COMPILED RESPONSES[1] TO REQUEST FOR PUBLIC COMMENTS ON ABCD: CONTINUING THE ARC OF DEVELOPMENT EXPERT PANEL MEETING

Respondent 1

How do the ambassadors feel about apps for RECEIVING information (findings, resources) v. data collection? Do they think their phones have enough storage for data collection on their phones?

Respondent 2

What are the considerations for privacy for participants? Especially with location tracking and social networks

Are the multiple dimensions of social behaviors/relationships that are not the traditional interactions accounted for? Thinking about interactions in the real world but also digitally - and the differing levels/contectiveness

Qualitative data will be important for contextualizing data - certainly want to collect such data (and meta data) to understand these complex relationships

Respondent 3

We could poll the existing ABCD cohort to determine what level of social media and geolocation tracking they would be comfortable with.

Respondent 4

I think the two most important and immediate factors that susceptible youth to substance use are drop out from the school and having friends who are using substances. so, If we are going to be efficient in data gathering, we need to ask questions about them.

Respondent 5

Related to the neurocognition in the setting of substance use risk and resilience, wondering if there is a way to link the ABCD with HBCD or OBOE studies to detect early changes and later risk or resilience? Will there be a plan to recruit/roll over the subjects in the HBCD and OBOE studies into the ABCD? Thank you.

Respondent 6

While I recognize the burden associated with additional data collection, I just want to add that acquiring EEG data in this cohort would be amazing, as it offers temporal resolution and neural dynamics that fMRI alone can't capture.

I recommend retaining measures of executive function/inhibitory control, working memory, and

[1]All responses appear as received – the only edits were to remove attributions, salutations, and closings/signatures

processing speed from the NIH Toolbox. These core cognitive domains are strongly implicated in the development of mental health and substance use disorders during young adulthood. Executive function and working memory are central to self-regulation and decision-making, while processing speed reflects general cognitive efficiency, which is often disrupted in psychiatric conditions. As a researcher, I believe continued assessment of these domains will be critical for understanding neurocognitive risk pathways over time.

Respondent 7

I think if we are tying physical health to brain health/cognitive functioning/mental health, the 2 main systems would be cardiovascular and GI. (Inflammation would be good too.)

But someone brought up Pain assessments, and I think we could/should do more assessments of GI functioning (which includes abdominal pain) and tie that to brain health. We can get some of that with dietary intake and stool microbiome, but if we could assess gut motility or other measures (like inflammation and LFTs) that would be great.

Pain assessments are out of my realm, but we should consider that maybe with survey, or EMA?

Respondent 8

While I recognize this may be a long shot, incorporating the HiTOP-PRO (also referred to as the HiTOP-SR) in at least a subsample of the ABCD Study would be highly valuable, given the limitations of the CBCL and ASR in capturing the full spectrum of psychopathology. As the field increasingly moves toward comprehensive dimensional models of psychopathology, it would be an important opportunity to validate this emerging framework within a large, diverse, and deeply phenotyped sample.

Respondent 9

Potential areas of value to add/modify in A-ABCD:

- Using AI or natural language processing to analyze free-text or oral responses (that are captioned during the interview to create documents that can then be processed via AI) would be very useful in this study. May also be engaging for the participants and help with retention. Several topics could be assessed this way:
    - Asking a few key short-answer/free text questions about their social well-being, connection to others, values, or self-identity may be quite valuable and to the point.
    - Value of assessing "future orientation", optimism vs. pessimism, moral distress, living in congruence with your values.
    - How do people cope with stress?
- If we have mid-level funding, could we do EMA to obtain physical behaviors, substance use, and medical conditions (what is physically happening at this time?, what are you doing?), and then tie questions about their current mental health, motivation, values, coping (how are you feeling?, how are you coping?) to these activities or situations.

- With all these assessments, can we vary or alternate when certain domain topics are asked.

Physical Health Domain:

- Go to the participants home to get assessments: LightShip, ExamOne?
- Potential to do a sub-study with more intensive and less intensive assessments for several domains (dietary intake, physical activity, substance use) and evaluate how reliable the "light" assessments are.
- Getting Dexa scans for participants (or Bioimpedence). Conducting PFTs or spirometry during this visit to assess Lung Function
- Increasing blood tests to include inflammatory markers and LFTs, Chem 7 (or just get CBP)
- Could also assess other nutrition labs in addition to getting dietary intake data
- Coordinate these measures with ECHO and All of Us.
- Consider doing a sub-study to capture changes with pregnancy
- Make sure to assess Life's Essential 8
- Add Cardiac MRI to scanning protocol, measure arterial thickness, endothelial dysfunction, measuring widening of the pulse pressure
- Add PaxGene tube collection for storage and later use

Respondent 10

Want to emphasize the importance of characterizing adulthood especially in processes that have stabilized, as one of the major goals is to understand individual variability and this data is optimal for predictive models. Many disorders do not become established until later adulthood and having their developmental trajectory becomes critical to inform etiology, prevention, and intervention.

Respondent 11

Please consider this attached article when considering any change in the ABCD resting state scans. Those of us promoting a movie resting state scan have been proposing it in addition to the resting state scan and to harmonize with HBCD's proposed movie scans that could also tap into social processing which ABCD does not currently measure very well.

Longer scans boost prediction and cut costs in brain-wide association studies

I think it is important to note based on the conversation of fMRI tasks that the ABCD en-back task does in fact predict mental health outcomes, stress, community violence and discrimination so I would hope that the committee seriously consider the ABCD literature before considering replacing tasks with new ones that tap into stress and executive functioning given the emotional n-back task tapes into both based on many papers.

Also the fMRI tasks were based on changes during the extended period of adolescence into the 20s as well as related to substance and alcohol abuse. This information is in the original ABCD grant submission by the consortium.

Respondent 12

Here are some thoughts related to the imaging session:

1. Access to derived metrics from established research groups such as those led by Thomas Yeo would be amazing. As a small neuroimaging lab, my group faces substantial logistical and computational barriers to downloading and processing the full ABCD raw imaging data. Sharing high-quality derived data not only enhances accessibility and equity across research groups but also promotes methodological consistency. There is also a growing awareness in the neuroimaging community of the environmental impact associated with large-scale data storage and processing. Recent efforts to measure and reduce the carbon footprint of neuroimaging pipelines underscore the importance of avoiding redundant computation. Generating and sharing metrics in a coordinated, standardized manner—rather than having multiple groups independently replicate the same resource-intensive preprocessing steps—supports both sustainability and scientific rigor. This reduces unnecessary energy consumption, aligns with open-science principles, and ensures that our field moves toward more efficient and environmentally responsible research practices. Rather than wait for groups to approach the study, ABCD could put out a call to all neuroimagers to see who has metrics to share. Other neuroimagers who have independently processed raw ABCD imaging data besides Thomas Yeo and who may be interested include Damien Fair, Ted Satterthwaite, Marc Berman, and Neil Woodward.
2. One consideration that I did not hear raised is the challenge of working with the emotional N-back task. While this paradigm was a creative attempt to simultaneously probe working memory and emotion processing, it has well-known limitations due to the confounding of cognitive load and emotional reactivity. In practice, it has proven difficult to include this task in grants and publications, as it is not straightforward to disentangle the contributions of affective processing from those of working memory demands. This ambiguity complicates interpretation and limits utility for answering more targeted questions in either domain. That said, I understand and support the need for continuity in imaging protocols across longitudinal waves of ABCD and recognize that maintaining consistency may require continued collection of this task. I would just encourage careful consideration in the selection of any new paradigms—particularly those designed to serve dual purposes. While "two-for-one" tasks are appealing from a time-efficiency perspective, they often introduce interpretive trade-offs that may reduce their usefulness for hypothesis-driven research.

Respondent 13

ABCD 2.0 should consider recruiting a smaller subset of lower income individuals. We know that this is the group that has been the hardest to retain and is underrepresented in the ABCD 1.0

sample. Though the new sample would not have longitudinal data from the past, we would be set up to include them in future waves.

Respondent 14

There is emerging psychological and imaging data that 18-21 year olds look more similar to younger teens than > 21 year olds (e.g. https://pubmed.ncbi.nlm.nih.gov/26911914/; https://pubmed.ncbi.nlm.nih.gov/30762417/#&gid=article-figures&pid=figure-1-uid-0; https://pubmed.ncbi.nlm.nih.gov/28009272/). This raises the important question of when is adolescent an adult? As such if imaging is reduced from every 2 years to perhaps every 3-5 years then please allow this study to address this trajectory that is so important for laws and health policies by acquiring data when they are 20-21, 25-26, 29-30. To only scan at 20 and 25 might will miss additional changes from 26-30 and to only scan at 25 and 30 would miss the critical data for 20-21 olds who often serve as adult comparisons when in fact there are continued changes.

Respondent 15

The mindLAMP app is used in a multitude of research studies and settings. The app consists of four pages, spelling the acronym LAMP.

Learn: Patients can access helpful mental health resources and tips. The clinician can specify what resources are available to each patient.
Assess: Patients can complete surveys about their symptoms, moods, and activities. These surveys are customized by the clinician and patient to address specific needs.
Manage: Patients can complete activities and learn skills to manage symptoms such as a mindful breathing activity, a journaling feature, and more. Here, the clinician can also create activities for each patient.
Prevent: In this section, patients can view all data collected in the app and track their own treatment progress. This section also allows patients to leave messages for their clinicians.

Respondent 16

Adding thoughts from Day 2:

- Would be great to fund some "super data users" who know the dataset well enough to be able to run analyses for outside researchers (using imaging data and tabulated data).
    - People could apply to access their services, and work with them to run analyses. Or if people want to run their own analyses, they can submit an application to NIH, but part of the analytic team would be at this "hub" for analysis.
    - Working with stats people who know the data well, would really help the larger community of researchers.

