Minimal Risk Protocol: Autism ALERT

1) Protocol Title

Autism Access Link for Early Referral and Treatment

2) Objectives

Autism Access Link for Early Referral and Treatment [ALERT], the intervention proposed in this application, is a novel state-wide referral and case management platform that PCPs can activate to ensure that a child with suspected Autism Spectrum Disorder (ASD) receives all necessary ASD diagnosis and treatment resources in a single referral, radically simplifying a complex diagnostic and treatment process. We hypothesize that Autism ALERT will have strong acceptability and high rates of use among primary care providers as well as among diverse low-income patients of children at risk for ASD, and that we will see higher rates of child ASD educational evaluations within six months, and shorter time between referral and ASD treatment,.

3) Background

Children with ASD can be accurately identified as early as two years old. Children identified early and placed promptly into comprehensive treatment models [CTMs] such as applied behavioral analysis programs, show improvements in language, IQ and adaptive functioning. Still, average age of ASD diagnosis in the US is around 4 years old, and is older for low-income and racial/ethnic minority children. Low-income and minority children are also less likely to be diagnosed with ASD, and are more likely to have severe features (e.g. comorbid intellectual disability). Although access to evidence-based ASD therapy is rapidly expanding, most children with ASD are not treated with evidence-based interventions, and minority children use Early Intervention and CTM therapies at the lowest rates. Thus, there is a strong need for interventions that connect low-income and minority children with existing services that they are eligible for and could access. Primary-care based screening for ASD and other developmental delays is increasing. As a result, more children with suspected ASD are identified and referred from primary care. However, unlike other conditions for which early identification and treatment are critical (e.g., hearing impairment, congenital metabolic disorders), there exist no statewide or national systems to ensure that children identified with ASD risk are promptly evaluated and treated. While ASD services are theoretically available for most children in the US, they are often not accessed, leaving a critical gap between identification of suspected ASD in primary care and access to ASD diagnostic and treatment services, particularly for low-income and minority children. Research by our team suggests that this gap exceeds 2 ½ years on average. However, our prior research has also shown that when PCPs help families connect with ASD services, ASD diagnosis and treatment is timelier, and timely diagnosis is associated with increased use of evidence-based services. As a result, we propose a model statewide intervention to close the gap between identification of suspected ASD in safety-net (i.e., underserved setting) primary care clinics and use of diagnostic and treatment resources, for low-income and minority children.

4) Study Design

We propose a pilot clustered interventional trial with two arms. Clinics in the intervention arm receive Autism ALERT plus an ASD screening intervention (START Autism), and clinics in the comparison intervention (control) arm receive only START Autism (no Autism ALERT). As this is a pilot trial, primary outcomes of interest are feasibility and acceptability. We will additionally assess mechanism of outcome, preliminary efficacy, and protocol fidelity. Feasibility and acceptability will be assessed in intervention clinics. Mechanism of action and preliminary efficacy will be assessed by comparing intervention to control clinics. Fidelity is assessed in both arms. We will pilot test Autism ALERT in 6 safety-net primary care clinics in Oregon: 3 clinics will serve as intervention clinics, receiving both Autism ALERT and START Autism, and 3 clinics will serve as controls receiving START Autism only. Study arm will be assigned via coin-flip randomization of clinics, stratified for size and urbanicity, by a statistician who is not otherwise part of the study team.

In 2023 we received new funding from CareOregon to expand the project. As a result, this pilot study will be expanded to all of Portland-metro area. It will no longer include a control arm. Participants will be recruited off of Autism clinic waiting lists in the PDX metro area, and will be enrolled into the study to receive family navigation services from our partners at Help Me Grow.

5) Study Population

a) Number of Subjects

The three subject groups include clinics, child/parent dyads, and providers. We seek to enroll 7 safety net primary care practices. 70 child/parent dyads will participate in this study (20–baseline condition, 25–intervention, 25–control). We estimate that 30 providers will participate in this study (15–intervention; 15–control). The number of participants per site will depend on the size of the participating clinics.

Per the expansion to all of Portland-metro area, we estimate that there will be around 300 children enrolled in the next 3 years.

b) Inclusion and Exclusion Criteria

There are different eligibility requirements for clinics, children/parents, and providers.

To meet eligibility criteria, participating clinics must have >30% Medicaid enrollees or uninsured patients. Family medicine clinics must have >30% children. The study will be initially offered to safety-net primary care practices in 3 Oregon counties. We seek to enroll 6 clinics; if more than 6 clinics initially express interest, we will randomly choose 6 interested clinics, reserving at least two spots for non-metropolitan clinics. If fewer than 6 express interest, we will open recruitment to an additional two counties. Additional counties will be considered if recruitment is inadequate.

