

Conditions Affecting Neurocognitive Development and Learning in Early Childhood (CANDLE):

Manuscript Analysis Plan Proposal (MAPP) Guidelines 3/2018

Prior to submitting a research proposal to the CANDLE Emerging Science Coordinator, please read the following MAPP guidelines. The goal of these guidelines is to ensure that high quality publications are produced in a timely fashion and that analysis plans do not substantively overlap.

Manuscript Analysis Plan Proposal (MAPP) Guidelines:

All investigators that would like to use CANDLE data for conference or publication purposes must submit a Manuscript Analysis Plan **Cover Form** and **Proposal**. Analysis Plan Cover Forms and Proposals should be submitted to the CANDLE Emerging Science Coordinator. These forms must be completed and submitted electronically via the CANDLE website. The Analysis Plan Proposal must include the following submitted in ONE DOCUMENT (Word .doc or .docx format):

1. **Title of the Project:** Please provide a title that clearly identifies the primary predictors and outcomes in your proposed research. Titles such as “Investigating Stress Effects on Development” or “Examination of Biomarkers Associated with Child Socioemotional Outcomes” are too broad and will not allow for adequate tracking.
2. **Investigator List:** (please include all investigators that will provide substantial guidance on the manuscript and co-author any resulting manuscripts). Please note who will be leading the statistical analyses and details of his or her level of expertise in that domain. Students will be permitted to be the primary author on submitted projects only if specific conditions are met: the student must demonstrate the necessary expertise in the area of study, provide evidence of adequate supervision from their mentors, and propose a novel and publishable project. Student/trainee applicants hoping to obtain CANDLE data for their own statistical analysis and write-up must be working closely with an existing CANDLE investigator and must provide the information set out in the document ‘Trainee/Mentor Analysis Plan Agreement Form’. Please see details on CANDLE authorship below.
3. **Background and Significance:** Please provide a suitably comprehensive review of the literature pertaining to your topic to demonstrate the need for the proposed analyses, the novelty of your research proposal, and its potential contribution to the literature. Also summarize why CANDLE provides a suitable population for your study. Please note that applications capitalizing on the unique characteristics of the full sample will be given priority.
4. **Study Aims and Hypotheses:** In addition to general aims, please provide clearly articulated and specific hypotheses. These hypotheses should be directional and indicate specific outcomes and predictors (for example, it is not sufficient to “test relations with socio-emotional development”). This is essential to ensuring that we avoid overlapping proposals, and analysis plans without specific hypotheses will be rejected without being reviewed. Similarly, proposals must demonstrate appropriate scope (i.e. a defined research question within a single, larger outcome area), and plans may be returned to the investigator if they are too broad in scope. Please see our example analysis plan for further clarification.

5. **Approach:** Please provide a detailed description of the methodological approach you will use to test your hypotheses, including *specific* statistical analyses to be used for each step of your project (e.g. rather than state “moderation analyses will be conducted” state the analytic methods by which moderation will be tested). This should also include a description of primary dependent, independent, and potential confounding variables, as well as a justification for why those variables were selected.
6. **A list of all variables to be used in the analyses:** Please review the codebook provided and measures available before formulating an analysis plan. This plan must include a concise variable list that reflects familiarity with the CANDLE measures. The Publications & Presentations committee *will not review applications without a detailed variable list that matches variable names within CANDLE.*

When uploading your Cover Form and Proposal, you will also be required to upload the CVs of the lead investigator, and any co-investigators (please be sure to include co-investigators with substantive expertise in the topic area if this expertise is not held by the lead investigator). If this is a trainee project, the CV of the primary mentor is also required. There will be space for multiple CVs to be uploaded if needed, but at least one CV is required in order to submit.

Note on manuscripts: Each analysis plan should be designed to result in at least one manuscript and a maximum of two manuscripts should results merit separate papers. Manuscripts should reflect the originally proposed specific aims. If resulting manuscripts do not reflect original aims and no amendment to the analysis plan has been submitted, investigators may not receive approval for submission.