- We could also do more regular outreach (like monthly) to participants to alert them of new study findings or something new that's happening at an ABCD site. (Modeling this after the All of Us study)

Respondent 17

On the topic of feeding back to participants about their own trajectory data - there is a free research tool for analysing and visualizing longitudinal data (including individual-level trajectories) which may be relevant: https://academic.oup.com/ije/article/54/4/dyaf095/8186977 (full disclosure, I was involved in developing this software).

Respondent 18

I imagine that compensation may need to increase in ABCD 2.0. I don't know what they get now, but in my own lab, I have found that while 100 dollars for a three-part study (7 hours total) was a strong incentive for 12-17 year olds, for adults this is not enough. We had participants say that it was not worth the cost of taking off work/finding a babysitter just to participate. Just pointing out that maintaining participant retention will likely require more age-appropriate compensation.

Respondent 19

I've been watching the video cast and one thing that has not been mentioned is the potential value of obtaining DNA samples/ whole-genome genotyping for the PARENTs of the ABCD participants. Genetics is an enormously valuable aspect of the study, and the existing whole-genome genotypes and sequencing on the participants are fantastic, but having familial information would add substantial value (please see dot: 10.1038/s41586-024-07721-5).

Respondent 20

RESOURCE: Nutrition for Precision Health, powered by the All of Us Research https://commonfund.nih.gov/nutritionforprecisionhealth

Respondent 21

RESOURCE: SnapCalorie taps AI to estimate the caloric content of food from photos | TechCrunch
https://techcrunch.com/2023/06/26/snapcalorie-computer-vision-health-app-raises-3m/

Respondent 22

Below are three practical points I hope you will consider.

First, it is very difficult to sustain the staffing model that has been required for ABCD 1.0. The funds provided allow for a staff mostly made up of post-baccalaureate trainees who are seeking experience before medical school, graduate school, law school, etc. However, this leads to a significant training burden for the PIs and annual staff turnover. With the current funding, it is impossible to build a team with more senior associates (e.g., research scientists or research associates who wish to remain in those roles). The latter would be more desirable to reduce training demands, minimize turnover, and have a professional staff with continuity. Of course,

the specifics may depend on how data are collected (e.g., self-guided online surveys vs. remote calls vs. in-person visits).

Second, time and funding need to be allocated to developing a more automated scheduling and communication platform. We should be able to auto-send reminders to families and allow them to schedule appointments online, similar to a doctor's office. We should not be relying on Google spreadsheets and other basic platforms that are not well-integrated with the PII/REDCap systems. A significant amount of time and effort—equivalent to a full-time staff member—is currently spent on tasks that could largely be automated.

Finally, the value of the imaging data is immense. However, its feasibility is uncertain given the increasing likelihood that participants will relocate. At our site, we are already seeing fewer participants from surrounding states. Greater clarity on how these data will be collected in the future would be helpful.

Respondent 23

I would strongly encourage the collection of peripheral inflammatory measures in blood in the next wave of data collection. I would also strongly encourage continued collection of data about exposure to various social adversities such as violence, poverty, and social isolation. I would suggest stopping collecting the stop signal task as a fMRI task because it's really only analyzable behaviorally and the fMRI data are very difficult to analyze. I would instead recommend collecting a learning task. I think it's important that we collect data on educational and vocational pursuits in ABCD participants as they transition into young adulthood.

Respondent 24

The Importance of Thinking Developmentally: This may seem obvious—ABCD has "Development" in the title—but it may not be, because it also has "Adolescents" in the title. The ABCD study has been studying this sample as adolescents, but it is important to recognize that they are not adolescents any more. I urge you not to think of this as an "extended adolescence" or "late adolescence" or you will miss many of them most interesting things about them at this age. Prior to age 18, it is normative in American society for adolescents to live with their family of origin; to be attending secondary school; to be experiencing the massive physical changes of puberty; to be a minor under the law; and to be not in the workforce or working only part-time. By age 20, none of these are normative any longer. So what is now normative? Very little! They have many kinds of living arrangements; many varieties of education, training, and employment; and many variations of involvement (or not) in romantic relationships. During the decade of the twenties they will change jobs, residences, and romantic partners more often than in any previous or subsequent decade of life. What chaos. And what a goldmine. Be sure you acquaint yourself with some of the literature on emerging adulthood so you can gain some ideas about what new questions are most important to ask about this phase of the lifespan that may not have pertained to them as adolescents. I will also be happy to help with this upon request.

Culture is Crucial: The US is a country of remarkable and rapidly growing cultural diversity. The past 30 years have been a period of massive immigration, adding to an already immense

range of cultural diversity. Despite the recent political backlash to this diversity, it is and will remain a crucial part of growing up in the US. The cohort that is the subject of the ABCD study is the most culturally diverse in American history.

So, it is essential in the ABCD to recognize, document, and explore how cultural factors influence development. It is vastly different to enter emerging adulthood as a child of recent Central American immigrants, or of urban African Americans, or 3rd generation Asian Americans, among many other variations. **Using ethnic group as a demographic variable in quantitative analyses is not enough!** In addition, it will be crucial to use measures that investigate **cultural identity**, which is crucially important especially in the period of emerging adulthood.

Add a Qualitative Component: For cultural identity as for so many aspects of development, there is only so much you can learn from saliva samples and brain scans. Those are important, too, but if that is all you have you will miss many of the important and fascinating aspects of their development. To understand development fully, a qualitative component is absolutely essential. This is especially true in emerging adulthood, when so much self-reflection is occurring as part of their identity development. They are the best authorities on their own development at this age! Listening to them is not only deeply informative but fascinating and compelling. Their social cognitive development advances greatly from adolescence to EA, and as part of that they typically have a lot of insights into their own development that they would not have been capable of as adolescents.

Obviously you can't collect qualitative data on all 11,800 participants (and their families!). A diverse subsample of 200 might be enough, although it might need to be more than that to cover the span of their cultural backgrounds even moderately well. But don't miss this opportunity to hear from the participants themselves about their development during this life stage. I would be happy to share my standard emerging adult interview upon request.

I recommend this as someone who has done both quantitative and qualitative research throughout my career. I recently published a paper using Census data with samples in the hundreds of thousands, on mental health trends across adulthood during the COVID-19 pandemic. But now I am following this up with a qualitative study with an N of about 40, to find out what is really going on. I have always learned far more from qualitative data than from quantitative data. Yes, qualitative methods have limitations, but so does every method. Qualitative interviews will give you important answers to questions you had not even thought to ask.

Here's one more thought to consider as you begin what will be a full and hopefully fulfilling day.

Digital Natives. Among the many variables included in the ABCD study, surely there are some good ones on their digital activities? They were born around 2006 and in 2007 the first iPhone came out, so they are **the first generation to grow up immersed in the digital world from birth**—"digital natives" as they are sometimes called, a term I like. Electronic activities are central to their lives, all day long, so if you want to understand them there has to be some recognition of this and some measurement of their involvement in it and their uses of their

electronic worlds. **Be sure to think of it as USES, not just EFFECTS.** They make choices, all day long, about what to pay attention to in their digital universes and how to respond to it all. **Because their electronic activities are so ubiquitous, everything else you wish to know about them, from their substance use to their mental health to their family relations, will be connected to this**. This is an especially important arena for qualitative data. Simple correlations between, say, their time on social media and their levels of anxiety and depression, can be highly misleading. You will have no way of knowing whether their social media use is driving their anxiety/depression or the anxiety/depression is relieved by their social media use—or both. ASKING them about their daily digital activities will lead to complex data, because their uses of their digital worlds are so diverse. But that's the only way to find out what all that electronic activity means for their development.

Respondent 25

I am grateful for the opportunity to provide thoughts and suggestions for the next stage of ABCD. Having assisted in the initial ABCD grant writing [redacted], and been involved in 6 ABCD Workgroups over time, I am personally invested in ensuring the success of ABCD for many years to come. The NIH, NIDA, the 21 study sites, the CC, and the DAIRC all deserve many accolades for the tremendous success of the project thus far. With that in mind, I do have some thoughts for A-ABCD/ABCD 2.0:

- I'd caution against thinking that moving to remote batteries inherently lowers cost. As noted in the ABCD Arc of Development meeting, certain individuals will be lost with remote, independent data collection. This means that retention will depend on deliberate, intentional, and time-consuming staff follow-up (which is already what happens). Thus, **retaining staff is key for retaining participants, and staffing needs to be adequate to support data collection (even remote)**. In line with this, there needs to be formal support for professional development, as this is a direct tool for retaining staff (and therefore participants) and improving data collection quality as staff have more buy-in and come to care more about and better understand why we do what we do.
- As a major user of the passive sensing of phone use (EARS) data and Fitbit data, I understand the draw of an EMA study, continued collection of Fitbit, and more passive sensing data. In my dream world, I would want all of these things. However, led the EARS pilot and worked with staff on Fitbit, I have significant concerns regarding the amount of burden this presents. **Young adults change, lose, and run out of space on their smartphones frequently**. **Anything that requires an app is going to be more difficult to collect and maintain.** Web browser-basedsurveys can be used, even for EMA, with much less staff burden. Other studies (e.g., All of Us) have already shown "bring your own device" data collection strategies for Fitbit and other devices can be sued successfully. If any EMA or sensing device type elements are included in the protocol, I would hope they would be considered opt-in/substudies.
- Especially as discussions of 3.0 and 4.0 are already raised, **explicit support and roles for early career investigators** (post-bacs through early career faculty) would be very beneficial. More junior faculty should be trained up now to be the future leaders of ABCD for decades to come. They also may have different

insights into the protocol (given prior roles in collection and/or extensive experience with data analysis) and should be included with senior investigators in protocol decision making, even at these early stages in planning 2.0. Once launched, trainees at all levels need support for data analysis (methods, trainings, NIST-compliant environments, funding).