Child/parent dyads are eligible for inclusion when the child's PCP suspects the child has ASD. This can be for any reason, including the child having a high-risk ASD screen, or clinical concern. Children with prior ASD diagnoses or prior history of diagnostic evaluation for ASD are excluded. Enrolled children must be between age 12 and 54 months at enrollment to ensure EI/ECSE eligibility.

Provider subjects must be pediatric primary care providers (e.g., physician, nurse practitioner, physician assistant) licensed in Oregon, and must see children age 1-5 for well-child care. Subspecialists are excluded.

For the expansion, any child aged 1-5 years old on an Autism clinic waiting list at OHSU, Randall Children's Hospital, Providence Child Development Institute, Mindsights, or The Children's Program, or a referral from an Autism ALERT trained provider is eligible to join the study, if they have not previously been medically diagnosed with Autism.

c) Vulnerable Populations

This study will include children under 7, as described in the inclusion criteria. The study may also incidentally include pregnant women, as there are no exclusion criteria for the parent in a child/parent dyad. However, pregnancy is not a focus of the study. We will not obtain information about parent pregnancy status as part of this research. The study excludes neonates, decisionally impaired adults, and prisoners.

d) Setting

Autism ALERT services will be administered through Help Me Grow (HMG) Oregon. HMG is a national model system promoting optimal early childhood development via cross-system connectivity. Universal HMG components include: a centralized telephone access point to help families and professionals connect children with community-based programs and services; family and community outreach to advance developmental promotion and grow awareness of developmental resources; healthcare provider outreach to support early detection and intervention; and data collection to support program evaluation, bolster advocacy, and guide quality improvement.

In Oregon, HMG is part of the Swindells Resource Center at Providence Portland Medical Center. Swindells is a statewide disability support organization with offices in Portland, the Columbia River Valley, and Southern Oregon. In addition to HMG, Swindells has a family navigation program for children with developmental disabilities with experienced family navigator staff. Swindells is located in the same building as Oregon Pediatric Society, which will oversee the comparison intervention. Thus, colocation of Autism ALERT and HMG within Swindells places Autism ALERT and its staff in a supportive environment that is rich in information about childhood disability, and which is poised for statewide dissemination. The study Navigators are employed by HMG and the Swindells Resource Center. Swindells staff involved in the project are considered part of the study team and have submitted (or will submit in the future, in the case of the navigators as they have not yet been hired) required training documents. An IAA is being requested with Providence.

Additional data will be collected through a chart review performed by administrators at participating clinics. The clinic administrators will be considered engaged in research, and will complete and Individual Investigator Agreement (IIA), in addition to completing an IRB and study procedures training from the study team. The administrator will be compensated at a rate of $40 per hour at 6 sites and at a flat rate of $200 at one site that would not allow hourly payment.

This study is being designed with input from Emily Feinberg, an advisor and collaborating researcher from Boston Medical Center. Dr. Feinberg will interact with the study team and may provide training to the Navigators, who are part of the study team, but she will not interact with

or interview subjects, she will not be involved in the consent process, and she will never have access to identifiable private research data.

The CareOregon funding will provide a means of expansion to help families navigate Autism diagnosis services in all of Portland-metro area. While navigation services will still be provided through Help Me Grow, the service areas will now include all of Portland-metro. Specifically, any child on an autism clinic waitlist, or any child who has received an autism clinic referral can access navigation services through our program.

e) Recruitment Methods

The study has a clinic-based recruitment strategy. In order to assure that the intervention addresses the needs of diverse children who are underserved in autism care, study inclusion criteria mandate that participating clinics have at least 50% Medicaid or uninsured patients. In addition, to make sure sample size is adequate, Family Medicine clinics must have at least 30% children. Since one of the study's goals is to ultimately reduce racial and ethnic disparities in the early identification of ASD, we will strive to attain a racially and ethnically diverse family sample by specifically approaching clinics that serve a diverse patient base, including recruiting clinics in rural areas. Autism ALERT will initially be offered to all Oregon primary care clinics meeting inclusion criteria in selected counties. We seek to enroll 6 clinics; if more than 6 clinics initially express interest, we will randomly choose 6 interested clinics, reserving at least two spots for non-urban clinics. If fewer than 6 express interest, we will open recruitment to additional counties. In this way, we hope to recruit a sample that would be representative of primary care clinics who will ultimately participate in a larger-scale study.

Clinics will be recruited to the study with the help of the Oregon Pediatric Society. They will be approached initially via an approved recruitment email (see "Autism ALERT Email Templates"). The recruitment process will include a training session for all clinic staff, at which initial provider surveys and patient study packets will be distributed.

