Supporting Statement Part B

The Study to Explore Early Development (SEED) Follow-up Study

New

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Table of Contents

1. Respondent Universe and Sampling Methods.....3
2. Procedures for the Collection of Information.....9
3. Methods to Maximize Response Rates and Deal with Nonresponse.....14
4. Testing of Procedures.....14
5. Contacts for Statistical Aspects and Data Collection.....19

1. Respondent Universe and Sampling Methods

Since 2007, three phases of the Study to Explore Early Development (SEED) have been completed (SEED 1: 2007 to 2011; SEED 2: 2011-2016; SEED 3: 2016-2021).[1] Each phase of SEED collected developmental, medical, and risk factor data from caregivers and children aged 2 to 5 years with and without autism spectrum disorder (ASD). The SEED Follow-up Study (SEED F/U) will involve longitudinal follow-up of these participants. The purpose of SEED F/U is to collect data on the health, mental health, and development of SEED children as they age towards adolescence and young adulthood and better understand how these health-related outcomes differ between children, adolescents, and young adults with and without ASD. Follow-up data will be collected on three groups of children: children with autism spectrum disorders (ASD), children with other (non-ASD) developmental conditions (developmental disability [DD] comparison group), and children from the general population who were initially sampled from birth records (POP comparison group). SEED F/U data will be collected from SEED caregivers and/or their children at three different stages:

Stage 1: **Initial follow-up of SEED 1-3 participants** – SEED F/U includes one 60-minute survey for caregivers of SEED 1-3 children. All caregivers will be asked to complete of a set of core questions (i.e., the core survey) on their child's health service use/need, community/social support, bullying, discrimination, child safety, daily living skills, and family/financial impact as well as one of three survey supplements based on their child's original participation in SEED 1, 2, or 3.[2] The following eligibility criteria will be used to select the initial SEED F/U sample:

- **Criterion 1: At completion of SEED 1, 2, or 3 the child was given a final classification of ASD, DD, or POP.**
  *This criterion excludes children who participated in SEED but were given a final classification of **POSSIBLE/INDETERMINATE CASE** because they dropped out of the study prior to completing the assessments needed to assign a more definitive final classification or because they underwent the aforementioned assessments, but the results were not adequate to provide determinate final case status.*

- **Criterion 2: Caregiver gave consent for future follow-up.**
  As part of their original participation in SEED 1, 2, or 3, the child's caregiver was asked to sign a consent form that included consent for future follow-up.

[1] The OMB control numbers are 0920-0741 for SEED 1, and 0920-1171 for SEED 3. Please note that SEED 2 inadvertently received a clinical exemption and thus did not go through OMB review. A follow-up pilot study of SEED 1 participants, known as SEED Teen (OMB control number 0920-1219), was also conducted during the same time as SEED 3.

[2] The reason for basing the survey supplement on the child's participation in SEED 1, 2, or 3 is because each cohort represents children from relatively distinct developmental periods (i.e., SEED 1 = young adults; SEED 2 = adolescents; SEED 3 = school-aged children). As such, the survey supplements were designed to gather information on relevant key outcomes among children, adolescents, or young adults and clarify the specific behavioral, medical, and psychiatric conditions and service needs that emerge at these different stages of life.

- **<u>Criterion 3a</u>: Child completed the in-person developmental assessment as part of their participation in SEED 1, 2, or 3.**
  This criterion establishes that the SEED 1-3 participants included in the SEED F/U sample completed most study data collection instruments given before the developmental assessment and needed for longitudinal analyses (e.g., parent-report questionnaires, caregiver/maternal interview).

<u>OR</u>

- **<u>Criterion 3b</u>: For SEED 3 children in the DD group, the child's caregiver completed the Child Health History (CHH) form.**
  SEED 3 children in the DD group were not required to complete the in-person developmental assessment in order to receive a final classification of DD. As such, the criterion of having completed the in-person developmental assessment was replaced with completion of the CHH form by the child's caregiver.

Table 1 provides sample estimates of SEED 1-3 participants who met the eligibility criteria listed above from each site and will be selected for potential recruitment into initial follow-up study. The overall estimated sample size of eligible participants is 6,362.

Table 1. SEED F/U Cohort Description by SEED Site

SEED Site	SEED Phases Implemented	Approximate Age range in years in 2022	Estimated eligible participants in SEED F/U (ASD, DD, POP)
Colorado	1, 2, & 3	4-19	1,111
Georgia/California*	1, 2, & 3	4-19	1,952
Maryland	1, 2, & 3	4-19	935
Missouri	3	4-8	361
North Carolina/ Pennsylvania*	1, 2, & 3	4-19	1,796
Wisconsin	3	4-8	207
Estimated Total Eligible	1, 2, & 3	4-19	6,362

*Georgia and North Carolina will recruit eligible participants from the California and Pennsylvania sites, respectively, under the terms of a data use agreement to share contact information.

Based on participation rates from our preliminary follow-up of SEED 1 participants (i.e., SEED Teen), we estimate that we will establish contact with approximately 97% (N=6,171) of those eligible for the initial follow-up and that up to 60% of these participants will complete the core component of the first follow-up survey (3,703 participants), with roughly 1,000–1,300 participants per study group (i.e., ASD, DD, and POP).