- As is unsurprising for anyone who knows me, I believe continued and expanded collection and analysis of hair samples for assaying is essential. [Redacted] are currently completing analyses to assess the generalizability of hair samples tested to date in data release 6.0, and finding that, at **Year 6, weighted estimates indicate a national prevalence of 7.1% of 15-16 year-olds demonstrate moderate-to-heavy cannabis use** (paper to be submitted to a preprint server and journal in August). This maps on well to MTF data, which shows 9.5% of 10th graders report past-month cannabis use. **We believe that ABCD data is therefore showing more substantive (more frequent, more heavy) cannabis use, since that is what hair measures**, than the general pattern we are seeing in MTF. Importantly, while concordance in self-report is increasing (45% of youth with positive cannabinoids in hair also self-report cannabis use), it is not perfect. Further, toxicological analyses reveal important insights such as CBD and Δ8-THC concentration of those who use. It is also important to note that, **while hair is much preferred, ABCD's lab (USDTL) has pioneered remote data collection of nail samples which can then be used to provide overlapping information as hair samples**, were remote study sessions required.
- **Longitudinal data structures need preserved**. Data collection may be reduced, but measures should not be changed at the cost of longitudinal validity. Changes should be scientifically substantiated. Many of the measures originally chosen (e.g., **NIH Toolbox**, **RAVLT**) were also picked because they are often demonstrated to be consequences of substance use onset/mental health challenges. Therefore, these measures need to be continued at least a couple more times in 2.0. In line with this, research aims should not drastically change from ABCD. We are not through the arc of development, we are in the midst of it, and new aims largely do not seem to be required.
- In the ABCD Arc of Development meeting, there were also a number of interesting ideas for new measures. My sincere hope is that **any new measures have direct clinical utility**. E.g., the Substance Use Workgroup wants to look more at types of treatment and outcomes. Adding more cognitive neuroscience measures is fascinating, but particularly given current priorities for prevention and long-term health, it would appear more beneficial, to me, to select measures that speak to these priorities. It is one reason the **RAVLT is so valuable**—as a measure regularly used in neuropsychology clinics across the country, it is easy to assess the actual clinical implications of analyses which employ its use. It also has multiple domains covered within it (e.g., working memory, learning, memory). If new measures are added, it seems like there is much interest (and rightly so) in executive functioning. Q-Interactive now has a mobile version of the D-KEFS, which covers numerous subdomains of executive functioning. ABCD has previously used Q-Interactive (admittedly it is not a favorite platform by staff, though newer versions may have improved). But I bring this up because the D-

KEFS is another measure which has clear clinical translation in addition to covering the domains in which ABCD is interested.

- I appreciated the ABCD Arc of Development discussion around citizen science and scientific teams contributing to data management. At the same time, I would hope the success of ABCD data releases don't depend on research teams to "volunteer" these types of time- and effort-intense projects rather than providing adequate funding to ensure the needs of ABCD 2.0 are met. Or that specific NOFOs are planned to support these projects, if not done within the ABCD consortium itself.

I again want to thank the NIH staff and especially our NIDA colleagues. I consider myself fortunate to get to be part of this groundbreaking and important study.

Respondent 26

I am writing to provide public comment after the Adolescent Brain Cognitive Development (ABCD) Arc of Development meeting earlier this week on the continuation of the ABCD study. I have summarized my main comments below:

- I think it will be important to focus on continuity from the previous protocol and utilizing similar measures to track trajectories of development. I know that this will need to be balanced with reducing participant burden which requires cutting down on the protocol. However, I would hate if the measures were changed for an alternative option that does not overlap with the previous protocol as that would limit the ability of researchers to accurately examine long-term trajectories.
- I wonder if reducing the number of imaging appointments might be helpful for alleviating some of the strain on the budget and participants. Maybe having just two more imaging appointments over the course of the 5-7 years instead of imaging sessions every other year.
- I think that the role of RAs and staff at sites will still be critical. Even as participants may be moving around the country, the personal connections built between staff and participant families cannot be underscored enough.
- Finally, I believe that we should continue to emphasize parts of the protocol that pertain to substance use. The substance use protocol is a core portion of ABCD's aims and should be prioritized given the point of development ABCD participants will be experiencing as substance use will continue to increase during this period.

I appreciate all the wonderful discussion that was had during the Arc of Development meeting and appreciate all the hard work that has been conducted by NIH on the project.

Respondent 27

I would like to voice my strongest support for extending the ABCD study into adulthood. In the next 5-10 years, it is estimated that 110 children in the ABCD Study will develop schizophrenia between the ages of 18-25 (1%); another 3.8% or about 400 children in ABCD will develop bipolar disorder.. 28% will develop a substance abuse disorder in this age range. These numbers

are sufficient to identify causes of these and many other disorders. The ABCD Study is unprecedented in that it has longitudinal data from before these diseases are expressed, including brain, genetics, schools, neighborhoods, social environment, screen time, sleep, to name the smallest subset of potential causal factors. Adolescence is where there pre-cursors of these disorders are established, but young adulthood is when they are expressed. Extension of this study, with its open data access policy, will provide information that can lead to prevention early intervention and possibly cures for these disorders.

I will add that although I have been involved in ABCD as a scientist, I am now retired, and will not myself benefit from funding awarded for this. But like all the ABCD investigators I am committed to seeing this resource meet its maximum potential. Thank you

Respondent 28

My name is [redacted], and I am a post-doc at the Medical University of South Carolina working with [redacted] and [redacted]. I wanted to reach out to ask if ABCD had considered adding a gambling questionnaire to ABCD 2.0. In recent months, I have heard anecdotally and through media outlets that there has been a substantial rise in youth gambling, particularly online sports betting. After attempting to review current literature on the matter, I noticed there was a substantial gap in this area despite alarms being raised among the general public. I have included some of those articles[2] here which highlight an increase in general and problematic gambling, specifically among young men.

All that said, I was curious to hear if folks in the ABCD consortium have discussed and/or are open to adding a gambling questionnaire. If so, I have included a recent systematic review of different measures that could be implemented (Montiel et al., 2021). While I am no expert on gambling, I am very interested in better understanding the true nature of the public's concern as well as potential risks and protective factors, and I believe ABCD is well positioned to clarify these issues.

Thank you in advance for your consideration, and I will be on the lookout for such changes in ABCD 2.0.

[2]Gonzalez-Roz, A., Fernandez-Hermida, J.R., Weidberg, S., Martinez-Loredo, V., Secades-Villa, R. (2017). Prevalence of problem gambling among adolescents: a comparison across modes of access, gambling activities, and levels of security. *J. Gambl Stud, 33,* 371-382. https://doi.org/10.1007/s10899-016-9652-4

[2]Montiel, I., Ortega-Baron, J., Basterra-Gonzalez, A., Gonzalez-Cabrera, J., Machimbarrena, J.M. (2021). Problematic online gambling among adolescents: a systematic review about prevalence and related measurement issues. *Journal of Behavioral Addictions, 3,* 566-586. https://doi.org/10.1556/2006.2021.00055

[2]Stefanovics, E.A., Gueorguieva, R., Zhai, Z.W., Potenza, M.N. (2023). Gambling participation among Connecticut adolescents from 2007 to 2019: potential risk and protective factors. *Journal of Behavioral Addictions, 12(2),* 490-499. https://doi.org/10.1556/2006.2023.00027

[2]Yeola, A., Allen, M.R., Desai, N., Poliak, A., Yang, K.H., Smith, D.M., Ayers, J.W. (2025). Growing health concern regarding gambling addiction in the age of sportsbooks. *JAMA Internal Medicine, 185(4),* 382-9. https://doi.org/10.1001/jamainternmed.2024.8193

Respondent 29

I'm a member of the team working on the ABCD study. I have seen first hand the incredible depth and value of the data already collected for the study. This data is being used worldwide to improve the health of communities and children. The next phase of ABCD is a necessary continuation of this data collection—by following our participants throughout their young adulthood we'll be able to even further increase the massive value of the data collected (and to be collected). Following these participants into the next stage of their lives will allow us to create significant conclusions on the effects of childhood experiences on adulthood. The value of ABCD cannot be overstated. As the most ambitious and longest-running study of its type, it's critical to continue this momentum for the good of public health.

Thank you for considering these thoughts, and thank you for all the work done at the NIH.

Respondent 30

Talking points:
Size and value of data
Importance for public health
Data already used for thousands of studies worldwide

Respondent 31

I'm attaching a word doc[3] with comments summarizing feedback we received from some of our ABCD users that are in the human brain mapping community. Please see attached document, which also summarizes the objectives and additional details of our Roundtable session.

Respondent 32

In full transparency, I am a researcher who has been tangentially involved in ABCD and have been very impressed with the administration of the study, and the data that are being produced. Please find my thoughts for ABCD for the future.

Sustaining the ABCD Study: Recommendations for Continued Investment and Strategic Direction
The Adolescent Brain Cognitive Development (ABCD) Study represents a landmark effort in longitudinal neurodevelopmental research. With its unprecedented sample size, multimodal assessments, and commitment to open science, ABCD is uniquely positioned to illuminate trajectories of brain, behavioral, and health development through adolescence. The NIH's recent decision to fund an extension of the study (re)affirms its scientific value and underscores the ongoing commitment to this cohort. Still, the long-term impact of ABCD will depend not only on continued funding but on decisions to ensure that data yield remains rigorous, inclusive, and usable across disciplines, and by investigators across the country.

[3]See Appendix I.

With such a large and complex dataset, the risks of overfitting, analytic flexibility, and cohort-related confounds are non-trivial. NIH could strengthen its role as a steward of high-quality secondary use by formally requiring pre-registration, transparent code sharing, and the use of harmonized analytic pipelines for funded research drawing on ABCD data. Additionally, ABCD's depth and breadth of data open meaningful opportunities for methodological leadership. Tools such as Bayesian integrative mixed models (e.g., BIPmixed) and network-based prediction frameworks are increasingly being applied to ABCD data to tackle the high-dimensional structure of its multi-site, nested design. Continued support for the development, validation, and dissemination of such methods, along with readily accessible code that can be immediately implemented by scientists doing applied (i.e. non methodological) research will be essential. The NIH might also consider investing in focused data challenges or cross-consortia hackathons to accelerate methodological translation and training.