Families will initially receive a study packet from their provider at the time of the referral. The packet will contain a children's book, information about autism, an Early Intervention Referral Form, and a Study Interest Form. Aside from the study interest form and the phone scripts that are used for screening there are no other recruitment materials (e.g., emails, flyers) for family participants at this time. They will learn about the study first from the study interest form. The Study Interest Form will include some general information about the study, as well as a HIPAA authorization allowing disclosure of family contact information and some health information to the study team. The parent will sign the interest form, allowing the clinic to pass the family's contact information to the Navigator team. Navigators will then reach out to the family to complete the online consent process, or phone consent process as necessary (see more information below). Please see Family Consent Form attachments. Family enrollment will be incentivized with a children's book and $50 stipend per survey completed for both experimental and control groups. Provider participants may receive Continuing Medical Education credits and/or Part IV Maintenance of Certification credits, if desired, as part of their participation in this study. Clinics may also be entered into a raffle to incentivize their patients' referral to the study, based on whether they refer any patients to the study in a given time period. The raffle incentive will be a gift or food basket costing less than $100. Control arm clinics will also be given a box of chocolate on Valentine's day to further increase enrollment as enrollment is lagging in that arm.

For clinics in the OHSU system, referrals to the Autism diagnostic clinic will also be monitored for potential study recruitment. The diagnostic clinic staff will provide a list of MRNs of patients referred to the OHSU Autism Clinic, which will be transmitted via secure OHSU emails to the referring primary care provider and study team for inclusion in the study. Data will be transmitted as a list of MRNs, which the provider can use EPIC to identify and consider. If the provider gives permission, the study team will directly contact the family. No PHI will leave OHSU.

For the expansion, we will be recruiting participants through Autism clinic waitlists. We already have access to Providence and OHSU system waitlists as study staff are at both sites. We are requesting a HIPAA waiver to access patient contact information for all sites. We will contact participants off the waitlist to enroll in the study. We will also be providing Autism screening training to providers and clinics in Portland-metro who express interest. These providers will also be receiving CME credits. These providers can then refer children they suspect may have Autism to our project, in addition to sending in a referral to their nearest Autism clinic.

We will be contacting autism clinics to see if they would like to offer Autism ALERT enrollment to families from their site; if so a HIPAA Waiver will be completed for that site. If a family is intended to be recruited off the autism clinic waitlist, we will also be sending them an advance letter through either email or mail 2 weeks before proceeding to call them for enrollment. If possible, we will also attempt to contact parents through their Electronic Health Record portal such as MyChart. They will be instructed to contact the study team if they would like to opt-out via email, text, or phone.

f) Consent Process

There are two informed consent processes in this study: one for primary care providers, and one for children and their parents.

<u>Providers:</u>

For providers, an IRB-approved information sheet providing all elements of an informed consent will be provided by the study team at the clinic-based training. Providers will be given the option to opt out of the project entirely both initially and subsequently at any point. They do not have to offer the study intervention (Autism ALERT) to any family for whom it may seem inappropriate. Providers will sign a line at the end of the information sheet to indicate their consent; an electronic consent form will also be available for providers who miss the initial project meeting but who still want to participate.

<u>Families:</u>

The consent process for families (in the intervention and control groups) was different than that for primary care providers. Families for whom ASD is suspected will be handed a study interest form by their PCP. The PCP will ask if they are interested in learning more about the study. If so, they will indicate their interest by completing a study interest form. This study interest form will serve as authorization to allow the PCP to release information to the researchers for recruitment purposes. This signed interest form signifies study interest but is not a consent for the study. Interested parents will then be contacted by the study team via phone, text or email, to secure electronic signed consent or verbal consent.

Text messaging, using the secure Twilio app hosted by OHSU, will be utilized for scheduling phone calls. Text messaging will not be used to obtain consent but will be used to schedule a phone appointment to obtain consent. After consenting, the family may also choose to receive text messages from the navigator or study team with updates, reminders, or other scheduling requests.

Electronic consent: Families will sign consent electronically through a form built in Research Electronic Data Capture (REDCap). The software allows consent forms to be emailed directly to the email address that the participant provides upon signing the Study Interest Form. Per OHSU OCTRI requirements, participants will click a radio-box for yes or no, and if yes is selected, will enter their first and last name. This will be used in conjunction with the timestamp on the REDCap form to confirm consent to the study. In most cases, participants will provide electronic consent while on the phone with a Navigator, who will be able to confirm their identity through phone, email, and signature congruency.