An important goal of SEED F/U is to enable examination of SEED 1-3 participants in the ASD vs. non-ASD classification groups and to assess associations with low-frequency exposures. Given this, the expected sample size will allow SEED investigators to assess differences between the ASD and POP group as well as the ASD and DD group on most health and developmental indicators with an expected population prevalence of 5% or higher and for which the ASD:POP or ASD:DD prevalence ratio (PR) is 1.5 or higher (see **Table 2**). This sample size also provides

sufficient power to assess more rare health and developmental indicators (e.g., population prevalence < 5%) with slightly higher prevalence ratios (e.g., PR ≥ 1.75) as well as sufficient power to assess other health and developmental indicators with 10% or higher population prevalence but lower prevalence ratios (e.g., PR ≤ 1.5).

Table 2. Sample size required for analyses under various assumptions of health or developmental indicator prevalence and prevalence ratio comparing ASD vs POP or ASD vs. DD

Health, Developmental Indicator Prevalence (%)	Prevalence Ratio	Sample Size Needed in ASD Group
1	1.50	2319
5	1.50	1471
10	1.50	686
20	1.50	294
30	1.50	163
1	1.75	913
5	1.75	714
10	1.75	330
20	1.75	138
30	1.75	74
1	2.00	474
5	2.00	435
10	2.00	199
20	2.00	82
30	2.00	42
1	2.50	352
5	2.50	222
10	2.50	100
20	2.50	39
30	2.50	19

Note: all calculations assume 80% power, 5% alpha error, 1:1 ratio ASD vs. POP or ASD vs. DD.

Given the SEED 1-3 cohorts are roughly similar in size and the age-specific supplements will be administered at the same time as the core survey, we estimate a final sample of approximately 350-450 for each study arm and age cohort (middle childhood, adolescent, and early adult). This sample size provides sufficient power to assess differences between the ASD versus POP group or ASD versus DD group on health and developmental indicators with an expected population prevalence of 5% or higher and PR ≥ 2.00 (**Table 2**), as well as sufficient power to assess more common health and developmental indicators (e.g., 20% or higher population prevalence) with lower prevalence ratios (e.g., PR < 1.5).

Stage 2: **Second follow-up of SEED 1 participants** – After completion of the first follow-up survey, both caregivers and adult children from SEED 1 will be invited to take part in a second follow-up survey that consists of two study arms - one for the caregiver and one for their young adult child (hereinafter referred to as "young adults"). The purposes of the second follow-up surveys are to a) assess changes in service access and utilization that may occur following high school exit; and b) gather information only reliably obtained by self-report from young adults.

The following eligibility criteria will be used to select caregivers and young adults from SEED 1 to participate in a second follow-up survey:

1. **Caregiver completed the core survey and supplemental study instruments included in the first follow-up.** *This eligibility criterion is needed to assess if any changes in services, health, daily activities, etc. have occurred since high school.*
2. **Young adult is 18 years or older at the time of the survey**
3. **Young adult has exited high school**
4. **Young adult has the cognitive ability to participate.** *SEED 1 Caregivers participating in the Second Follow-up survey will be asked to assess the capacity of their young adult child to complete a similar survey independently, or with assistance.*

For the second follow-up survey of SEED 1 caregivers, we expect a response rate of 85% of those who completed the first follow-up survey. This is based on our recent experience with the SEED Teen study, in which 84% of participants who enrolled completed the study. Therefore, of the 1,234 SEED 1 caregivers who are expected to complete the first survey, we anticipate roughly 85% (N = 1,049) will complete the second follow-up survey with approximately 300-400 participants per study group (i.e., ASD, DD, and POP group). This sample size provides sufficient power to assess differences between the ASD versus POP group or ASD versus DD group on most health and developmental indicators with an expected population prevalence of 10% or higher and PR ≥1.75 and relatively rare health and developmental indicators with higher prevalence ratios (e.g., PR > 2.00) (**Table 2**).

For the second follow-up young adults, we will be contacting participants through the sample pool of caregivers who completed the first follow-up survey. Hence, we will have the same starting pool of 1,234, but we anticipate a lower response rate (40%) due to the need to obtain consent from the adult child, and because some of the adult children will not have the capacity to complete the survey because of significant language or cognitive difficulties. We therefore anticipate a final sample of 494 with approximately 150 to 200 participants from each of the three study groups (ASD, DD, & POP). This sample size provides sufficient power to assess differences between the ASD versus POP group or ASD versus DD group on health and developmental indicators with an expected population prevalence of 30% or higher and PR ≥1.5. It also provides sufficient power for less common health and developmental indicators (10% population prevalence 10%) with higher prevalence ratios (e.g., PR > 2.5) (**Table 2**).

Stage 3: Follow-up in-person assessment of cognitive abilities - The third stage of the SEED F/U involves an in-person clinical assessment on a subset of SEED children who participated in

either SEED 1 or SEED 2. This in-person assessment will provide an opportunity to re-evaluate the cognitive abilities of SEED children from the ASD and DD groups as they age into adolescence and adulthood in order to inform public policies on service eligibility and factors associated with developmental trajectory. The following eligibility criteria will be used to select participants for the in-person assessment:

- **Caregiver completed the core survey and supplemental study instruments included in the first follow-up.** *This is needed for future analyses examining the relation between cognitive ability and key outcomes assessed in the follow-up survey as well as to facilitate recruitment for the in-person assessment using more recent/current/accurate contact information.*
- **The participant completed the SEED developmental assessment during SEED 1 or SEED 2.** Note: *This eligibility criterion applies for the in-person assessment because the participant must have completed a baseline measure of cognitive abilities. Children from SEED 3 will not be included because children classified as DD in SEED 3 did not receive an assessment of cognitive abilities and because they will not be 8 years old at the time of recruitment, the age at which cognitive abilities become more stable.*
- **The participant was assigned a final classification of ASD or DD in SEED 1 or SEED 2** *Preschool children in the POP group have mean scores for cognitive ability in the average range and previous studies suggest that cognitive abilities are relatively stable for these children.*
- **Family's participation in SEED 1 or 2 was in Colorado, Georgia or Maryland.** *These three sites were funded to conduct assessments of cognitive abilities and will be scheduling and conducting in-person evaluations.*
- **The participant does not have uncorrected hearing or vision loss.** *The cognitive assessments completed during the follow-up in-person assessment are not valid for individuals who are deaf or blind; these individuals will therefore be excluded if hearing or vision loss is uncorrected.*

Table 3 provides sample estimates for children who met these eligibility criteria from each site and will be selected for potential recruitment for the follow-up in-person assessment.

Table 3. Estimated number of eligible participants for the in-person assessment

Sites conducting the in-person assessment	ASD	DD	Total
CO	153	180	333
GA	164	221	385
MD	146	117	263
Total	463	519	982

Additionally, previous SEED analyses [36] found that about 70% of children whose mother completed a telephone interview completed an in-person developmental evaluation.

Therefore, we estimate that 70% of the eligible children will complete the in-person assessment of cognitive abilities (N=687 Total, n= 324 for ASD, and n=363 for DD). Based on the power calculations [37] of an overall sample approaching 700 we will have strong statistical power (1-β ≥ .95) to detect small to medium effects and answer basic research questions such as a) whether cognitive abilities change from early childhood to adolescence or young adulthood (**Figure 1a**), b) whether cognitive abilities differ between adolescents/young adults with ASD and adolescents/young adults with other (non-ASD) developmental disabilities (**Figure 1b**), c) whether cognitive abilities are associated with a health or developmental outcome (**Figure 1c**), and d) whether cognitive ability in early childhood is predictive of cognitive ability in adolescence/young adulthood (**Figure 1d**).

Figure 1a.

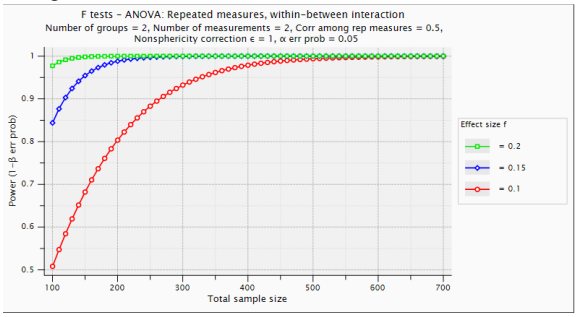


Figure 1b.

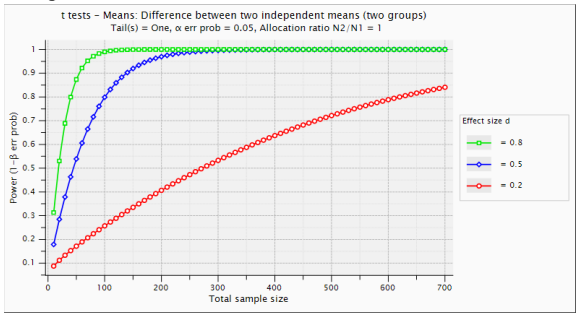


Figure 1c.

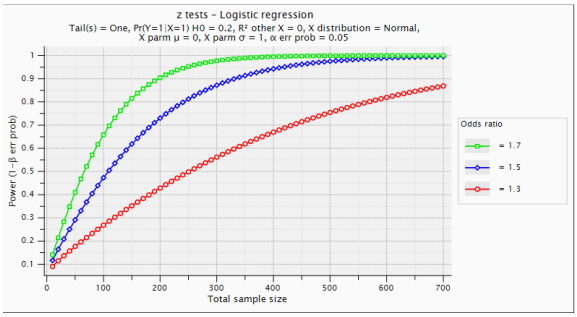
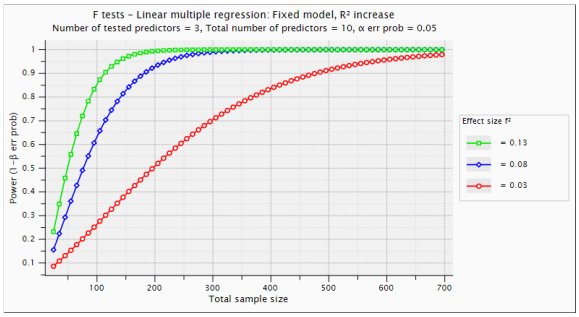


Figure 1d.



2. Procedures for the Collection of Information

Data collection for the SEED F/U will primarily consist of surveys (first follow-up survey of SEED 1-3 caregivers; second follow-up survey of SEED 1 caregivers; and second follow-up of SEED 1 young adults). For the surveys, participants will be encouraged to complete responses online to allow them to take advantage of information technology efficiencies; however, they will be offered the option to complete the surveys by the phone or by mail.

Assessments of cognitive abilities will be completed through in-person testing of individuals who were child participants in SEED 1-2.