Note on conference abstracts: Abstracts for conferences will not be considered separately, as abstracts should represent manuscripts already submitted or in progress. If an investigator would like to submit an abstract to a conference, they are welcome to do so in the context of an approved analysis plan that is intended to result in a manuscript within the 9-month grace period. Please carefully attend to the timelines listed to allow for the MAPP review to be completed before relevant conference submission deadlines.

Manuscript Analysis Plan ID Number

Once a complete application is received, each manuscript analysis plan proposal will be given a MAPP ID#. Please reference this number in email subject lines and in all future verbal communication with CANDLE staff.

MAPP Application Review Process

All submitted proposals will undergo the same review process described below. Investigators will receive feedback on their proposals within 6 weeks of their submission, although efforts will be made to provide feedback more quickly. Please note that under NO circumstances will this proposal review process be expedited.

1. Review by the CANDLE Emerging Science Coordinator to assess completeness of the application and overlap with existing plans. Plans will be rejected at this stage if they 1) significantly overlap with an existing plan, or 2) are incomplete. All other plans will be forwarded to the Publication and Presentation (P&P) Committee.
2. Review by the Publication and Presentation (P&P) Committee
 - a. Two members of the CANDLE P & P Committee with substantive expertise in the area of the proposed project and a biostatistician will be assigned by the Principal Investigator and Co-Directors. This team will review the proposal for significance, innovation, methodological approach, and the qualifications of the investigators. Comments and recommendations regarding approval will be provided. If specific CANDLE investigators have made significant scientific

contributions to the CANDLE study or possess required expertise for the execution of the proposed work, submitting authors will be asked to include these investigators as co-authors.

3. Investigators will be contacted with one of the following outcomes:
 - a. The Analysis Plan is approved
 - b. The Analysis Plan is pending and requires investigators to respond to issues raised by the P&P committee and resubmit their proposal.
 - c. The Analysis plan is rejected due to significant overlap with an existing project, lack of expertise on investigative team, or limitations in the research proposed.

Data Use Agreement

The investigator must sign a Data Use Agreement Form if he or she is given direct access to the data. This agreement includes a commitment to analyzing the data only for the purposes laid out in the Analysis Plan, and to destroying any datasets received once analyses are completed. If a Data Use Agreement is required for your project, the Emerging Science Coordinator will contact you for more details.

Using covariates in the CANDLE study:

One of the many strengths of the CANDLE study is the very rich data that characterizes the experiences of both mothers and children in the cohort. As a result, it is possible to include many potential confounders in models designed to test specific hypotheses. When chosen based on prior literature or with empirical justification, the inclusion of covariates can greatly strengthen one’s ability to make causal inferences using the CANDLE data. As a result, many MAPPs will include a large number of covariates. In general, we believe this is a great strength of the CANDLE data an encourage investigators to include thoughtfully selected covariates in their analysis plans.

However, one challenge with this approach is that final analyses may appear similar to each other if all effect estimates are presented in final tables. For example, a regression model that examines the relation between birth weight and cognitive performance many look very similar to a regression model looking at maternal stress and cognitive performance if that model also includes the covariate of birth weight and all effect estimates are presented. In both of these final papers, an effect estimate for the relation between birth weight and cognitive performance would be presented even though this is not the primary aim of the latter paper.

To address this, we suggest that whenever possible, CANDLE investigators do not show the effect estimates for all the covariates in their models when presenting their regression results. Instead, we suggest that investigators present the effect estimates for their primary predictor(s) and summarize their covariates in a footnote at the end of the table. An example of this approach is available in the following paper (see Table 3, pictured below):

TABLE 3. Adjusted Means of Infant Growth Parameters According to WIC Participation

Outcomes	No WIC (Access Problems) (N = 340)	No WIC (No Perceived Need) (N = 188)	WIC (N = 5,395)	P Value*
Weight-for-age z score	-0.23	-0.02	0.009	.008
95% CI	-0.41, -0.10	-0.18, 0.22	-0.03, 0.04	
P value†	.002	.74		
Length-for-age z score	-0.23	.21	0.002	.003
95% CI	-0.43, -0.09	0.001, 0.45	-0.05, 0.03	
P value†	.006	.04		

Multivariate regressions are adjusted for study site, race/ethnicity of infant, infant birth weight, months breastfed, infant’s age, caregiver’s employment status, caregiver’s education, household’s receipt of housing subsidy, caregiver’s receipt of public insurance, whether infant’s family received TANF benefits, and whether infant’s household received food stamps. CI, confidence interval.