Verbal Consent over the Phone: For families lacking internet access, a verbal consent via telephone will be provided in lieu of electronic signed consent. For these families we have requested a HIPAA waiver/alteration.

Family consent for Expansion: Children who are referred from their primary care providers will follow the same consent process as the pilot project, wherein a team member will reach out to them to receive electronic or verbal consent. We will request a HIPAA waiver to reach out to children on the OHSU CDRC, Providence Health Systems, and Legacy Health, Mindsights, and The Children's Program waitlists. This will allow us to contact families off the waitlist and ensure all families have the option of receiving a family navigator, as it is impractical to recruit every single primary care clinic in the Portland metro area to provide referrals to us.

In the pilot study - Medical record review: One member of the administrative staff of each participating clinic will be engaged in research, and will complete an IIA in addition to a specialized training on IRB and study procedures (see attachment). (This medical record review process will not be continued in the expansion) They will perform medical record review for each clinic to ascertain autism and developmental screening rates throughout the project. This person will have access to patient medical records as part of their usual work. The administrator will transmit de-identified medical record review information on PCP screening rates and referral patterns using the Medical Chart Review Tool to the study team via fax or secure email.. For this portion of the research, no identifiable patient information will be collected or relayed to the study team. Since no individual identifiers will be collected or transmitted, this portion of the study would not be considered human subjects research. It is not possible to obtain parent consent for this variety of work since thousands of children would be seen in pediatric practices during this time period (in our prior research study of similar design, it was >2000 visits over 6 months). Obtaining consent from this volume of patients in the pediatric office setting would make this project impossible to conduct, since no community pediatric practices would agree to participate. It is also

unnecessary because we are not getting any information that would readily identify individuals based on this chart data we obtain from the clinics.

The research team will repeatedly emphasize to community providers and study team members that participation is optional, and that families should not be coerced to participate. Given that many families of children at risk for autism have low literacy and/or limited English proficiency, all study materials including consent documents will be available at a 6th grade reading level in English and Spanish, and a study research assistant and family navigator will speak both languages fluently. Families speaking languages other than Spanish or English cannot enroll in the study but can be referred to Swindell's existing family navigation services (not part of the research study) if PCPs choose. We cannot enroll non-English/non-Spanish speakers in the study, because from a scientific standpoint their resource use would be quite different. In addition, the low numbers of enrollees in this group might create imbalances in the intervention and control arms that would make data interpretation challenging.

Pregnant women are only enrolled incidentally as part of the general parent study population; no study procedures will entail any risk to pregnant women or their fetuses. This project will not enroll human fetuses, neonates, or prisoners.

Modifications to the Consent Process

For the pilot, It should be noted that primary care sites are only obtaining authorization to share family contact information with the study team and not directly obtaining informed consent. Given the realities of community primary care (e.g., 15 to 20 minutes for an entire well child check), it is not possible for community primary care providers to obtain informed consent. In addition, doing so would require the study team to engage 30 community primary care providers in research, which it is unlikely that they would be consistently willing to do. Whenever possible, signed consent and authorization will be obtained electronically. However, we are requesting a waiver of consent documentation for families that cannot access the internet. This will allow us to obtain consent and authorization verbally for those individuals when it is not practicable to get signed consent and authorization. We have also submitted the necessary HIPAA documentation to allow for this verbal consent and authorization. Since families will be located all over the state of Oregon it will not be possible to mail and mail back a signed consent form in a timely way, and this delay might contaminate time-sensitive study outcomes. Therefore obtaining a signed consent in these cases is not possible.

For the expansion, we will need to obtain a HIPAA waiver to consent families off the Autism clinic waitlists. We are requesting a HIPAA waiver because it would not be possible to contact families to secure their interest in Autism ALERT without getting some information to contact them with. Having participating clinics contact families would place an unreasonable burden on clinic administrative staff, who are already overwhelmed by very long wait lists for autism services.

Non-English Speaking Subjects

Study materials will be available in English and Spanish. At the time of the referral, Spanish speaking patients can receive a study packet, including the study interest form, in Spanish. Navigator services in Spanish will also be available, so Spanish signed consent can be obtained by the study team. We cannot enroll non-English/non-Spanish speakers in the study, because

from a scientific standpoint their resource use would be quite different. In addition, the low numbers of enrollees in this group might create imbalances in the intervention and control arms that would make data interpretation challenging.

For the expansion, we will offer non-English/non-Spanish speakers the Autism ALERT navigation support; however, they will not receive the program evaluation measures because they have not been validated in other languages. We are working to make the evaluation measures available in more languages currently.