In sum, the ABCD Study has established itself as a generational resource. Its scientific promise is clear, and its infrastructure is mature. What remains is to ensure that future analyses are both methodologically sound and readily applicable across multiple disciplines and geographic locations. NIH's continued investment, if paired with strategic alignment to rigor, and innovation, will help ensure that ABCD is not merely a large study—but a lasting one.

Respondent 33

Thank you for inviting input on the next phase of ABCD. As [redacted] and a member of the planning team since inception, I offer the following recommendations.

Why ABCD must continue

- ABCD is the only U.S. cohort of nearly 12,000 youth with longitudinal multimodal MRI, deep environmental profiling, and rich biospecimen data.
- A proven open-science pipeline (>1500 publications) and diverse participant base maximize return on prior federal investments.
- Extending follow-up through age 27 captures the developmental window when ~75% of lifetime psychiatric disorders begin and when education, vocation, relationships, and parenting trajectories are set.

Existing assets to leverage

- Large, well-characterized, representative cohort with high retention
- Secure, scalable data infrastructure and share-ready pipelines
- Multidisciplinary investigators covering neuroimaging, genetics, digital environments, substance use, mental and physical health, sleep, activity, and cognition
- Robust participant engagement

Proposed high-value aims for 2027-2034

- Chart normative vs. atypical trajectories of brain and cognitive maturation across adolescence into emerging adulthood, aligned with educational, vocational, and family milestones.

- Identify environmental and digital-ecosystem exposures (social media patterns, online peer interactions, wearable-based context) that heighten or buffer risk for mental-health disorders.
- Map pathways to substance use, addiction, and recovery, including interactions with neurodevelopment and co-occurring mental disorders.
- Determine how physical-health conditions (obesity, cardiometabolic risk, sleep disruption, chronic pain) co-evolve with brain development and behavior.
- Integrate multimodal data to predict functional outcomes (productivity, wellbeing, civic engagement) and generate evidence-based recommendations for clinicians, schools, and policymakers.

Capitalizing on ABCD's unique strengths to meet these aims will provide the nation with actionable guidance on promoting healthy, productive adult lives.

I appreciate NIH's commitment to this flagship study and am happy to elaborate on any of these ideas.

Respondent 34

Very excited to see the next phase of ABCD when we will be able to assess the results of different aspects of development on adult trajectories and build predictive and risk models that can inform preventive and treatment approaches. This is a unique an critical opportunity for important health discoveries.

Respondent 35

Thank you for the opportunity to provide input with regards to the A-ABCD study. At the outset, I would like to say that extending the study into adulthood is critical for building upon and multiplying the influence and enormous information already gained from the ABCD study. It is critical to know how brain development and experiences in adolescence shape whether or not individuals go on to have a healthy, happy and productive adulthood. For example, many youth experiment with substances during adolescence, but a critical question is which factors, most notably those associated with brain structure and function, predict which individuals which pass through this developmental phase without ill effect and which individuals will instead transition into addiction.

From my perspective, the following elements are crucial for the next phase of the study. Ideas on how those elements might be achieved and commentary on them are provided under the numbered points.

1. More emphasis should be placed on the brain aspect of the study, which is its unique characteristic. With that in mind, I would place the most emphasis on the following:

    a. The frequency of data collection on brain imaging should remain the same and not be reduced. What makes ABCD so special is the *longitudinal* brain imaging data. These data are an unparalleled and unique resource as compared to any other

study. While brain imaging is expensive and logistically difficult, it is the truly distinct piece of data that is provided by the ABCD and potentially the A-ABCD study.

b. To provide better insights into brain function in the early adult years, the tasks should be modified to be more challenging (e.g., adding a 3-back condition to the N-back task).

c. As brain responsiveness to risk taking behaviors have peaked in mid-adolescence, it probably would be useful to replace the Monetary Incentive Delay task with a task that assesses cognitive flexibility, abstract reasoning, inference, or other aspects of executive function that are needed for adaptive adult behavior.

2. More emphasis should be placed on understanding brain processes and linking them to behavior, making that the core central aspect of the study (which also makes it unique).
    a. From my perspective, there has been too much "mission creep" in the ABCD study with the addition of numerous new domains and factors being studied. As a result many analyses have focused on relationships between various behavioral measures or between behavior and demographic/environmental/experiential variables. These issues are well examined in other, often larger, data sets than ABCD. Designing A-ABCD so it can focus on what critical information brain measures can provide would be a welcome approach.
    b. To aid in this endeavor, more emphasis should be placed on the data informatics core providing the brain data in a curated and timely fashion for analysis. The amount of data is too huge for any reasonable voxel-based analyses. Priority should be given to parcellated data. More consideration should be given to how atlases used for parcellation of anatomical and functional data (which are different) can be overlaid to enable the co-localization of effects.
    c. Training should be provided in using the tools that have been created to analyze such data in a computationally tractable manner (e.g., FEMA) so that analysis of the data can be an achievable endeavor for a larger portion of the scientific community.

3. A-ABCD should place priority on obtaining information on how successfully individuals are transitioning to independent adult roles in their lives.
    a. To this end, more emphasis should be placed on the assessment of executive functions, including decision making, cognitive flexibility, goal-setting and goal attainment, and alike. Less emphasis should be placed on risk taking and reward processing.
    b. Assessments of the social indicators of having adult-like roles in life should be prioritized (e.g., stable employment, romantic partnering, children, friends, involvement in community groups/activities).

4. More emphasis should be placed on discerning indicators of causal relationships and mechanisms, as much of the research provided to date by ABCD has been correlational in nature.
    a. In the spirit of this goal, the genetic aspect of the study should be retained, both with regards to the twin portion of the cohort and GWAS information provided by

the study. Such information has the unparalleled ability to provide insights into the genetic predispositions to adult behavior.

b. Emphasis should be placed on the creation and dissemination of tools to allow for the analysis of longitudinal data so as to ascertain the predisposing factors that might influence later adult behavior.
c. Ideally, it would be advantageous to provide support and funds for theoretical "affinity" groups (e.g, for small mini-conferences) to bring together scientists to discuss and present analyses that are relevant to particular conceptual questions (e.g., "What is the evidence that adolescent drug usage affects the brain?"; "What aspects of brain development appear to be more or less complete by late adolescence?"). Whereas one might think this task would fall under the purview of the working groups, those groups are instead too busy ensuring that the data being collected is useful, curated, and cleaned. In addition, such affinity groups could include individuals beyond ABCD investigators.

Once again, thank you for the opportunity to provide input. It is much appreciated.

Respondent 36

As leaders of the Linked External Data (LED) Environment and Policy working group and in thinking about the next stage of the ABCD Study, we imagine an exciting opportunity to significantly enhance ABCD's analytical capabilities in the next phase. Please find attached via PDF[4] our thoughts about the next phases of the ABCD LED work. In completing a **S**trengths, **W**eaknesses, **O**pportunities, and **T**hreats (SWOT) analysis (**Appendix A**) based on the existing ABCD LED work (**Appendix B**), we believe the next phase of ABCD's LED would best be supported through the development and integration of an 'NIH Brain Development Cohorts (NBDC) Geospatial Hub' (**Appendix C**).

We would welcome the opportunity to discuss how this geospatial infrastructure could enhance ABCD's next phase objectives and would be happy to arrange a presentation or answer any questions you may have.

Respondent 37

I'm writing to share a public comment regarding the future of the ABCD Study, with a focus on participant retention as adolescents reach adulthood.

As participants begin to turn 18 and face life transitions, such as moving away for college, work, or other opportunities, it's crucial that the study offers flexible participation options to maintain engagement. This includes establishing clear, standardized protocols across sites for long-term remote participation, guidelines for those who move far from an ABCD site, and considerations for participants who relocate internationally.

To improve retention into the next phase of ABCD, I believe it is important to provide

[4]See Appendix II.

participants and their families with transparent expectations and flexible options *before* these major life transitions occur.

Thank you for the opportunity to share feedback. I'm excited to see how the ABCD Study evolves in its next phase.

Respondent 38

The ABCD project is an exceptional longitudinal study that should be continued. Building on the unique cadre of students and families combined with the knowledgeable, talented university and NIH staff at this transition from youngsters to young adults will provide an unprecedented opportunity to impact young people, families and communities while continuing to grow our research understanding.
I highly encourage NIH to continue to support its investment in ABCD.

Respondent 39

Hair toxicology for drug use.

Engagement with AI tools:
• Usage as a tool for education/problem solving
• Usage for companionship or romantic connection
• Usage for personal development/goal setting

Electronic health records!!

Social networks/connectedness
• How often are they seeing friends in person
• **Social trust:** this is a construct in economics that predicts social mobility

SES Outcomes:
• Income
• Education: College Major, University,
• Trade school, employment.

Appendix I.

Shaping the future of the ABCD Study: A roundtable discussion

Conference: Organization for Human Brain Mapping (OHBM)

Date, Location: July 26, 2025. Brisbane, Australia

Panelists: [Redacted]

Attendees: ~70+ people in the room. Lots of engagement with a steady stream of questions, most people stayed for the full hour. Included comments from [redacted]

Format and Objective: This was a one-hour roundtable organized by [redacted] to gather feedback from the human brain imaging community on what they would like to see in the next phase of the ABCD Study. One of the main objectives of this session was to have an active dialogue between ABCD investigators and the user community to help shape the next phase of the ABCD Study ("ABCD 2.0"). This roundtable session also allowed participants to provide feedback on tools and data sharing features that would be useful in the future.