* Three-group comparison.

† Two-group comparison (each No WIC group versus WIC group).

Reference: Black, M. M. (2004). Special Supplemental Nutrition Program for Women, Infants, and Children Participation and Infants' Growth and Health: A Multisite Surveillance Study. *Pediatrics*, 114(1), 169–176.

We realize that depending on the disciplinary backgrounds of the reviewers at a given journal, full regression models may be requested. We will examine these requests on a case-by-case basis and work with investigators to find a solution.

Amendments to the Analysis Plan Including Additional Data Requests:

If, in the process of data analysis or manuscript development, additional data is required and/or the main objectives deviate from the original plan, the first author is responsible for submitting a Manuscript Analysis Plan Amendment. If you are requesting additional data, a brief description of why the variables are required for the analysis must accompany each request. If the variable request and justification suggests a departure from original aims, either an amendment or new analysis plan will be requested. These documents should be sent to the Emerging Science Coordinator prior to initiating the new work and include:

1. Manuscript Analysis Plan Amendment Form
2. A revised Manuscript Analysis Plan Proposal that accurately reflect new aims, hypotheses, required variables and appropriate literature review to match the new focus of inquiry. See details for formatting in the Manuscript Analysis Plan Amendment Form.

Amendments are reviewed by the same process as new analysis plans. While amendments may be approved in a shorter time frame depending on the extent of changes, please allow 3 weeks for amendments to be approved. If the P & P committee decides that the amendment is too great a departure from the original plan, a new plan will be requested (the original AP # will be closed and a new one assigned).

Expiration of Manuscript Analysis Plans

Manuscript Analysis Plans remain current for 9 months from the date of approval. If the Emerging Science Coordinator has not received a complete manuscript draft within 9 months, the Analysis Plan will enter a probationary period. At this time, the investigator's progress will be evaluated and barriers to completion assessed. If sufficient progress has not been made, the project may be claimed by another investigator—either as a new, independent effort or in collaboration with the original investigators. If no new investigator has shown interest in the area of focus, the original investigator may request that their Analysis Plan be extended (See Section M).

If investigators knowingly choose to cease effort on an MAP, either due to lack of time and interest or due to unpublishable results, the investigators should immediately inform the Emerging Science Coordinator so that records can be updated in a timely fashion.

Review and Approval of all Abstracts, Manuscripts and Grants

Once analyses are completed and investigators must work with the CANDLE scientific management team prior to presenting their findings to the scientific community. All conference abstracts, manuscripts, and grants must be submitted to Emerging Science Coordinator prior to submission (allow two weeks for the review of abstracts/presentations, and four weeks for the review of manuscripts and grants). No submission of any kind will be approved if there is not a current, approved analysis plan associated with the project, so be sure to allow time for that process.

1. For each type of submission, the investigator is responsible for submitting the abstract, manuscript or grant and the corresponding review form (Abstract/Presentation approval form, Manuscript Approval Form, Grant Approval Form, respectively) to the Emerging Science Coordinator. Separate requests for approvals need to be submitted for an abstract submission as well as the subsequent poster or presentation.
2. The P & P committee will review submissions and inform primary investigators if they are approved. The primary reasons for review, and criteria for approval at this stage are 1) confirm fidelity to the approved analysis plan, 2) ensure that no CANDLE data would be disclosed by the publication,

- 3) identify potentially patentable intellectual property which would be disclosed by the publication, and
 - 4) to confirm that the privacy rights of individuals are adequately protected. The PI or study designee manuscript review may provide comments on the technical merit or scientific content of the proposed publication.
3. A list of CANDLE authors that must be included in manuscripts using CANDLE data will be provided at that time as well, which will include, at a minimum, all members of the CANDLE leadership team. This team is responsible for funding cohort maintenance and biospecimen assay, data acquisition and processing, study management, and providing information that allow analyses and write up of the CANDLE data; all individuals to be listed as co-authors will be expected to meet ICMJE uniform authorship requirements (described below).
 4. Copies of all final submissions, presentations, and accepted manuscripts must be shared with the Emerging Science Coordinator at the same time that they are submitted.