Assent of Children and Parent Permission

Since the children in the children/parent dyads in the study will be 5 years old or younger and have developmental difficulties, the capability of the children is so limited that they cannot reasonably be consulted about this research. For this reason, parental consent as described above and child assent will not be obtained.

Adults Unable to Consent/Decisionally Impaired

Adults who are unable to consent or who are otherwise decisionally impaired will not be considered eligible for the study at this time.

6) Procedures

Data collected from children and families includes process data about interactions with families, family survey data, and administrative data about children's medical and educational services use. Process data about interactions with families will be collected by family navigators (who are part of the research team) using the Care Coordination Management Tool and the Navigator Fidelity Checklist, which are study tools adapted from existing measures. Only members of the study team will have access to these data, and these data will be securely kept on the OHSU Sharepoint secure cloud storage throughout the study. These data are collected for the purposes of evaluating this research project.

Survey data from families will be collected in both study arms primarily via a mailed and/or online survey. The survey will be sent upon enrollment and 6 months after enrollment in Autism ALERT or the comparison intervention. Prior to the 6 month post-enrollment survey, a letter will be sent to families informing them of the upcoming survey and the $50 incentive for completion. A $50 cash or gift card incentive will be provided for survey completion. The survey will initially be sent 3 times via a secure RedCap link. Then non-responders will be contacted via telephone. Subjects who do not respond to either email or telephone will be sent a survey mailing with a $5 Dutch Bros coffee card. The survey will be marked with a study number only and will contain no personal identifiers. The study team will have a separate locked document that has the key linking study ID to personal information (see below). Completed surveys will be mailed back to the study team in an envelope and entered into a secure database behind the OHSU firewall. Original copies will stored in a locked file cabinet in the study team area.

For the expansion, survey data from families will be collected primarily via a mailed and/or online survey. The survey will be sent upon enrollment and 6 months after enrollment in Autism ALERT. Prior to the 6 month post-enrollment survey, a letter will be sent to families

informing them of the upcoming survey and the $10 incentive for completion. A $10 cash or gift card incentive will be provided for survey completion. The survey will initially be sent 3 times via a secure RedCap link. Then non-responders will be contacted via telephone. Subjects who do not respond to either email or telephone will be sent a survey mailing with a $5 Dutch Bros coffee card. The survey will be marked with a study number only and will contain no personal identifiers. The study team will have a separate locked document that has the key linking study ID to personal information (see below). Completed surveys will be mailed back to the study team in an envelope and entered into a secure database behind the OHSU firewall. Original copies will be stored in a locked file cabinet in the study team area.

Study team members will also be reaching out to families via email and/or phone, about participating in a semi-structured phone interview regarding their experiences with navigators, and the overall Autism diagnosis process. Families will be contacted via email and telephone to schedule these interviews. Participating families will receive $50 for completing the interview. Interviews will be recorded using WebEx or a digital audio recorder. These recordings will then be sent to GMR Transcription (HIPAA-compliant) to provide transcripts. Finally, the study team will code the interviews using Dedoose software to get a better understanding of parents' experiences in the Autism evaluation process.

Administrative data about children from the ecWeb (EI/ECSE) database will be governed by a Data Use Agreement (DUA) between Dr. Zuckerman (PI) and the Oregon Department of Education (ODE) . Consistent with our prior DUA's, we will request ecWeb access for only families with signed consent and a FERPA release for each child's educational data. The study team will submit names and dates of birth of people who signed consent and authorization to ODE staff, and ODE staff will allow the study team direct access to these individuals' data within ecWeb, ODE's database for Early Intervention. ODE staff are only releasing data and will not be considered engaged in research. These data include details on the dates and times of each child's referral, evaluation, and service plan. ODE staff will provide access to these data, which study team members will analyze, and are not considered part of the study team.

After consent, secure emails may be transmitted between the family navigator and the PCP, which may contain family information. These emails will be sent via encrypted email using the OHSU Secure Mailbox. This technology requires outside users to log into a website behind the OHSU firewall to send/receive the encrypted email, which minimizes the risk of privacy breach. Secure messages also automatically expire 30 days after creation and are removed from the Secure Mailbox server. Autism ALERT will also have a PCP interface in which PCPs can contact the study team and monitor the status of their patients. This interface will be part of OHSU's RedCap database and thus will also be hosted behind OHSU's firewall. It will require a unique user ID and password, which the study team will assign to each PCP. Each PCP will only be allowed to view his/her own patients on the secure website.