Points raised during roundtable & our offered solution if applicable in sub-bullet below:

ABCD 2.0

- [Redacted] describes lessons from generation R study for ABCD 2.0 - balance between longitudinal data and deep phenotyping. What about deep phenotyping on select things related to mental health (at specific ages)? Add a new random sample? Can there be some creativity regarding variables that are removed due to executive orders?
- Plans to improve clinical descriptions?
    - mental health workgroup is looking at remote platforms for mental health assessments. Will do more 'trained assessor' assessments in 2.0 as well (structured interview clinical assessment). Users can also expect to see SIPS interviews for psychosis for some portion of the sample going forward (will be released as part of 1.0)
- Measuring cerebrovascular health. Perfusion measures? Important for Alzheimers risk, etc. Considering adding an ASL imaging acquisition.
    - [Redacted] mentions that PCASL is in HCP-D and HCP-A
    - [Redacted] adds there is potential to add one-off acquisitions

- Adding sensory processing sensitivity measures to the imaging and/or behavioral battery
- Different ways of measuring SES
    - [Redacted] describes changes that are already happening in ABCD 1.0 (asking youth directly about their income/job status/etc as they become emerging adults, area deprivation index, ladder scale)
- A couple votes to maintain the rsfMRI scan length going forward
- What data will ABCD 2.0 collect on participants that become pregnant?
- Some mentions of maintaining continuity of imaging parameters vs. starting multi-echo imaging
- Understanding the impact of microplastics on developing brain
    - it's possible we may be able to gather some of this info with biosamples that we have banked with new research proposals
- Possibility of looking at development of social cognition & adding social cognition measures generally. Hyper-scan (interaction between parent-child, interactions between peers)?
- One participant brings up collecting EEG data, given that it is more cost effective, maybe collect every other year. Unclear whether resting or task would be preferred here
- Assessing the Gut-brain axis, fecal sample (microbiome)
- Suggestion to talk to people at ISMRM, as they are at the forefront of novel imaging acquisitions
- Adding app based remote assessments (EMA)
    - [Redacted] describes that as a consortium we have started to look into this; the big question is, do we eliminate the standard assessments and move them all to app-based measures? Or do we use apps as additional complementary measures?
- Quantitative imaging sequence (targeting myelin)
- Can we add eye-tracking during the resting state fMRI to see if they are asleep?

Data curation & release

- Desire for careful metadata curation in imaging (released in BIDS, carefully annotated, to assist in harmonization, better clearly described metadata)
- Releasing our human phantom data to look for reliability of inter-site, inter-scanner (for harmonization).
- We got lots of thanks from early career researchers, the ABCD Study has really helped people launch their research programs
- Concerns around variability in preprocessing: will there be standardized preprocessing?
    - [Redacted]: not much has changed to the standard (minimal) preprocessing, we let users decide on their own pipelines after that. Maybe we can move towards more options in the future. [Redacted]'s pipeline is available (community ABCC).
- Would it be possible for users to upload their own preprocessed data given this diversity in pipelines that folks are using?
    - Revisiting part of our initial plans in the DAIRC for the community to share resources/code/etc.
- One common & computationally intensive pre-processing step is the structural connectome from DTI data- users would like to see released tractography data

- Lots of questions around the DUC and NIST, which panelists helped clarify based on information the consortium has received around this
- Users would like to see a guide to compare ABCD to other big data (HCP, UKB, ADNI, etc)?
    - [Redacted] responds that the DAIRC is actively working on this
- Can Freesurfer data be made available?
- Can we process diffusion data with NODDI?
    - [Redacted]'s lab has processed all of ABCD data with NODDI, he's happy to work with us – goes back to point above re: community sharing processed outputs

Additional questions/comments from OHBM app chat:

- myelin-targeted imaging: quantitative MRI, ihMT, QSM
    - a few people asked for this. One would prefer qMRI over task and ASL
- There were also a few endorsements for ASL
- Request to gather more info on MRI experience to contribute to broader understanding of how we interact with participants in the MRI space
- Scan the parents & participant's future offspring (a couple votes on this!)
- Maintain resting state at 20min to retain reliability

Appendix II.

July 29, 2025

Dear ABCD Leadership,

As leaders of the Linked External Data (LED) Environment and Policy working group and in thinking about the next stage of the ABCD Study, we imagine an exciting opportunity to significantly enhance ABCD's analytical capabilities in the next phase. In completing a **S**trengths, **W**eaknesses, **O**pportunities, and **T**hreats (SWOT) analysis (**Appendix A**) based on the existing ABCD LED work (**Appendix B**), we believe the next phase of ABCD's LED would best be supported through the development and integration of an 'NIH Brain Development Cohorts (NBDC) Geospatial Hub' (**Appendix C**).

To date, our work in ABCD has included mapping 70 sets of variables from 40+ data sources (for a total of 900+ variables) to the primary residential address when the children enrolled in the study were ages 9-10 years. The ABCD consortium and researchers worldwide have shared with us that the geospatial insights have been very valuable. Multiple studies using these data have also been cited in proposing new public health policies. What many may not know is that, beyond these initial data, our working group has procured external funding [R01ES032295 (PI Herting); R01-ES031074 (PI Herting)], which allowed us to lead and oversee all efforts over the past 5 years, revamping and implementing a new lifetime address standard operating procedure, creating novel visual timelines, and developing a rigorous quality control pipeline for residential time series data for ABCD. Thus, as we embark on ABCD-A, ABCD has lifetime address data from birth through the present day; ultimately allowing for us to ask novel and important questions about how earlier life exposure (prenatal to study enrollment) as well as ongoing exposures during adolescence, and now into young adulthood, impacts changes in brain, behavior, and health.

With ABCD-A, we believe the LED geospatial scope of work is three-fold: 1) update our rigorous data collection protocol to be securely collected via the web by the (now) adult participants themselves (reducing both cost and RA burden), 2) link existing exposure datasets retrospectively and prospectively in order to create time-weighted lifetime exposure estimates for ABCD participants, as well as 3) applying our expertise and knowledge gained in this domain to build a 'NBDC Geospatial Hub'. We believe this initiative would transform how we analyze environmental influences on brain development by moving beyond traditional static residential approaches to capture the dynamic, spatiotemporal nature of where participants spend their time in terms of their homes, schools, and workplaces. We believe this proposed idea offers ABCD several compelling advantages, including expansion of current efforts to provide the scientific community with:

- Secure, web-based infrastructure that seamlessly integrates existing ABCD protocols for data collection of address, school, and workplace locations into a harmonized data structure
- Comprehensive lifetime (i.e., time series data) for residential, school, and workplace geocoding for all ABCD participants
- Integration with advanced exposomics data spanning macro-community factors (school quality, healthcare access) to micro-individual exposures (air quality, noise, chemicals) to get both developmentally weighted and study-visit specific exposures (i.e., exposures for each age of development versus exposure 1 year prior to each study visit)

Given ABCD-A will need the resources and expertise to achieve these goals, we believe the development and support of a 'NBDC geospatial hub' will maximize communication, resources, efficiency, and ensure harmonization among ABCD and HBCD to facilitate the scientific discovery of *when, where, and for whom* environmental interventions may be most effective. This approach addresses a critical gap in current research that treats environmental factors as isolated, static variables rather than the dynamic, interconnected influences they truly are. By combining and expanding into a harmonized geospatial hub, this plan could significantly amplify NBDC's scientific impact and translation potential. For additional context, we have also included a) a summary of the LED Working Group's work so far (**Appendix B**), and b) a proposal for an NBDC Geospatial Hub developed alongside key collaborators (**Appendix C**).

We would welcome the opportunity to discuss how this geospatial infrastructure could enhance ABCD's next phase objectives and would be happy to arrange a presentation or answer any questions you may have.

Best regards,

[Redacted]

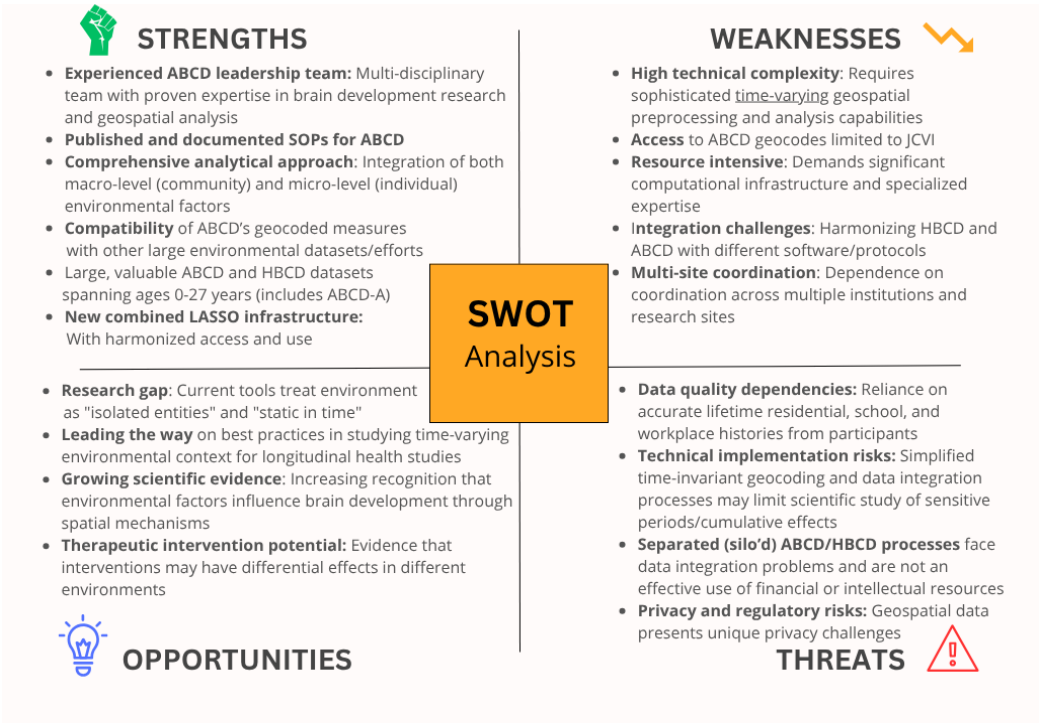
APPENDIX A

Strengths, **W**eaknesses, **O**pportunities, and **T**hreats (**SWOT**) **Analysis of Linked External Data (LED)**

Addressing Ongoing Challenges Through New Opportunities. Our current strengths and the opportunities moving forward include: **(1)** experience and expertise can be adapted to other LED data (e.g. LED school working groups dealing with similar issues as well as needed to capture exposures as individuals move schools at different times within a year) as well as **(2)** providing the larger field with harmonized LED Environment data for ABCD and HBCD and leading the way to provide best practices and resources for contextualizing the environment that can easily be adapted into other health studies.