First follow-up surveys

For the first follow-up survey of SEED 1-3 caregivers, initial contact with each participant will be an invitation letter mailed to the primary residence of the prospective participant (**Attachment 2a**). The invitation letter will include the following:

- Brief statement of the study purpose
- Brief description of what the participant will be asked to do, and anticipated time required
- Description of token of appreciation for time and effort
- Brief statements regarding the voluntary nature of study and protection of participant confidentiality
- Description of the ways the invitee can contact the site directly
- Statement informing the prospective participant that SEED study staff will follow-up soon with a phone call unless they opt out of contact.

Along with the invitation letter, potential participants will receive a response card allowing participants to "opt in" or "opt out" (**Attachment 2b**), and a tape measure – as a small token of appreciation for their previous contribution to SEED and to measure child's height for the SEED F/U Health and Development Core Survey.

For most potential participants, an invitation and enrollment call will be conducted after the potential participant has returned the response card expressing interest in the study. However, for some potential participants for whom a valid address could not be located, or they did not return a response card within 3 weeks, the first contact may occur via phone. A call guide has been developed and will serve as a detailed standard for study staff conducting the call (**Attachment 2c**). Calls will include the following components:

1. Interviewer introduces themselves and confirms that respondent is the correct invitee.
2. Brief discussion thanking respondent for past participation in SEED and providing a brief recap of the consenting process for that study – i.e., to describe that we are only contacting participants who previously gave permission for future contact.
3. Brief introduction to SEED F/U and request to conduct eligibility screen.
4. Conduct the eligibility screen.
5. If from the eligibility screen it is determined that the SEED F/U invitee is no longer the sampled child's caregiver/legal guardian, the study staff will query the respondent to determine if the child is living with another caregiver or legal guardian that may be interested in participating in the SEED F/U.
6. Once the correct invitee is contacted and the child is determined to be eligible for SEED F/U, study staff will provide a more detailed explanation including a discussion of the SEED F/U data collection instruments. The description will include a brief overview of content and time needed to complete each instrument.
7. Study staff will discuss the $30 token of appreciation for their participation in SEED F/U once the data collection instruments are completed.
8. Following this detailed explanation of the study, study staff will answer any questions from the invitee. Once all questions have been answered, study staff will

ask the respondent for verbal consent to participate in SEED F/U (**Attachment 2c**). As part of the verbal consent process, staff will explain that participation in SEED F/U is voluntary in nature and will describe the measures that will be taken to protect their privacy and confidentiality. This information will also be given to participants in a participant information sheet delivered by mail or email (Attachment 2d).

9. Study staff will indicate online completion is the preferred mode, but if caregivers indicate they are unable to complete the survey online, they will be given the option to complete study materials by phone and then by mail.
10. Study staff will also discuss optional consents that participants may choose to provide, independent of their decision to participate in the current SEED F/U protocol:
    a. Consent to be contacted for future studies and to have study data linked to other data sources. This consent will be requested verbally during the invitation and enrollment call (**Attachment 2c**).
    b. Consent to share genetic data from biosamples that were collected in the original SEED 1 study with genetic research consortiums established and maintained by the National Institutes of Health (NIH) (**Attachment 2e**). ***Note****: This consent form will only be discussed with parents/caregivers of SEED 1 children who provided consent to store biosamples, with identifiers, collected during the SEED 1, and did not enroll in the SEED Teen pilot follow-up study; SEED Teen participants were already provided the opportunity to provide consent to sharing their genetic data. This consent form will not be discussed with SEED 2 and SEED 3 participants who were already provided the opportunity to provide consent for sharing their genetic data.*

Following the invitation and enrollment call, the first follow-up core survey (**Attachment 2f-h**) and appropriate age supplements (middle childhood, **Attachment 3**; adolescent supplement **Attachment 4**; and young adult supplement, **Attachment 5**) will be administered according to the mode selected by the participants. Study staff may follow-up with all participants via phone, irrespective of initial mode of administration, to obtain responses on missing items and to clarify inconsistent responses.

Second Follow-up of SEED 1 Caregivers and Young Adults

Caregivers:

Following completion of the first follow-up survey, study staff will review the supplemental survey completed by SEED 1 caregivers (**Attachment 5**) to determine if the caregiver expressed interest in participating in a second follow-up survey and if information was provided about when their young adult child is expected to exit high school.

SEED 1 caregivers who express interest will receive an invitation email (**Attachment 6a**) that includes information about the purpose of the second follow-up survey and what they will be asked to do. Approximately 5-10 days after sending the invitation email to the caregiver, study staff will conduct the invitation and enrollment call (**Attachment 6b**). This call will include the

following components:

1. Study staff will introduce themselves (or reintroduce if the staff member had prior contact with the parent during the initial follow-up) and confirm that the caregiver is the correct invitee.
2. A brief discussion thanking respondent for recent participation in the first SEED F/U survey and providing a brief recap of the consenting process for that study.
3. Brief introduction to the purpose of the second F/U and provide caregivers with the option to complete the enrollment call at that time, or schedule the enrollment call for a later date that is more convenient.
4. Conduct the eligibility screen.
5. Following the description of the study instruments, study staff will ask the caregiver additional screening questions to determine if their young adult child can complete the study instruments independently or, with some assistance.
6. Once it is determined that the young adult can complete the study instruments independently or with some assistance, study staff will ask the caretaker if they can contact their young adult child directly to assess their interest in participating in the second follow-up.
7. Study staff will discuss the $5 gift card that the caregiver will receive as a token of appreciation for returning the survey.
8. Study staff will answer any questions the participant might have and then obtain verbal consent for participation (**Attachment 6b**). As part of the verbal consent process, study staff will explain that participation is voluntary in nature and will describe the measures that will be taken to protect privacy and confidentiality. This information will also be given to participants in a participant information sheet delivered by mail or email (Attachment 6c).
9. Staff will describe the survey materials participants will receive (**Attachment 6d**) and the different options for completing the study instruments. Study staff will indicate online completion is the preferred mode, but caregivers who indicate they are unable to complete the survey online will be given the option to complete study materials by phone and then by mail.