We will also survey providers about intervention fidelity, feasibility and acceptability. Survey data on providers will be collected via a mixed mode (in-person, email, mail, fax) survey, upon enrollment, at the end of subject enrollment (about patient portal use only) and at the end of the study intervention period. The survey will be sent to all providers whose clinics participated in the study, whether or not they were assigned to the study intervention or actually used Autism ALERT. Surveys will initially be sent to providers in person or via an email link, which will connect to a secure RedCap server. The survey will require entry of a study number only and will contain no individual identifiers. Non-responders, identified by a locked

key document to associate their names with their study IDs, will be sent follow-up emails, and will also be given the option to complete the survey via mail or fax. Paper surveys will be stored securely at OHSU as outlined above and destroyed approximately 6 months after publication of study results. The patient portal survey will be anonymous and no study ID or PHI will be entered. In addition to the survey, chart review data will be collected which contains information about each provider's practice patterns. These data are collected once every 3 months, in both arms. These data include number of children screened for ASD and number of children referred to EI/ECSE for an ASD concern. Note that referrals to Early Intervention are a separate process that is standard of care, and is not related to enrollment in the study. Providers will be encouraged to adhere to standard of care in terms of screening children for autism and referring to Early Intervention; however this process can be accomplished by usual methods without enrolling children in the study if providers prefer. Number of children screened for ASD, and screening test results, will be collected by a practice administrator, using an existing form that we have used in prior research projects. The administrator will be considered engaged in research through an IAA. This form will be encrypted and sent to the study team electronically using OHSU's secure server. Finally, fidelity data (e.g., PCP-Navigator Contact Log) will contain information about interactions between the PCP and the navigator. This file will be kept encrypted and stored on OHSU Box, a secure cloud server.

Follow-up provider interviews: Using data already collected from participating clinics, study team members will review referral rate data from all 41 participating pediatricians and stratify each according to referral rates; then, we will identify the highest-referring (top) and lowest referring (bottom) quartiles. High- and low-referring pediatricians will be invited to participate in a video qualitative interview, via email solicitation from the study team. **Providers will be emailed the information sheet as part of their study invitation; the information sheet will be reviewed and and a verbal consent will be recorded prior to the interview.** . They will be compensated $**100 via clincard** for participation after the interview. The interview will use Chart Stimulated Recall, a case-based interviewing technique which explores clinical reasoning and management decisions by guiding pediatricians to reflectively review medical records. For each pediatrician, the study team will select 2-3 patients with positive screens to Early Intervention services. With the study team, the pediatrician will review each patient's chart to discuss their recollection of the screening process, and why they did/did not refer the child to EI. The interviewer will also ask general questions regarding decision making about positive screens. All interviews will be recorded and professionally transcribed for analysis.

The pediatrician interview will last 45 minutes and use CSR methods. CSR, derived from the field of medical anthropology, is a case-based interviewing technique which explores clinical reasoning and management decisions by guiding pediatricians to reflectively review patient medical records. It permits patient, environmental, system, and other factors that can influence clinical decisions to emerge. CSR has been successfully used in other primary care research settings, such as with HIV screening. For each pediatrician, the study team will use the Autism ALERT database to select 2-3 of their patients who screened positive for ASD. Guided by the study team, the pediatrician will review each patient's chart notes **with PHI redacted** to discuss their recollection of the screening process, and why they either ultimately choose to refer or not

refer the child to Early Intervention Services. At the end of the CSR, the interviewer will ask general questions regarding decision making about positive ASD screens.

Qualitative Interview process. Interviews will be via telephone or videoconference **on Webex**, per subject preference, and last approximately 45 minutes. Immediately after each interview, the interviewer will create a structured memo describing the interview's key findings, interviewer reflections, and areas for future investigation. Memos will be distributed to all team members for review. All interviews will be recorded and professionally transcribed for analysis.

7) Data and Specimens

a) Handling of Data and Specimens

Four types of data are collected: System Process Measures, Family-Reported Measures, PCP-Reported Measures, and Administrative Measures. Data will be stored behind an OHSU firewall on Onedrive/Sharepoint io, a contracted secure cloud storage provider. Data will be destroyed about 6 months after publication of study results. Study interest forms will be sent via fax to the study team. The website providing PCP and Navigator access will be built by the OHSU IT department in RedCap, and will have the same security as any OHSU web applications.

b) Sharing of Results with Subjects

A summary of the study's findings will be shared at multiple community meetings around Oregon. As a result, some patients and providers will be notified of study results. However, we will have no consistent system for notifying patients or providers of study findings. Families who wish to receive copies of study publications can notify the study team.