Yet, we believe the major existing weaknesses for the current LED environmental work is three-fold: **(1)** high-technical complexity of geospatial time series data (i.e. people split homes, move over time, neighborhood change), **(2)** logistical barriers (e.g., limited access to geocodes despite mechanisms to securely provide access to LED ABCD members) and **(3)** resources (outside NIEHS R01-level funding ended on 7/1/2025). Moreover, we already see notable existing gaps in applying these 'hard lessons learned' across ABCD and HBCD to ensure both the data quality as well as the harmonization and implementation to account for the nuances of the timeseries inherent to this work (i.e., people move, share homes, periods of exposures over time, etc.). Despite multiple attempts at coordinating efforts, key organizational differences between the ABCD and HBCD Consortia have led to siloed geospatial/LED efforts with duplicated resources and funding gaps, significantly limiting the potential impact of both geocoding initiatives. For these reasons, the NBDC Geospatial Hub (Appendix C) represents our most cost-effective path to transformative environmental analysis capabilities within ABCD and HBCD. Rather than developing separate geospatial capabilities, the proposed collaboration with USC's Spatial Science Institute and the NEXUS Network will provide additional resources as we work to harmonize ABCD and HBCD geospatial data collection, delivering comprehensive environmental analysis tools that neither study could achieve independently while maximizing shared infrastructure investments.

Figure 1. SWOT Analysis for LED Data



APPENDIX B

Summary of the LED Environment's Working Group's Effort So Far

A. Linked External Data (LED) - Environment. The ABCD consortium's Linked External Data (LED) Environmental workgroup is currently led by co-chairs Dr. Herting (since 2020) and Cardenas-Iniguez. A full list of working group members can be found here: https://abcdstudy.org/scientists/workgroups/. The mission of our working group is to advance the integration and utilization of linking external environmental and policy data sources to residential history-derived geocodes in the ABCD Study. Its members strive to promote the adoption of external datasets that may provide additional insights into child and adolescent environments, which can help to contextualize primary data collected, and ensure that researchers use residential-history-derived geocoded measures responsibly.

The work conducted as part of the LED-Environment working group is considered a sub-study (via the ABCD SERG process) and has been traditionally funded by outside support made possible from NIEHS R01-ES032295 (PI Herting) and R01-ES031074 (PI Herting). While these grants are focused on air quality, they have provided substantial funds (~$800,000 over 5 years) to the DAIRC to support the time of staff to conduct all portions of this work under direct leadership of the LED co-chairs. Following the ABCD consortium's open science framework, our initial grant's support of LED workgroup activities has generated rich environmental data linked to the primary addresses at the baseline study visit when the children were ages 9-10 years. This baseline dataset has been utilized by other researchers in over 160 publications by researchers worldwide (**Figure 2**).

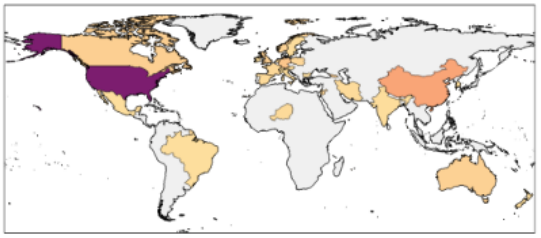


Figure 2. Global distribution of author affiliations from 160 papers focused on ABCD LED constructs. *Countries are shaded by frequency of contributing authors.*

B. Existing ABCD LED Environment & Policy Data Thru Release 6.0. The currently available geospatially linked environment data in the ABCD Study (through release 6.0) are largely based on up to three concurrent caregiver-provided residential addresses corresponding with the baseline data collection (2016–2018) when the ABCD participants were 9-10 years-old. Specifically, participants have linkages for a single primary address if > =80% of their time was spent residing at one location; if < 80% of their time was reported at a single address, informants could report up to two additional addresses. Given a number of challenges our working group faced with the originally collected residential data (see section C below), the past 5 years have been focused on two concurrent efforts, including **(1)** establishing a framework, processes, and linking environmental factors to these baseline residential addresses and **(2)** updating the standard operating procedures for residential data collection and developing rigorous preprocessing and quality control pipelines to capture nuances in residential addresses over time (i.e. time series based analyses). We discuss these efforts in more detail below:

(1) ***The Adolescent Neural Urbanome Framework.*** Extensive research across diverse fields, such as environmental health, social epidemiology, developmental psychology, cognitive neuroscience, sociology, and economics, has shown that environmental conditions – beyond the home – play a crucial role in brain development. ABCD's LED Environment and Policy data expands researchers' ability to explore how various environmental features of individuals' residential locations – particularly – relate to myriad neurodevelopmental, cognitive, mental, and physical health outcomes. At baseline, 80% of ABCD Study participants lived in an Urban Area or Cluster as defined by the CDC. Urban residence is a double-edged sword. On one hand, it offers many advantages, such as diverse social networks and well-developed infrastructure that may increase access to healthcare, education, employment opportunities, and social services and support. On the other hand, urban living often presents significant challenges. Children in urban settings may be exposed to higher levels of

pollution and noise. Furthermore, urbanization often engenders spatial stratification. Thus, building on the initial work of the LED working group, we worked to capture additional facets of the environment in which adolescent development unfolds. Using a framework that we call "the Adolescent Neural Urbanome," this approach guides developmental neuroscience research on environmental factors by: (1) refining community and individual contextual constructs to extend beyond sociodemographic composition and (2) integrating these constructs into an "urbanome" theoretical framework. Research evaluating environmental conditions and their impact on brain and psychological processes often examines indirect, proxy measures usually associated with household socioeconomic status (i.e., income, education) or employs neighborhood measures of socioeconomic status derived from geocoded data that are linked to the American Community Survey (ACS) in the United States. Moving beyond these SES proxies, the Adolescent Neural Urbanome environmental framework for the ABCD Study considers spatially patterned exposures alongside specific community- and neighborhood-level constructs that may operate as key mechanisms through which social and built environments impact neural and behavioral development. Details of these efforts can be found here:

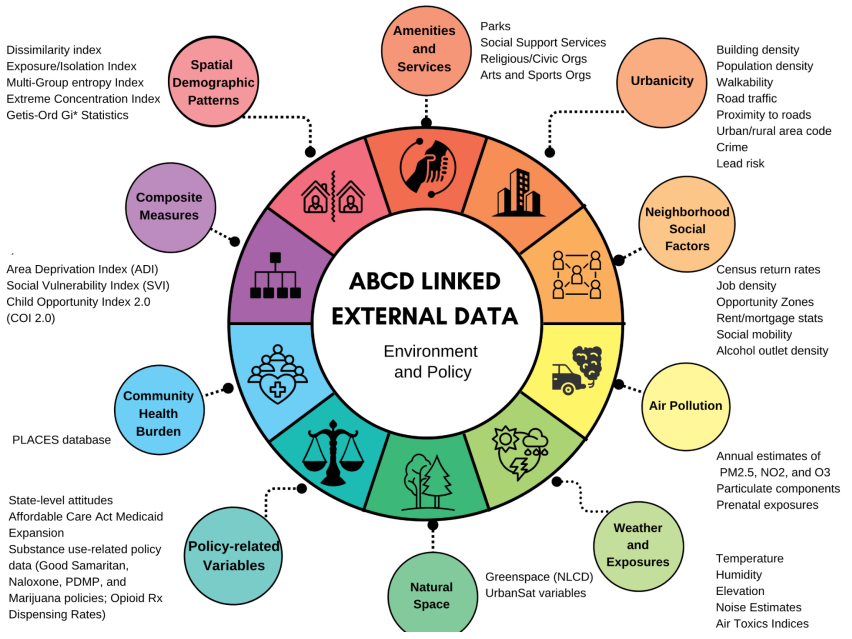


Figure 3. The Adolescent Neural Urbanome. *A framework of exposures and contextual variables linked to the ABCD Study, consisting of 900+ variables from over 40 data sources, the Urbanome provides opportunities for researchers to link ABCD constructs to real-world data related to environmental and social drivers of adolescent health.*

[Cardenas-Iniguez C, Schachner JN, Ip KI, Schertz KE, Gonzalez MR, Abad S, Herting MM. Building towards an adolescent neural urbanome: Expanding environmental measures using linked external data (LED) in the ABCD study. Dev Cogn Neurosci. 2024 Feb;65:101338. doi: 10.1016/j.dcn.2023.101338. Epub 2024 Jan 3. PMID: 38195369; PMCID: PMC10837718.]