Study staff may follow-up with all participants via phone, irrespective of initial mode of administration, to obtain responses on missing items and to clarify inconsistent responses.

Young Adults:

Young adult participants from SEED 1 will not receive an invitation email until their caregiver grants study staff permission to contact them directly during the caregiver invitation and enrollment call for the second follow up study. If the caregiver indicates their young adult child would not be able to complete the survey due to their cognitive abilities, the young adult will be removed from the pool of eligible participants for the young adult survey. If permission is obtained, study staff will send invitation email (**Attachment 7a**), which is again a brief statement of the purpose, what participants will be asked to do, a description of the token of appreciation participants will receive for completing the survey, the voluntary nature of the

study, and a brief statement that a CDC representative will soon be given them a call. Approximately 5-10 days after sending the invitation email to the young adult, the invitation and enrollment call will take place. A detailed invitation call guide has been developed (**Attachment 7b**). This call will include the following components:

1. Brief introduction to the purpose of the second follow-up.
2. Conduct eligibility screen to ensure the invitee meets the following eligibility criteria for the second follow-up of SEED 1 participants.
3. For all young adults determined to be eligible for the second follow-up, study staff will provide a more detailed explanation of the study including estimated time needed to complete (approximately 40 minutes), and the $20 gift card that the young adult will receive, as a token of appreciation for their participation.
4. Following this detailed explanation, study staff will answer any questions the participant might have. Once all questions have been answered, study staff will obtain verbal consent to participate in the second follow-up study from the young adult (**Attachment 7b**). As part of the verbal consent process study staff will explain participation is voluntary and will describe the measures that will be taken to protect privacy and confidentiality. This information will also be given to participants in a participant information sheet delivered by mail or email (**Attachment 7c**).
5. Young adults will also be told that some questions included in the survey will ask if they have *ever* experienced unwanted sexual contact or *ever* had suicidal thoughts or behaviors. They will be instructed that they may choose not to answer these questions if they are not comfortable doing so. Due to the sensitive nature of these questions, the data collection packet for young adults will also include a brochure (**Attachment 7d**) of additional resources for the young adult should they have any questions or concerns about a mental health condition or having experienced sexual assault or suicidal thoughts.
6. Staff will describe the survey materials participants will receive (**Attachment 7e-h**) and the different options for completing the study instruments. Study staff will indicate online completion is the preferred mode, but young adults who indicate they are unable to complete the survey online will be given the option to complete study materials by phone and then by mail.

Study staff may follow-up with all participants via phone, irrespective of initial mode of administration, to obtain responses on missing items and to clarify inconsistent responses

In-Person Assessment of Cognitive Abilities

Following completion of the initial follow-up survey (including the core survey and survey supplement), study staff will review the supplemental survey completed by SEED 1 and 2 caregivers (**Attachment 4a and 5**) to determine if the caregiver expressed interest in having their child participate in the in-person assessment of cognitive abilities. For interested participants study staff will first send an invitation email (**Attachment 8a**), and then will make a

total of five attempts over 3 weeks to recruit participants for the in-person assessment through a recruitment call. A detailed recruitment call guide has been developed (**Attachment 8b**). Scheduling will be completed during the recruitment call whenever possible.

Informed consent will be obtained at the beginning of the clinic visit. The clinician working with the participant will describe the purpose and the tests and type of information that will be collected. The clinician will also describe other aspects of informed consent (e.g., voluntary participation), solicit questions from the participants. Written consent forms have been developed for caregivers (**Attachment 8c**), along with written assent for all participants in the assessment under the age of 18 or under a legal guardianship (**Attachment 8d**). Separate written consent forms have been developed for participants 18 years or older participating in the assessment (**Attachment 8e**).

Based on information from test publishers, it is estimated that the clinic visit will take about 90 minutes to complete including informed consent/assent (Attachment 8c-e) and completion of the clinic assessment (**Attachment 8f-g**). Participants will be given a $45 token of appreciation for time and effort, and will also be mailed a feedback letter describing their results (**Attachment 8h**).

3. Methods to Maximize Response Rates and Deal with Nonresponse

We are recruiting a group of individuals that completed nearly all SEED 1-3 study steps including an in depth in-person interview. Moreover, we are only contacting individuals who consented to future contacts. Thus, we have a motivated target study population for SEED F/U.

While we have kept in touch with families by sending periodic newsletters (unless they opted out of these mailings), we have not actively followed them to ensure we have current contact information. Study staff will utilize tracing procedures to locate the most recently available contact information for study participants. One or more people search engines such as Accurint, USPS, White Pages, and/or Google Maps, as well as social networking sites, will be used. These search engines will also be used to trace potential new contact information for participants who appear to have moved since their last SEED contact.