An anticipated incidental finding is that children are found to have another developmental condition (instead of autism) in the context of their evaluation by Autism ALERT. We expect that this may be the case in 30-40% of children referred to the program. In these cases, the Autism ALERT navigator will connect these children to appropriate developmental resources for that condition. Because the Swindells Resource Center has expertise in a large number of developmental conditions, the navigator should have the resources to do this. In addition, the information will be communicated back to the child's PCP via the secure Autism ALERT interface.

c) Data and Specimen Banking

This study will be registered at ClinicalTrials.gov upon IRB approval. Study findings will be submitted to ClinicalTrials.gov according to its submission policy. All consent materials will include a specific statement relating to posting of clinical trial information at ClinicalTrials.gov. OHSU has an internal policy in place to ensure that clinical trials registration and results reporting occur in compliance with policy requirements.

For the initial intervention only, we will also report data to the National Database for Autism Research (NDAR), which is part of the NIMH Data Archive. All consent materials will include a specific statement relating to posting of study information at NDAR. NDAR data may be used for future unspecified research. The OHSU researchers will not otherwise save or use the data for future research so there is no OHSU repository. Only data on individuals who

signed authorization for release will be submitted to NDAR and ClinicalTrials.gov; i.e. no chart review or screening data will be submitted.

8) Data Analysis

Process data from CCMT and Navigator Fidelity Checklist will be used to calculate contact attempts, time to first contact, total time spent per family, and counts of specific navigator activities. Families who complete all calls will be compared to those who broke off contact, and specific points of participant drop-off will be calculated. We will assess whether specific intervention activities varied by family demographic characteristic and clinic site, to assess variability in acceptability, using bivariate analyses. Family survey data will also be used to assess feasibility and acceptability. Initial analyses will focus on families who participated in ALERT, assessing experience of care and improvement suggestions. Next, post-intervention family experience will be compared in intervention vs. control clinics using bivariate analyses with an intention-to-treat approach. We will also examine variation in experience outcomes overall, and by study arm, by demographic characteristics, in order to assess whether the intervention was appropriate for diverse families, and to target improvements. Parent responses to open-ended items will be assessed via conventional content analysis. Using the parent interviews, we will also qualitatively assess families' feelings towards the evaluation process, and for the intervention arm we will also be looking at experiences with family navigators.

PCP process data will be used in a similar fashion. PCP/Navigator interactions will be descriptively characterized, using the PCP-Navigator Con-tact log and use of the PCP Website. PCP survey data will be used to characterize PCPs' post-intervention experiences. PCPs' overall experiences will be compared in both arms using bivariate testing, and open-ended questions will be coded.

We will refine our mechanism hypotheses and measurement by examining change in family-and provider-reported outcomes (e.g., stress, empowerment) pre-and post-intervention, in both study arms, primarily using descriptive and bivariate tests. Exploratory analyses will assess whether mechanism outcomes differ by family race/ethnicity, English proficiency, or insurance type, both overall and by study arm, using bivariate or limited multivariable regression analyses. This will allow us to gather valuable descriptive data on variation in engagement of target mechanisms, which might allow for individualized messaging in future research.

We will compare efficacy outcomes in the Autism ALERT group to the baseline and control groups, using bivariate analyses and Kaplan-Meier curves for time to treatment variables. Estimated effect sizes for the subsequent R01 will be measured using Cohen's d. To test engagement of target mechanisms, we will assess whether efficacy outcomes differed by mechanistic outcome (e.g., whether parental stress was associated with time to treatment), using bivariate or limited multivariable models. We will also assess whether outcomes differ according to family demographic characteristics, both overall and by study arm, to test variability in intervention effects. Secondary and exploratory efficacy outcomes from ecWeb and Medicaid claims will be analyzed in the same framework.

Fidelity outcomes include both structural measures (e.g., receipt of program components) and procedural measures (e.g., quality of delivery of these components). We will use descriptive

statistics to assess delivery of the START Autism ± Autism ALERT training curriculum components. We will also use descriptive statistics to calculate navigator fidelity to the protocol, using the Navigator Fidelity Checklists. Checklists will also be cross-checked with recorded calls to assure accurate documentation. We will use descriptive statistics to characterize PCP use of the Autism ALERT website. To understand how Autism ALERT and START Autism altered PCP screening and referral behaviors, we will assess rate of ASD screening and EI/ECSE referral in both study arms in the baseline condition, and 3-and 6-months after initiation of START Autism ±Autism ALERT. As an exploratory analysis, we will assess whether racial/ethnic or language differences in PCP screening are present, and whether they vary by study arm or by PCP/clinic characteristics.

Our goals in this pilot study are to assess the feasibility and acceptability of the intervention and analysis, develop hypotheses regarding mechanism of action, and to provide context for defining meaningful differences and otherwise inform R01 power calculations. We intentionally have not powered to detect statistically significant differences. However, estimates will provide preliminary evidence of intervention effects, generate effect size estimates, and will help refine analytic strategy, efficacy hypotheses, and sample size estimates for a larger study.

