website. Our "Down Syndrome Clinic to You" (DSC2U) will be developed both in English and Spanish.

When people who do not speak English are excluded from participation in the research, provide the scientific rationale for doing so. Individuals who do not speak English should not be denied participation in research simply because it is inconvenient to translate the consent form in different languages and to have an interpreter present.

As our "Down Syndrome Clinic to You" (DSC2U) will be developed both in English and Spanish, both English-speaking and Spanish-speaking families will be recruited.

For guidance, refer to the following Partners policy:
Obtaining and Documenting Informed Consent of Subjects who do not Speak English
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Non-English_Speaking_Subjects.1.10.pdf

RECRUITMENT PROCEDURES

Explain in detail the specific methodology that will be used to recruit subjects. Specifically address how, when, where and by whom subjects will be identified and approached about participation. Include any specific recruitment methods used to enhance recruitment of women and minorities.

We plan to enroll 200 total parents/caregivers for the RCT.

In order to capture participants who do not have access to a DS specialty clinic, we plan to recruit our participants through multiple mechanisms and media (Appendix M): (1) the NIH's DSConnect®, a national contact registry, where parents/caregivers from around the country have indicated that they are interested in being contacted for potential research opportunities about DS, (2) e-newsletters, Facebook, and Twitter postings of DS advocacy groups around the country, (3) our own Facebook and Twitter postings, and (4) registering at the NIH's Clinicaltrials.gov. States/regions without a DS specialty clinic will be targeted initially and preferentially. While all patients with DS have a disparity as defined by their disability, we intend to mitigate the compounding disparities of geographic location, race/ethnicity, and socioeconomic factors for the majority. We have incorporated a strategy to maximize our study participants' retention by reaching out to study participants via up to 3 follow-up e-mails and a reminder phone call at various study points.

Provide details of remuneration, when applicable. Even when subjects may derive medical benefit from participation, it is often the case that extra hospital visits, meals at the hospital, parking fees or other inconveniences will result in additional out-of-pocket expenses related to study participation. Investigators may wish to consider providing reimbursement for such expenses when funding is available

Parent/caregiver participants of our RCT will receive $50 total for completion of the study: $10 after completing the Baseline Assessment, $10 after completing the two-week post-visit assessment 1, and $30 after completing the seven-month post-visit assessment 2. An additional $20 will be given to parents/caregiver participants in the validation set. PCPs will receive $40 after completing the two-week post-visit experience questionnaire. We will purchase online gift cards through Partners reloadable gift card service or from Amazon.com or other national retailer. The electronic links to these activated gift cards will be sent electronically to the caregivers after survey completion.

For guidance, refer to the following Partners policies:

Recruitment of Research Subjects

https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Recruitment_Of_Research_Subjects.pdf

Guidelines for Advertisements for Recruiting Subjects

https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Guidelines_For_Advertisements.1.11.pdf

Remuneration for Research Subjects
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Remuneration_for_Research_Subjects.pdf

CONSENT PROCEDURES

Explain in detail how, when, where, and by whom consent is obtained, and the timing of consent (i.e., how long subjects will be given to consider participation). For most studies involving more than minimal risk and all studies involving investigational drugs/devices, a licensed physician investigator must obtain informed consent. When subjects are to be enrolled from among the investigators' own patients, describe how the potential for coercion will be avoided.

Online consent form will be sent to all eligible participants via email. Eligible participants (parents/caregivers) will be able to view all of the elements of informed consent online in REDCap (Appendix C). Questions for the study could be sent to our study personnel via email. All consent will be obtained via REDCap. Two buttons (Yes and No) will be located at the end of study consent page. By click on the "YES, I AGREE TO PARTICIPATE IN THIS RESEARCH" button, parents/caregivers will be enrolled to our study. By click on "NO, EXIT THE PROGRAM" button, parents/caregivers will not be enrolled to the study and will be redirected to our study recruitment website main page. Online consent form can be printed and/or saved as PDF file. Eligible participants will have up to 5 days to provide his/her consent.

NOTE: When subjects are unable to give consent due to age (minors) or impaired decision-making capacity, complete the forms for Research Involving Children as Subjects of Research and/or Research Involving Individuals with Impaired Decision-making Capacity, available on the New Submissions page on the PHRC website:
https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb

For guidance, refer to the following Partners policy:
Informed Consent of Research Subjects:
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Informed_Consent_of_Research_Subjects.pdf

DATA AND SAFETY MONITORING

Describe the plan for monitoring the data to ensure the safety of subjects. The plan should include a brief description of (1) the safety and/or efficacy data that will be reviewed; (2) the planned frequency of review; and (3) who will be responsible for this review and for determining whether the research should be altered or stopped. Include a brief description of any stopping rules for the study, when appropriate. Depending upon the risk, size and complexity of the

study, the investigator, an expert group, an independent Data and Safety Monitoring Board (DSMB) or others might be assigned primary responsibility for this monitoring activity.

NOTE: Regardless of data and safety monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for protecting the rights, safety, and welfare of subjects under his/her care.

We will use REDCap (Research Electronic Data Capture), a secure, NIH-funded, and Health Insurance Portability and Accountability Act (HIPAA) compliant web-based application hosted by Partners HealthCare Research Computing to collect parent/caregiver baseline assessment, parent/caregiver post-visit assessment 1, and parent/caregiver post-visit assessment 2. Primary care providers can submit their PCP post-visit experience via regular mail or through REDCap. Parents/caregivers can submit their documentations of laboratory and procedural results via regular mail or e-mail.

Data collected via REDCap are secured and stored behind the Partners firewall and follow Partners Healthcare Information Security policies for authenticated, minimum access. Data collected via regular mail will be scanned and stored electronically in our secure, access-limited, password-protected research folder on the Partners shared drive, same as data that are collected via e-mail. Original copies of data collected via regular mail will then be disposed in the HIPAA-compliant bins at Massachusetts General Hospital.