Given the diversity of our study population, we are mindful that some participants may have low literacy level that might pose a barrier to participation in a study in which participants are asked to complete self-administered forms. To minimize this barrier, study staff will tell participants during the invitation call that they will be available to help them complete the data collection instruments over the phone even if the participant chooses to complete the study instruments online or by mail. For the follow-up in-person assessment of cognitive abilities, trained site staff will be available to answer any questions prior to visiting the designated clinic space where the in-person assessment will take place. Site staff will also provide participants with a visual representation of activities and tasks they will be asked complete as part of the in-person assessment.

4. Testing of Procedures

Subject matter experts from across CDC, including experts in developmental disabilities, genetics, survey methodology, and health statistics were involved and consulted in the development of the SEED Follow-up Study. CDC has also consulted with SEED F/U grantees and self-advocates (e.g., Autism Self-Advocacy Network), and external autism partners (e.g., National Institute Health [NIH], National Institute of Mental Health [NIMH], Health Resources and Services Administration [HRSA], Autism Science Foundation, Autism Society, Autism Speaks) in identify priority areas and developing the survey instruments.

Procedures for developing survey instruments included the following: 1) selecting individual questions from existing surveys that have already undergone cognitive testing; 2) selecting standardized assessments that have been previously validated and used in numerous studies and clinical evaluations of children.

First Follow-up Survey for SEED 1-3 Caregivers

The first follow-up survey contains a core survey administered to all SEED 1-3 participants, and age supplements specific to participants from the SEED 1, 2 and 3 cohorts.

SEED Follow-up Health and Development Core Survey (**Attachment 2f**)

Based on feedback received from SEED investigators, self-advocates, and external autism partners, the following domains were selected for the Core Survey:

- Child's health
- Child's health care services
- Child's developmental services
- Child's education
- Child's activities and social participation
- Child's experiences with bullying and/or discrimination
- Child's safety and stressful life events
- Child's strengths
- Family and financial impacts
- Information about the caregiver
    - Demographics
    - Health
    - Community
    - Relationship with child
- Information on family and household

Additionally, lessons learned from the SEED Teen pilot study have been incorporated into the SEED Follow-up Studies including the omission of several questions that did not provide useful data. All other questions included in the SEED F/U Health and Development Core Survey

instrument were selected from existing child and adult health and development surveys or standardized questionnaires that have been cognitively tested. Sources for all survey questions were taken from one or more of the following instruments:

- National Survey of Children's Health (NSCH)
  - Weblink: https://www.cdc.gov/nchs/slaits/nsch.htm
- National Health Interview Survey (NHIS)
  - Weblink: https://www.cdc.gov/nchs/nhis/
- National Health and Nutrition Examination Survey (NHANES)
  - Weblink: https://www.cdc.gov/nchs/nhanes/
- Pregnancy Risk Assessment Monitoring System (PRAMS)
  - Weblink: https://www.cdc.gov/prams/
- Behavioral Risk Factor Surveillance System (BRFSS)
  - Weblink: https://www.cdc.gov/brfss/
- Infant Feeding Practices Study II (IFPS 11) and Year 6 Follow-Up (Y6FU), a U.S. nationally distributed longitudinal study of maternal health and infant health and feeding practices
  - Weblink: https://www.cdc.gov/breastfeeding/data/ifps/index.htm
- National Longitudinal Transition Study-2 (NLTS2)
  - Weblink: http://www.nlts2.org/
- Interactive Autism Network (IAN)
  - Weblink: https://iancommunity.org/
- SEED case-control study maternal and child health history forms
- SEED Teen Health and Development Survey (created as part of SEED's pilot follow-up study of SEED 1 participants)

Additionally, two standardized assessments were included along with the core survey instrument:

- Behavior Assessment System for Children – Third Edition (BASC-3) (**Attachment 2f**)
  - Weblink: BASC-3
- Vineland Adaptive Behavior Scales – Third Edition, parent domain-level form (VABS-3) (**Attachment 2g**)
  - Weblink: VABS-3

For most of the above instruments, extensive pilot and field testing was completed when the instruments were developed. All questions have been previously implemented in other surveys or research studies and thus have the added advantage of experience from researchers who have previously developed and thoroughly tested these survey questions that cover our research domains and have analyzed the data obtained from these questions. Moreover, virtually all survey questions we used were taken from surveys of nationally representative samples of U.S. children. This holds an added benefit of allowing us to compare SEED F/U data obtained from all three study groups – ASD, DD, and POP – to external prevalence rates for health indicators in U.S. children in the general population.

In compiling questions into a single SEED F/U Core Survey, we made only minor revisions to some of these existing questions. For example, in the SEED F/U Health and Development Core Survey, we revised all applicable questions to use consistent phrasing, "DURING THE PAST 12 MONTHS" (or other timeframe of interest) and our default placement was the beginning of a question. In some instances, we added option(s) to an existing multi-response question. For example, we added an option on "use of wellness therapy or mindfulness" to a question on complementary and alternative health care treatments because we know this is a common complementary treatment used by families of children with developmental disabilities.

Lastly, slight modifications were made to some questions if there was consensus among SEED F/U study investigators that the original source question included older terminology that is no longer used in the field (e.g., intellectual disability is now preferred terminology over mental retardation).