Similar quantitative and qualitative approaches will be used for the expansion, except that there will be no control group so analyses will be primarily descriptive. We will also compare families who did versus did not engage in the Autism ALERT intervention after consenting.

Folllow Up Provider Interviews: Analysis of the provider interviews will use a phenomenological approach. We first will use structural coding to generate a limited set of predetermined codes to categorize data broadly. This initial coding structure will be reviewed after an initial read of 2 transcripts from each respondent class. Subsequently an emergent coding approach will be used by 2-3 trained research assistants, establishing novel codes to explore each global category with greater precision, using Dedoose. A final framework will be reviewed by 2 new pediatricians for triangulation.

9) Privacy, Confidentiality and Data Security

Administrative Safeguards: Only individuals on the study team have access to human subjects' materials. All electronic human subjects' data are stored on OHSU's network or Cloud behind OHSU's firewall. Individuals are only able to access human subjects' data through OHSU's network, which requires authentication through use of strong passwords. Access rights to folders will be granted only to project staff identified on the IRB protocol.

Physical Safeguards: All physical data (e.g., survey instruments, study consent forms, process data collected on patients and families) will be stored on the OHSU campus or at Providence Swindell's Center, in a locked file cabinet in the study team area, which is in a secured building. The study team area is separated from the rest of the building by a door that is locked at the end of each business day. All output containing individual identifiable information is treated as confidential data. This information is never transferred electronically via email or other protocols except via OHSU's Secure Mailbox. Shredders are used on any printed material containing individual identifiers. All physical human subjects' data (e.g., surveys) will be destroyed 6 months after publication of study results. Study interest forms will be faxed to the study team and securely stored on site.

Electronic Safeguards: All electronic data files for this study are kept on the OHSU network, behind the OHSU firewall. This network is monitored regularly and is accessible only to key personnel; as a result, the risk of unlawful penetration is very low. All data files are stored on the server, thereby eliminating the need to house data on laptop computers that are generally more of a security risk. OHSU's Information Technology Group (ITG) administers and maintains individual workstations, users' network folders, and group shared folders. Multiple daily snapshots of user network folders and group shared folders are made automatically and are available to be restored by the user without interaction by ITG. This makes version control of these folders very robust. Individual workstations are not backed up automatically; however, neither critical nor protected health information is stored on individual workstations.

10) Risks and Benefits

a) Risks to Subjects

Given that the probability of physical or psychological harm anticipated in this research is quite low, this study meets criteria for minimal risk research. However, there are some risks to both patients and providers. There is a risk of loss of protected subject data. This could happen during transfer of data from outside sites to OHSU or internally at any site. We will take multiple measures to mitigate this risk (see below).It is possible that families may experience discomfort or embarrassment as a result of the Autism ALERT intervention, especially since the family navigator may need to ask the family personal questions in order to better connect them with resources. It is also possible that patient's parents may falsely believe their child has autism if he/she is referred to Autism ALERT prior to receiving a full evaluation for autism. Thus it is possible that some families will be unnecessarily worried as a result of the intervention. However, research suggests that 90% of children who fail an autism screener have some kind of developmental condition, even if it is not autism. Thus, the risk of unnecessarily worrying families is rather low. We will connect families of children who are diagnosed with other developmental disabilities instead of or in addition to ASD, to the appropriate services. Similar risks may be applicable to providers—they may too experience discomfort knowing that a research team will be following up with patients whom they have identified to be at risk for autism. However, since enrollment in Autism ALERT is optional, providers who feel uncomfortable do not have to participate or enroll their patients, and individual providers can opt out of this research at any time.

b) Potential Benefits to Subjects

We anticipate that all subjects may benefit from the proposed research study, regardless of the arm of the intervention to which they are assigned (i.e., Autism ALERT + START Autism or START Autism only), because they will receive higher-quality ASD care overall. Providers in both arms of the study will benefit from the additional training around how to appropriately conduct developmental and autism-specific screenings. We anticipate that all providers will also benefit from additional information on the autism referral process, thus making them stronger practitioners for future patients. Further, we anticipate that families in the Autism ALERT + START Autism arm of the intervention will benefit from having an accelerated process in the diagnosis and treatment of autism; we anticipate that having a family navigator will

boost these family's empowerment and self-efficacy around making healthcare decisions for their child with autism. We anticipate that families in the START Autism only arm of the intervention will reap the benefits of the study indirectly from their child's health care provider, whom will train to better identify and treat autism.