Ancillary Study Policies

JHS Ancillary Study Policies

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Ancillary Study Policies

1. Purpose

The Jackson Heart Study (JHS) encourages investigators to propose and conduct ancillary studies that further the aims of the JHS and contribute to scientific advances and discovery. Ancillary studies enhance the value of the JHS and provide a unique opportunity for investigators to leverage the infrastructure of the existing cohort to conduct additional projects.

2. Definition of an ancillary study

A JHS ancillary study is a study that uses JHS resources (i.e., participant contacts, biospecimens, images, personnel) but is supported by sources outside of the JHS contract. Examples include studies funded by investigator-initiated NIH R01s, grants from academic institutions, or those funded by private resources.

A study that involves the *collection of new data directly from participants* (e.g., questionnaires, biospecimen collection, physical measures) is an ancillary study. This type of study typically requires subcontracts to support JHS Field Center and Coordinating Center activities. This type of study requires review and approval by the Ancillary Studies Committee, Lab Committee (if collecting biospecimens), Steering Committee, OSMB, and NHLBI.

A study that involves the *use of previously collected biospecimens* (blood, urine) is an ancillary study. This type of study typically requires subcontracts to support JHS Coordinating Center and JHS Central Lab Biorepository activities. This type of study requires review and approval by the Ancillary Studies Committee, Lab Committee, Steering Committee, OSMB, and NHLBI.

A study that involves the *use of previously collected images or other physical or digital study records* (e.g., medical records) is an ancillary study. This type of study typically requires subcontracts to support JHS Coordinating Center activities. This type of study requires review by the Ancillary Studies Committee and Steering Committee.

A study that involves *secondary data analysis only* is also considered an ancillary study. This type of ancillary study application requires review by the Ancillary Studies Committee and Steering Committee. A subcontract with the JHS Coordinating Center may or may not be necessary depending on the scope of the data needed, planned analyses, variables that will be generated, and adherence to the data management and sharing plan for integration into the parent dataset.

Ancillary studies must have all required approvals prior to submission for funding.

3. Review of an ancillary study

Ancillary studies are subject to the same policies, reviews, and approvals as the parent JHS protocol. The highest priority will be given to studies that:

a. Have the highest scientific merit;
b. Do not interfere with the parent study objectives;
c. Have objectives directly related to the parent study;
d. Produce the least burden on participants;
e. Require the unique characteristics of the JHS cohort; and
f. Can be integrated with the parent study or other ancillary studies to minimize participant burden and optimize operational efficiency.

In addition, priority for studies requesting biospecimens (blood, urine) will be highest if they:

a. Use thawed samples when possible;
b. Use assays that may be done on more than one sample type to allow selection of the most abundant type available (e.g., serum or EDTA plasma);
c. Use the smallest sample volume possible (volumes requested will be examined by the Laboratory Committee);
d. Do not request samples from participants with the least amount of sample; and
e. Can be integrated with other studies to conserve sample or limit freeze-thaw cycles.

4. Responsibilities of Ancillary Study Principal Investigators

a. **Costs.** The investigator applying for an ancillary study must provide all additional funds required to conduct the study. The JHS Field Center incurs expenses on behalf of ancillary studies when participant contact (e.g., mailings, calls, text messages) or review of medical records is required. The JHS Coordinating Center incurs expenses on behalf of ancillary studies related to regulatory approvals, generate pull list for biospecimens, data collection, data management, quality control, study coordination and communications, and reporting. The JHS Central Lab Biorepository incurs expenses to pull, aliquot, and ship specimens to outside labs. Therefore, PIs should consult with the JHS Ancillary Study staff (jhsanc@umc.edu) to determine what level of involvement will be required and the associated costs. This will result in subcontracts to be included in the PI's grant application.

b. **Confidentiality and identification of JHS participants.** Confidentiality of individually identifiable data about JHS participants must be assured. As a general rule, no personal identification of participants will be provided to ancillary study investigators and their staff. There are no assurances that participants will be able to be identified and contacted in the future for the purpose of an ancillary study if the parent study ends.

c. **Clinical implications of findings.** The proposing investigator must clearly delineate any findings of clinical significance that may result from the study, including genetic findings, and propose how these will be handled, including reporting to participants, and their physicians and providing recommendations for follow up. This includes incidental findings, such as pathology identified from an imaging study that is not the focus of the study.

d. **Genetic studies**. Genetic studies may include only participants who provided appropriate informed consent. Investigators should consult the JHS Coordinating Center to determine the number of participant samples eligible for analysis based on responses from the appropriate informed consent. Medical and other (ethical, legal, and social) implications of the findings and reporting of results must be addressed in the proposal.

e. **Early communication with JHS Centers.** The proposing ancillary study investigator should consult with the JHS Ancillary Study Staff (jhsanc@umc.edu) to discuss the anticipated involvement of the Field Center, Coordinating Center, Central Lab, and Reading Centers. Such discussions focus on feasibility and provision of necessary resources and do not constitute formal approval of the study.

f. **Inclusion of JHS Field Center and/or Coordinating Center Investigator.** A JHS Field Center and/or Coordinating Center-affiliated investigator must be included as a co-investigator (or co-PI as appropriate) on an ancillary study. This individual is responsible for reviewing the ancillary study proposal **before** it is submitted to the Ancillary Studies Committee; monitoring the study to assure continuing compatibility with JHS; and serving as a liaison to the JHS Steering Committee. In addition, manuscripts and abstracts are generally expected to include a JHS FC and/or CC-affiliated investigator. For assistance in identifying a JHS FC and/or CC-affiliated investigator, contact jhsanc@umc.edu.