Responsibilities of the Primary Investigator

It is the responsibility of the primary investigator to:

1. Keep his or her analysis plan up to date
2. Submit amendments or new analysis plans when appropriate
3. Ensure that all coauthors have been provided with adequate time to review and provide edits to the manuscript prior to sending it to the Emerging Science Coordinator for approval prior to submission.
4. Submit all abstracts, manuscripts, and grant applications for review and approval by the P & P committee *prior to submission* at conferences, journals or funding agencies, respectively. The P&P will review these products and provide feedback and/or approval within two weeks.
5. Submit all final CANDLE related research projects to the Emerging Science Coordinator (i.e. all accepted manuscripts, funded grants, and abstracts) so that the CANDLE archives remain current.
6. Maintain up to date IRB approval for their project in a manner in line with the expectations of their University.
7. Providing IRB approval to CANDLE staff when requested.

Investigators who do not take these responsibilities seriously will lose their good standing with the CANDLE study. This may result in consequences such as: revocation of permission to conduct analyses with CANDLE data, interruption in presentation or publication progress until requirements are met, denial of future proposals, and/or communications with respective University department leadership or scientific ethical conduct boards.

Authorship Guidelines for CANDLE Manuscripts

- 1) General Principles
 - a. Criteria for authorship on a CANDLE article should follow the uniform requirements published by the International Committee of Medical Journal Editors (ICMJE) (see www.icmje.org) in that a co-author should contribute to (1) conception and design, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) approve the final version of the manuscript or abstract. Each putative co-author must be given the time and opportunity to contribute substantially to the elements listed above. All authors, including the CANDLE leadership team, those that the CANDLE Publication Committee suggested collaborate on the manuscript, and co-authors selected by the Primary Investigator, must meet the ICMJE authorship criteria for inclusion as authors prior to submission. If necessary, the CANDLE Principal Investigator (PI) will be the arbiter of the final authors list for a manuscript. Acknowledgements on manuscripts may include more than one person associated with the CANDLE Study. CANDLE administrators will provide a list of individuals and funders who contribute/d significantly to the start-up or ongoing conduct of CANDLE and who should be acknowledged in all publications if they do not meet the criteria for authorship.

- b. Conference or Meeting Abstracts: Abstract submissions are only approved for previously-approved MAPPs. In general, the same principles for authorship on journal articles apply to abstracts submitted for presentation at meetings. However, given the preliminary nature of data contained in abstracts and the seemingly inevitable rush to meet deadlines, some flexibility is appropriate. In particular, lead authors may need to limit the abstract author list because of space restrictions. It should be assumed that for all abstracts submitted, a manuscript on the topic will be prepared, and those interested in co-authoring the manuscript should communicate with the principal author of the manuscript. Co-authors for an abstract should generally be co-authors of any corresponding manuscript; it is understood, however, that, because of personnel turnover and other reasons, this may not always be possible.
- c. Using CANDLE Biospecimens to Validate New Assays: In some cases, investigators may be approved to use CANDLE biospecimens to validate new assays that will be of use to the CANDLE study. When publishing manuscripts describing the new assay, CANDLE should be acknowledged as the source of the specimens. However, it may not be necessary to include additional CANDLE investigators as authors on the publication. Investigators interested in pursuing this type of study should discuss authorship with the CANDLE PI. Please remember that, prior to conducting any assays or developing resulting manuscripts, the Publication & Presentation Committee must approve these activities.

Archives

The Emerging Science Coordinator will maintain an electronic archive of all CANDLE publications, posters, presentations, etc. Electronic copies of the final version of all manuscripts will be available via the CANDLE website (See Section R). Electronic copies of abstracts and presentations are available upon request, and only with approval of the first author.