Survey Supplements for SEED 1, 2 and 3 Caregivers

*Survey Supplement for SEED 3 Caregivers (**Attachment 3**)*

The survey supplement for SEED 3 caregivers includes two standardized assessments:

- Behavior Rating Inventory of Executive Function, 2nd Edition (BRIEF2; **Attachment 3a**)
  - Weblink: BRIEF-2
- Short Sensory Profile 2 (SSP-2; see **Attachment 3b**)
  - Weblink: SSP-2

Note: this survey supplement only includes these two standardized assessments (i.e., no survey questions are included).

*Survey Supplement for SEED 2 Caregivers (**Attachment 4**)*

The survey supplement for SEED 2 caregivers includes additional survey questions pertaining to relevant adolescent outcomes such as planning for exiting high school, transitioning to adult health care, and sexual education (**Attachment 4a**) as well as one standardized assessment to assess current ASD symptomatology – the Social Responsiveness Scale, Second Edition (SRS-2; see **Attachment 4b**; https://www.wpspublish.com/srs-2-social-responsiveness-scale-second-edition).

All survey questions included in the Survey Supplement for SEED 2 Caregivers (**Attachment 4a**) were selected from national surveys or the previously approved SEED Teen Health and Development Survey and included as is or with only minor modifications as described above. Question sources include the following instruments:

- National Survey of Children's Health (NSCH)
  - Weblink: https://www.cdc.gov/nchs/slaits/nsch.htm
- National Health Interview Survey (NHIS)
  - Weblink: https://www.cdc.gov/nchs/nhis/
- National Health and Nutrition Examination Survey (NHANES)

    - Weblink: https://www.cdc.gov/nchs/nhanes/
- National Longitudinal Transition Study-2 (NLTS2)
    - Weblink: http://www.nlts2.org/
- Interactive Autism Network (IAN)
    - Weblink: https://iancommunity.org/
- SEED case-control study maternal and child health history forms
- SEED Teen Health and Development Survey

*Survey Supplement for SEED 1 Caregivers (**Attachment 5**)*

The survey supplement for SEED 1 caregivers includes additional survey questions designed to capture information on outcomes that are most relevant to young adults such as the transition plan for exiting high school, experiences with transitioning to adult health care, vocational training and support, transportation, and sexual health (**Attachment 5**).

Note: the survey supplement for SEED 1 caregivers does not include any standardized assessments.

All survey questions included in the Survey Supplement for SEED 1 caregivers were selected from national surveys or the previously approved SEED Teen Health and Development Survey. Question sources include the following instruments:

- National Survey of Children's Health (NSCH)
    - Weblink: https://www.cdc.gov/nchs/slaits/nsch.htm
- National Health Interview Survey (NHIS)
    - Weblink: https://www.cdc.gov/nchs/nhis/
- National Health and Nutrition Examination Survey (NHANES)
    - Weblink: https://www.cdc.gov/nchs/nhanes/
- National Longitudinal Transition Study-2 (NLTS2)
    - Weblink: http://www.nlts2.org/
- Interactive Autism Network (IAN)
    - Weblink: https://iancommunity.org/
- SEED case-control study maternal and child health history forms
- SEED Teen Health and Development Survey

As in the SEED F/U Health and Development Core Survey, we made only minor revisions or modifications to some of these existing questions.

Second Follow-up of SEED 1 Participants

Second Follow-up Survey for Caregivers (caregiver-report) (**Attachment 6c**)

The second follow-up survey for caregivers of adult children will survey questions about their child's loss or change in services, vocational training and support, transition to post-secondary education, daily activities, and social participation following high school exit. The survey will take approximately 5 minutes for caregivers to complete. All survey questions included in the

second follow-up survey for caregivers were selected from national surveys or the previously approved SEED Teen Health and Development Survey. Question sources include the following instruments:

- National Survey of Children's Health (NSCH)
  - Weblink: https://www.cdc.gov/nchs/slaits/nsch.htm
- National Longitudinal Transition Study-2 (NLTS2)
  - Weblink: http://www.nlts2.org/
- SEED Teen – Health and Development Survey

Second Follow-up Survey for Young Adults (self-report) (**Attachment 7**)

The second follow-up survey for SEED 1 young adults (i.e., self-report survey) is intended for young adults 18 years or older and includes similar questions to those included in the caregiver-report survey. However, many emerging issues surrounding the transition to adulthood among adolescents with ASD require self rather than caregiver report. Therefore, the self-report survey for young adults will also include survey questions related to job experience and satisfaction, financial support, health care service use and need, sex education and behavior, romantic relationships and sexual orientation, anxiety and depression, suicidality, substance use, and personal beliefs and interests.

All survey questions included in the second follow-up survey for young adults (**Attachment 7e**) were selected from national surveys or the previously approved SEED Teen Health and Development Survey. Question sources include the following instruments:

- National Survey of Children's Health (NSCH)
  - Weblink: https://www.cdc.gov/nchs/slaits/nsch.htm
- National Health and Nutrition Examination Survey (NHANES)
  - Weblink: https://www.cdc.gov/nchs/nhanes/
- National Longitudinal Transition Study-2 (NLTS2)
  - Weblink: http://www.nlts2.org/
- Youth Risk Behavior Survey (YRBS)
  - Weblink: https://www.cdc.gov/healthyyouth/data/yrbs/questionnaires.htm
- The National Longitudinal Study of Adolescent to Adult Health (Add Health)
  - Weblink: https://addhealth-navigator.cpc.unc.edu/
- National Survey of Family Growth (NSFG)
  - Weblink: https://www.cdc.gov/nchs/nsfg/index.htm
- SEED Teen – Health and Development Survey

In addition to these survey questions, young adults will also be asked to complete three standardized assessments designed to capture detailed information on quality of life and social camouflaging (i.e., monitoring and modifying behavior to mask ASD symptoms). These standardized assessments are described below.