(2) Rigorous Collection, Preprocessing, and Quality Control of ABCD Lifetime Residential Addresses. From study conception, updated residential address information was collected at each study visit, and starting at the 2-year annual follow-up visit, caregivers were also asked to provide up to 10 previous addresses for their child. However, the original ABCD Protected Health Information (PHI) platform did not validate geocodes in real-time and did not timestamp changes in addresses or adequately capture the complex residential histories experienced by various study participants. Collectively, this led to high amounts of missing data and poor geocode conversion rates. Thus, in 2020, as the working group sought to construct ABCD participants' lifetime residential histories to link exposure estimates for

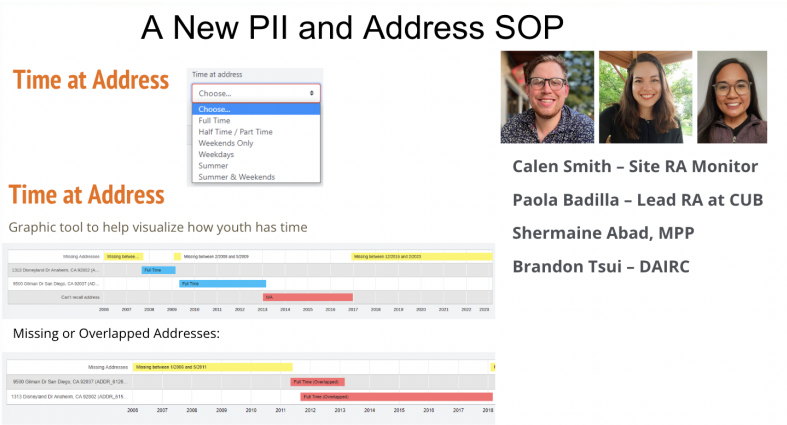


Figure 4. LED WG and ABCD Team Efforts to Build a Rigorous Interactive, Intuitive, and Rigorous Lifetime Address Protocol

the cohort, the initial retrospective address histories and prospectively collected addresses in ABCD were of insufficient quality. As such, we led the consortium to overhaul its residential address data collection and geospatial linkage standard operating procedures (SOP) (**Figure 4**). By year 4 of the project, we finalized a new lifetime address history SOP and implemented rigorous quality control measures. These efforts resulted in over 80% completion of lifetime address data for 89% of ABCD participants, compared to only 39% as seen upon taking over these efforts in 2020. These efforts and details have been published in detail:

Abad S, Badilla P, Marshall AT, Smith C, Tsui B, Cardenas-Iniguez C, Herting MM. Lifetime residential history collection and processing for environmental data linkages in the ABCD study. Health Place. 2024 May;87:103238. doi: 10.1016/j.healthplace.2024.103238. Epub 2024 Apr 26. PMID: 38677137; PMCID: PMC11132178.

Badilla P, Abad S, Smith C, Tsui B, Cardenas-Iniguez C, Herting MM. Lifetime residential data collection protocol for the Adolescent Brain Cognitive Development (ABCD) Study. MethodsX. 2024 Apr 3;12:102673. doi: 10.1016/j.mex.2024.102673. PMID: 38623304; PMCID: PMC11017270.

This means, as we embark on ABCD-A, we have the opportunity to use these rigorous ABCD protocols and existing, high quality lifetime address data from birth through the present day to begin to **(1) update our rigorous data collection protocol to be securely collected via the web by the (now) adult participants themselves (reducing both cost and RA burden),** and **(2) link the *Adolescent Neural Urbanome* exposure datasets over time;** ultimately creating time-weighted lifetime exposure estimates (i.e. nuanced time series data) for ABCD participants.

(3) An Example of the Potential Scientific Knowledge to Be Gained with Time Series Exposure Data: Sensitive Windows and Cumulative Effects of Environmental Exposures

Lifetime histories of where people have lived and gone to school provide unique data regarding what environmental and social factors our ABCD participants experienced prior to enrolling in our study (**Figure 5**). This information provides an unparalleled opportunity to understand what environmental factors may have influenced where each participant started in terms of their brain, behavior, and health at the beginning of the ABCD Study (i.e., their intercept) and provide additional information regarding how early life exposures map onto how ABCD participants develop over time (i.e., trajectories/slopes). Collectively, this allows for studying important questions regarding the Developmental Origins of Health and Disease (DoHaD) using lifetime LED data in ABCD. We provide an example using air pollution, but with additional resources, our LED working group aims to expand to link additional environmental exposures over time.

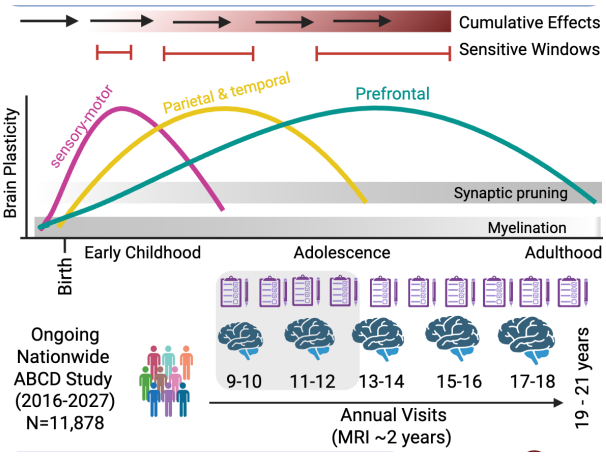


Figure 5. Lifetime addresses allow us to learn about the environmental context of our participants before they began our study. *Timeseries data allows for understanding if environmental factors have sensitive periods and/or cumulative effects on health.*

Per the study aims of our outside funding from NIEHS, we have used the rigorous residential addresses o map fine particulate matter (PM2.5) air pollution exposures from the prenatal period to the baseline study visit this past year. These data are slated to be included in the 7.0 release. Using these data, we provide an example of the scientific knowledge to be gained having rigorous lifetime exposures in the ABCD study. Using distributed lag modeling, our preliminary analyses reveal timing-specific effects on sensorimotor and temporal regions during early childhood, but cumulative effects on the prefrontal cortex and behavior. When examining a 4-μg/m^3

difference in $PM_{2.5}$ exposure (from the WHO guideline of 5 μg/m^3 to EPA standard of 9 μg/m^3), we observe significant lag-specific effects for cortical thickness at ages 9-10 (**Figure 6**) with timing-specific effects highlighting susceptible periods for sensorimotor (birth to age 4) and temporal brain (ages 5-8) regions. Cumulative effects of a 4-ug/m^3 difference in $PM_{2.5}$ exposure [9 vs. 5 μg/m^3] are also significantly associated with greater sensitivity to both punishment (i.e., higher behavioral inhibition system (BIS) scores) and rewards (i.e., higher behavioral activation system (BAS) scores) at ages 9-10 (**Figure 6**), as measured by the BIS/BAS scales. These types of behavioral traits have been linked to anxiety and depression[180], bipolar spectrum disorder[181], and substance use[182-184]. A similar pattern is seen for internalizing problems over time, albeit not yet reaching significance by age 9 (**Figure 6**).

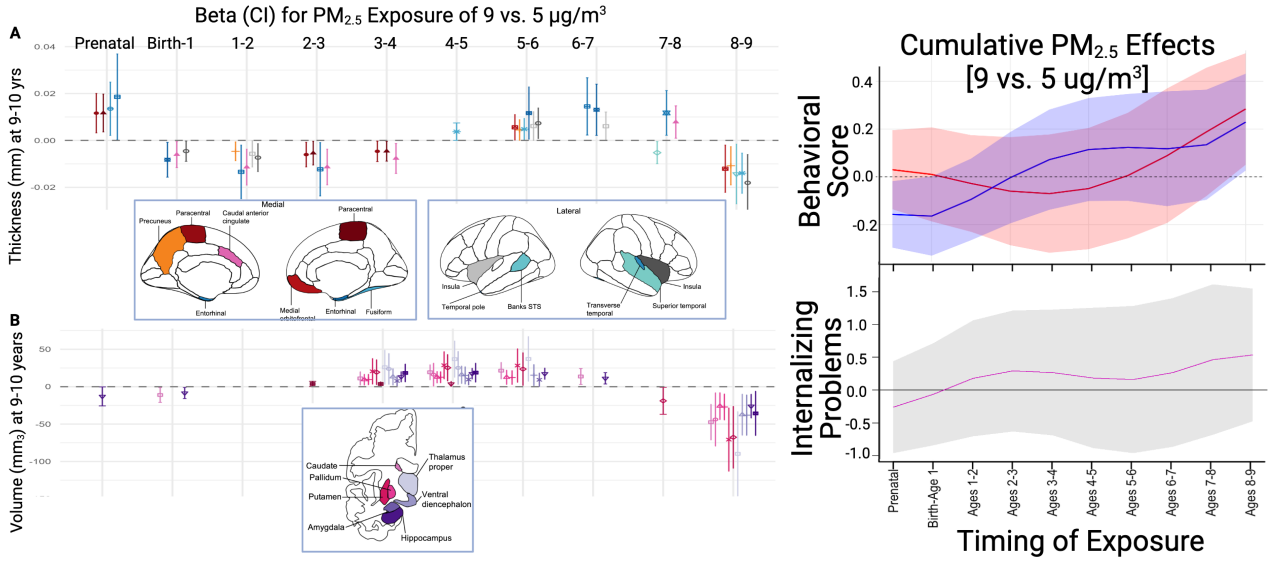


Figure 6 Sensitive windows and cumulative effects of air pollution on brain structure and behavior at study entry (ages 9-10). *All findings are adjusted for covariates with a sample size of n=7,812. Right-side plots A-B) These plots reflect the effect size (standardized beta and 95% CI) of how air pollution during discrete periods of development (spanning the prenatal period (i.e. 9-month average) and annual exposure at each postnatal age) impact (A) cortical thickness and (B) subcortical volumes at study baseline. Color coding of beta reflects the brain region shown on the schematic brain maps. (A) For cortical thickness, unique exposure windows exist for the precentral, paracentral, caudal anterior cingulate, and medial OFC (~birth to age 4 years), whereas sensitive periods of exposure for the temporal lobes are later during early to mid-childhood (age 5-8 years). (B) The hippocampus is more sensitive to air pollution exposure during prenatal and 1st year of life, whereas air pollution shows much stronger associations with other subcortical structures between the ages of 3-6 years as well as the year prior to ABCD enrollment. Left-side plots) Cumulative effect of air pollution on BIS (red) and BAS scores (top) and internalizing problems (bottom) at ages 9-10.*

APPENDIX C: NBCD Geospatial Hub Proposal

Title: Establishing NIH's Brain Development Cohorts (NBCD) Geospatial Hub for Integrative Brain Development Research

Authors: Megan M. Herting, Carlos Cardenas-Iniguez, Rima Habre, John Wilson

SPECIFIC AIMS. Brain development is fundamentally a spatiotemporal process, with critical periods of growth, connectivity establishment, and functional specialization occurring across distinct anatomical regions and developmental timeframes. Despite advances in neuroimaging and developmental neuroscience, our understanding of how brain development varies across populations, environments, and genetic backgrounds requires an integrated, spatially aware analytical framework for the environment in which a child grows up. Current efforts and analysis tools often treat the child's environment as isolated entities of place that are static in time, failing to capture the complex spatial relationships, place-based contexts, and behavioral effects that characterize where mothers, children, teens, and young adults spend their time, how they move between locales, and how temporal variations in their environmental exposures map onto normal and atypical brain development. The urgent need for a comprehensive geospatial approach to brain development research is underscored by growing evidence that environmental factors influence brain development through spatially distinct environment-specific mechanisms, and that therapeutic interventions may have differential effects at different macro (e.g., geographical and community) and micro (e.g., home, school, workplace) environments. **The overarching goal of this project is to establish a comprehensive NBDC Geospatial Hub that enables the integration and analysis of geospatial environmental and social exposure data across macro- and micro-level settings to advance our understanding of brain development across the lifespan.** This hub will provide researchers worldwide with unprecedented capabilities to analyze brain development through a spatial lens, enabling discovery of how environmental factors may drive or moderate risk factors to better inform therapeutic targets for neurodevelopmental disorders.