We will use a secure, web-based application, SproutScribe, to support the DSC2U intervention. SproutScribe was developed by the MGH Lab of Computer Science to support the intelligent transformation of collected structured data into custom narratives. The application has been reviewed and approved by Partners Information Security and is currently used to support clinical care reporting in the MGH Down Syndrome Program, the MGH Lurie Center for Autism and MGH Cardiology. Structured data collected from the DSC2U intervention form itself is secure and stored behind the Partners firewall and follows Partners Information Security policies for authenticated, minimum access.

Describe the plan to be followed by the Principal Investigator/study staff for review of adverse events experienced by subjects under his/her care, and when applicable, for review of sponsor safety reports and DSMB reports. Describe the plan for reporting adverse events to the sponsor and the Partners' IRB and, when applicable, for submitting sponsor safety reports and DSMB reports to the Partners' IRBs. When the investigator is also the sponsor of the IND/IDE, include the plan for reporting of adverse events to the FDA and, when applicable, to investigators at other sites.

NOTE: In addition to the adverse event reporting requirements of the sponsor, the principal investigator must follow the Partners Human Research Committee guidelines for Adverse Event Reporting

The attribution of any adverse events to this study is categorized as Unlikely. The principal investigator will, however, evaluate any adverse events and report these to the Partners Human Research Committee (PHRC). Any serious adverse events will be reported within 24 hours of the event, followed by a complete written report within 10 working days. Adverse events considered to be mild or moderate will be summarized in the progress report for the continuing review, as specified by the PHRC adverse event reporting guidelines.

MONITORING AND QUALITY ASSURANCE

Describe the plan to be followed by the principal investigator/study staff to monitor and assure the validity and integrity of the data and adherence to the IRB-approved protocol. Specify who will be responsible for monitoring, and the planned frequency of monitoring. For example, specify who will review the accuracy and completeness of case report form entries, source documents, and informed consent.

NOTE: Regardless of monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for ensuring that the study is conducted at his/her investigative site in accordance with the IRB-approved protocol, and applicable regulations and requirements of the IRB.

Only Principal Investigator (PI) and the study's research staffs directly involved in the data collection will have access to the identifiable information about study participants.

Data collected from the RCT will be stored electronically in our secure, access-limited, password-protected research folder on our hospital's secured drive. The original paper copies of any study-related materials will be discarded, after scanning, in the designated HIPAA-compliant blue recycling bins at MGH for confidential materials. Partners Information Services (IS), a division within Partner Healthcare Systems (PHS), manages all data and voice communication networks as well as other core infrastructure systems and applications across the Partners environment. All systems are secured behind the Partners firewall and follow Partners Healthcare Information Security policies for authenticated, minimum access. All systems are patched, monitored, and scanned routinely for vulnerabilities and intrusions by the systems administrator and PHS Information Security. All configuration changes that could affect accessibility or security are approved by management. All systems administrative personnel and support staff have completed the NIH training program in Computer Security and have additionally completed their certification in the Collaborative Institutional Training Initiative (CITI) program. CITI was developed by experts at PHS, MGH, and Brigham and Women's Hospital and with outside institutions in the

"IRB community" and consists of courses in the Protection of Human Research Subjects for Biomedical Research.

For guidance, refer to the following Partners policies:

Data and Safety Monitoring Plans and Quality Assurance
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/DSMP_in_Human_Subjects_Research.pdf

Reporting Unanticipated Problems (including Adverse Events)
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Reporting_Unanticipated_Problems_including_Adverse_Events.pdf

PRIVACY AND CONFIDENTIALITY

Describe methods used to protect the privacy of subjects and maintain confidentiality of data collected. This typically includes such practices as substituting codes for names and/or medical record numbers; removing face sheets or other identifiers from completed surveys/questionnaires; proper disposal of printed computer data; limited access to study data; use of password-protected computer databases; training for research staff on the importance of confidentiality of data, and storing research records in a secure location.

NOTE: Additional measures, such as obtaining a Certificate of Confidentiality, should be considered and are strongly encouraged when the research involves the collection of sensitive data, such as sexual, criminal or illegal behaviors.

Data collected via REDCap are secured and stored behind the Partners firewall and follow Partners Healthcare Information Security policies for authenticated, minimum access. Data collected via regular mail will be scanned and stored electronically in our secure, access-limited, password-protected research folder on the Partners shared drive, same as data that are collected via e-mail. Original copies of data collected via regular mail will then be disposed in the HIPAA-compliant bins at Massachusetts General Hospital.

SENDING SPECIMENS/DATA TO RESEARCH COLLABORATORS OUTSIDE PARTNERS

Specimens or data collected by Partners investigators will be sent to research collaborators outside Partners, indicate to whom specimens/data will be sent, what information will be sent, and whether the specimens/data will contain identifiers that could be used by the outside collaborators to link the specimens/data to individual subjects.

Not applicable

Specifically address whether specimens/data will be stored at collaborating sites outside Partners for future use not described in the protocol. Include whether subjects can withdraw

their specimens/data, and how they would do so. When appropriate, submit documentation of IRB approval from the recipient institution.

Not applicable

RECEIVING SPECIMENS/DATA FROM RESEARCH COLLABORATORS OUTSIDE PARTNERS

When specimens or data collected by research collaborators outside Partners will be sent to Partners investigators, indicate from where the specimens/data will be obtained and whether the specimens/data will contain identifiers that could be used by Partners investigators to link the specimens/data to individual subjects. When appropriate, submit documentation of IRB approval and a copy of the IRB-approved consent form from the institution where the specimens/data were collected.

Not applicable