- World Health Organization Quality of Life Scale - Brief Version (WHOQOL-BREF) (**Attachment 7f**)
    - Weblink: WHOQoL-BREF
- WHOQOL Disabilities Module (WHOQoL-DIS) (**Attachment 7g**)
    - Weblink: WHOQoL-DIS
- Camouflaging Autistic Traits Questionnaire (CAT-Q) (**Attachment 7h**)
    - Weblink: CAT-Q

Description of Study Instruments included in the In-person Cognitive Assessments

The in-person cognitive assessment will include two standardized assessments that measure verbal and non-verbal skills and how well a person can make sense of new information compared to other people the same age:

- Stanford-Binet Intelligence Scales, Fifth Edition (SB-5) (**Attachment 8f**)
    - Weblink: SB-5
- NIH Toolbox Pattern Comparison Processing Speed Test (**Attachment 8g**)
    - Weblink: NIH Toolbox

5. Contacts for Statistical Aspects and Data Collection

The development and implementation of SEED F/U is a collaborative effort between CDC's National Center on Birth Defects and Developmental Disabilities (NCBDDD) and five extramural SEED sites located in Colorado, Missouri, Maryland, North Carolina, and Wisconsin. CDC will serve as the sixth site in Georgia. CDC and extramural sites will jointly conduct the follow-up studies using a common IRB protocol.

CDC and extramural sites will jointly conduct the initial follow-up with SEED 1-3 caregivers and second follow-up with SEED 1 caregivers and young adults using a common IRB protocol.

For the in-person assessment, CDC will collect information in Georgia, and two of the extramural sites (University of Colorado Anschutz Medical Campus; and Johns Hopkins University) will do so in in Colorado and Maryland, respectively (3 sites total).

NCBDDD also funded Chickasaw Nation Industries (CNI) to provide scientific and technical support to facilitate SEED F/U research, including data collection, management, analysis, and research coordination. CNI will work collaboratively with all SEED F/U sites to recruit, enroll, and complete data collection.

NCBDDD is also supported through contracts with Allied Technologies, LLC. Staff members will provide administrative and program/data management support to the SEED F/U project. The Allied Technologies and CNI staff members are integrated with CDC staff and work on this and other projects in the Child Development and Disabilities Branch (CDDB), NCBDDD, CDC.

SEED F/U Key Staff at CDC

Karen Pazol (Team Lead, Epidemiology Team, CDDB, NCBDDD, CDC) is the Principal Investigator (PI) and Science Lead for the SEED F/U Studies. Dr. Pazol is responsible for scientific oversight and all project activities. Other CDC personnel currently involved in SEED F/U are Aimee Alexander (GA SEED F/U PI), Matthew Maenner (Acting CDDB Branch Chief), Seema Gupta (SEED Project Coordinator), Shericka Harris (Data Coordinator), Eric Jacobs (Epidemiologist), Katie Overwyk (Data Programmer), Patrick Powell (Co-Science Lead and Clinician), Lin Tian (Statistician), Sarah Tinker (CDDB Senior Scientist), and Lisa Wiggins (Co-Science Lead and Clinical Lead). These individuals also serve as co-investigators.

SEED F/U Key Staff at Extramural Sites

Colorado (CO), University of Colorado Anschutz Medical Campus: Carolyn DiGuiseppi is the PI for the CO SEED F/U project Component A, Cordelia Robinson Rosenberg is the PI for Component B, and Kristina Hightshoe is the Project Coordinator for both components. Co-investigators are Tessa Crume, Sandra Friedman, Jessica Sanders, Nuri Reyes, Ann Reynolds, Steven Rosenberg, and Sarah Schmiege. CO SEED collected data from participants in SEED 1, SEED 2, and SEED 3.

Maryland (MD), Johns Hopkins University: Christine Ladd-Acosta is the PI for the MD SEED F/U project Component A, Heather Volk is the PI for Component B, and Jamie Kaczaniuk is the Project Coordinator for both components. Co-investigators are Elizabeth Wise, Rebecca Landa, and Christine Hess. MD SEED collected data from participants in SEED 1, SEED 2, and SEED 3. Johns Hopkins University continues to host the repository of biospecimens from SEED 1-3.

Missouri (MO), Washington University at St. Louis: Robert Fitzgerald is the PI for the MO SEED F/U project Component A and Lauren Eck is the Project Coordinator. Co-investigators are John Constantino and Cy Nadler. MO SEED collected data from participants in SEED 3.

North Carolina (NC), University of North Carolina at Chapel Hill: Julie Daniels is the PI for the NC SEED F/U project Component A and Chyrise Bradley is the Project Coordinator. Co-investigators are Tanya Garcia, Rebecca Pretzel, and Alan Kinlaw. NC SEED collected data from participants in SEED 1, SEED 2, and SEED 3 and led the SEED Teen pilot project alongside CDC. NC will also be following up with SEED 1 and SEED 2 participants from Pennsylvania.

Wisconsin (WI), University of Wisconsin at Madison: Maureen Durkin is the PI for the WI SEED F/U project Component A and Leslie Seltzer is the Project Coordinator. Co-investigators are Maria Stanley and Hayley Crain. WI SEED collected data from participants in SEED 3.