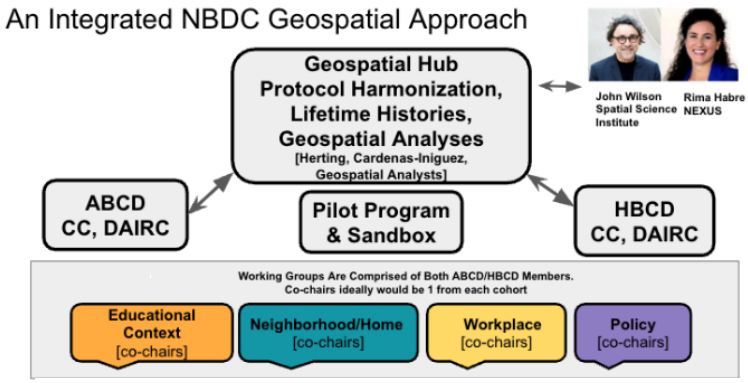


Figure 7 Concept for a proposed Geospatial Hub.

Aim 1: Develop a secure Geospatial Data Infrastructure for the Healthy Brain Cognitive Development (HBCD) and Adolescent Brain Cognitive Development (ABCD) Studies. We will leverage USC's Spatial Science Institute (https://dornsife.usc.edu/spatial/about/) to design and implement a secure geospatial preprocessing pipeline that integrates with the LASSO-based data infrastructure to harmonize HBCD and ABCD lifetime residential, school, and workplace histories with reproducible geocoding workflows and explicit metadata frameworks. The infrastructure will feature: (1) automated spatial geocoding and quality control pipelines, (2) standardized anatomical atlases with developmental trajectories, (3) secure multi-site data sharing protocols compliant with NIST privacy regulations, and (4) APIs for seamless integration with existing analysis platforms. **Expected Outcomes:** A robust, secure and scalable platform containing harmonized **lifetime residential history** data from >15,000 NBDC participants aged 0-27 years, with quality-controlled geo-coordinates for homes, schools, and workplaces, ready for geospatial analysis.

Aim 2: Integrate Exposomics Data and Analysis Structures to Map Comprehensive Geographic, Environmental, and Social Influences on Brain Development Across the Lifespan. We will establish formal partnerships with the Geospatial Sciences Hub of the NEXUS Network for Exposomics (https://www.nexus-exposomics.org/) in the U.S. to develop geospatial data generation and linkage frameworks and integrate a

comprehensive, exposomic scan of environmental and social determinants of health across multiple scales and timepoints, compatible with global and national data-intensive cohorts. This will include: (1) macro, community-level factors (school quality, healthcare access, food environment, social cohesion, etc.) and (2) micro, individual-level home, school, and workplace exposures (chemicals, air quality, noise, etc.). Advanced exposure modeling will incorporate activity-space analysis, GPS tracking data, and time-activity patterns to create personalized exposome profiles. **Expected Outcomes:** Comprehensive spatiotemporally resolved exposome profiles linked to brain development data for HBCD and ABCD participants, enabling the scientific community to include these environmental factors in their creation of personalized risk prediction models.

Aim 3: Create Advanced Geospatial Analytics Tools for Brain Development Research and Community Outreach. We will curate and share a comprehensive suite of geospatial analysis tools including: (1) spatial autocorrelation and graph-theoretic analyses for identifying developmental clusters and outliers, (2) spatiotemporal modeling frameworks for characterizing how factors map onto brain-behavior growth trajectories, and (3) environmental exposure mapping tools that link geographic location and activity space data with brain development patterns and personal wearable technologies. All tools will be implemented within the NIST-compliant LASSO environment, featuring user-friendly interfaces. **Expected Outcomes:** A toolkit of novel, spatiotemporally nuanced geospatial analysis methods compared to the traditional static approaches. We will catalyze collaborative research efforts by creating and sharing comprehensive training, responsible use, and outreach programs. Concurrently, we will establish a community engagement program featuring: (1) annual training workshops for researchers and clinicians, (2) collaborative research pilot programs to help facilitate adding community-identified linkages to NBDC data, (3) integration with existing neuroimaging initiatives and consortia, and (4) development of educational materials and best practices guidelines.

Impact: This project represents a paradigm shift toward environmentally enriched brain development research, moving beyond traditional residential approaches to embrace the dynamic importance of place and time. The project's innovations include the first comprehensive geospatial infrastructure for developmental neuroimaging, novel statistical methods adapted from exposure science and geography, and unprecedented integration of the external environment exposome with brain development patterns. The anticipated impact extends across multiple domains: researchers will gain powerful new tools for understanding brain development, and the broader scientific community will benefit from enhanced data sharing and collaborative opportunities. Ultimately, the NBDC Geospatial Hub will accelerate translation of neuroscience discoveries into improved outcomes by determining *when, where, and for whom*, place-based health preventions and interventions may best improve brain health for all.

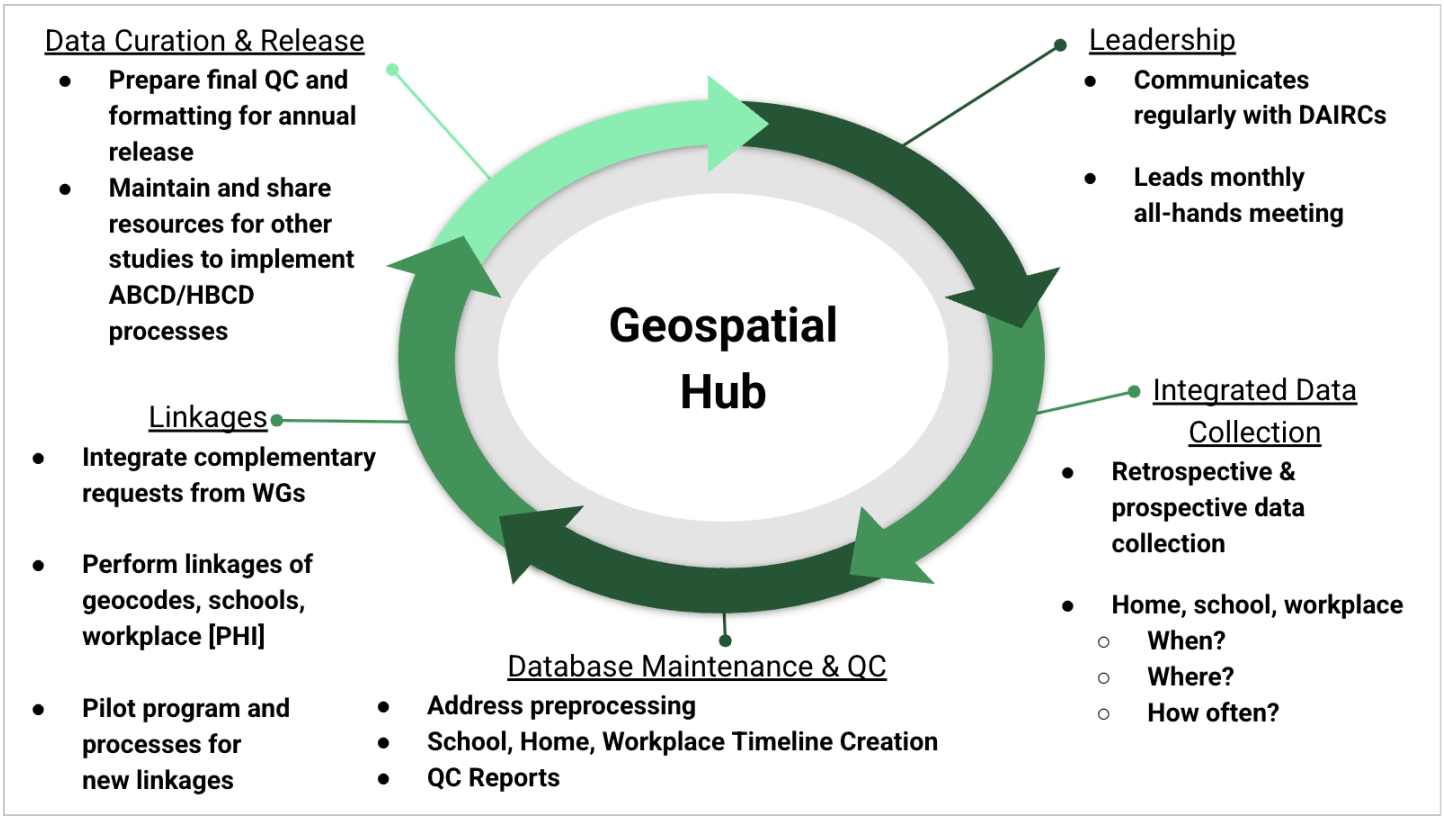


Figure 8 Geospatial Hub Workflow in the Research Cycle. *The geospatial hub centralizes integrated data collection, linkages, database maintenance & QC processing, and data curation for annual releases. In addition, the leadership of the geospatial hub communicates with ABCD working groups and DAIRC leadership and leads monthly meetings with researchers interfacing with the geospatial hub.*