g. **Data Management and Sharing.** NHLBI expects ancillary studies to adhere to NIH and NHBLI data-sharing policies regardless of funding source, as outlined in the agreement between the parent and ancillary study. Any limitation on sharing must be communicated to the parent study and strongly justified (e.g., Tribal sovereignty, consent restrictions). Ancillary studies funded through an NIH application submitted on or after January 25, 2023, are subject to the NIH DMS Policy and require a Data Management and Sharing (DMS) Plan. DMS plans will be reviewed by the NIH. Ancillary study DMS Plans must clearly reference the relevant parent study approved repository and parent study policies, as well as the ancillary study investigator's planned adherence to those policies. Changes to an NIH DMS Plan for an ancillary study must be discussed with the parent study before NIH submission and approval.

h. **Timeline.** All proposed ancillary studies must be submitted via the online portal. Ancillary study applications must be submitted **12 weeks** prior to the grant application deadline. Applications submitted after this deadline may not receive approval prior to the grant submission deadline, and will not be allowed to include JHS in the grant application. In addition, studies that involve subcontracts must have their final budget negotiated and approved for internal institutional review no later than **2 weeks** prior to the grant application deadline.

i. **Final application or proposal.** The JHS Ancillary Studies Staff and/or NHLBI Project Officer may request a copy of the final grant application submitted for funding.

j. **Industry participation.** Proposals for industry sponsorship or collaboration will be evaluated in accordance with the procedures described above. In addition, it will be the responsibility of the PI to obtain agreement through an appropriate contractual mechanism that all data relevant to the JHS ancillary study will be shared with the CC. As an initial step in planning, the PI should contact the NHLBI Project Officer to determine if an agreement between NHLBI and industry is required or to approve the agreement between industry and the investigator's institution. Industry-sponsored ancillary studies shall include participants who provided informed consent allowing for-profit collaborations and must comply with current NHLBI guidelines. The NHLBI Third Party Involvement Guidelines can be found at http://www.nhlbi.nih.gov/funding/policies/thirdparty.htm.

k. **Progress report.** The ancillary study PI must provide semi-annual progress reports to the JHS CC with updates on the progress of the study (including funding status, start date, changes in protocol, and any publications or presentations). These reports will be included in the Steering Committee, NHLBI, and OSMB reports.

l. **Amending an ancillary study proposal.** If there are changes to the science or scope of an approved ancillary study, either before or after becoming active, then an amendment request must be submitted for review by the Ancillary Studies committee. Review by the Lab Committee, Steering Committee, OSMB, and NIH may also be required depending on the extent of the request. The PI must submit the request to the JHS Ancillary Study staff (jhsanc@umc.edu) and include:

- A revised study proposal with changes from the approved version tracked; and a clean copy of the revised proposal.
- A brief memo summarizing the requested changes and the rationale for the changes.

Examples of changes requiring review and prior approval:

- request for additional specimen or use of different assays/platforms;
- request to add new outcomes or change the primary exposures;
- any additional participant burden;
- change of PI;

For minor changes that do not impact the science or scope of the ancillary study, the ancillary study PI must send a memo to the Ancillary Study staff for JHS administrative review and approval.

- Request to add co-investigators;
- Request to modify the analytic approach.

m. **Review of publications and presentations.** Manuscript proposals based on ancillary study data require approval by the JHS Publications and Presentations (P&P) committee. Publications, presentations and abstracts from an ancillary study must be reviewed and approved by the JHS P&P committee prior to submission or presentation, in accordance with the general rules for publications and presentations.

5. Incorporation of data from an ancillary study into the parent study database

The data collected by the ancillary study are first provided to the JHS Coordinating Center for integration into the main database, after which the ancillary study investigators will receive the integrated file containing necessary data from the parent study. The JHS De-identified Data Distribution Policy describes additional requirements that must be met to receive the integrated file, including an approved JHS manuscript proposal, a fully executed JHS Data and Material Distribution Agreement (DMDA), and evidence of IRB review. The ancillary study PI will be given the exclusive opportunity to analyze, present, and publish data collected under the auspices of the ancillary study. After data collection and review are completed (and in accordance with NIH data sharing policies and the submission timeline for the parent study), the ancillary study data will be made available for use by other investigators. Collaboration with the ancillary study investigators will be encouraged. It is the responsibility of the ancillary study PI to submit a formal written request to the Steering Committee and NHLBI if there are special circumstances that would affect adherence to these guidelines for data sharing.

For more information on the NHLBI data sharing policy:

https://www.nhlbi.nih.gov/grants-and-training/policies-and-guidelines/nhlbi-policy-for-data-sharing

https://www.nhlbi.nih.gov/grants-and-training/data-sharing-policy-faq-ancillary-studies

6. Data sharing with a consortium

Ancillary study investigators who wish to share ancillary study data and some contract-derived variables (e.g., age, sex) with a consortium must bring a proposal describing the consortium to the Steering Committee for review. Such consortia often have their own data sharing plans and their own P&P committees, and these arrangements need to be reviewed and approved by JHS before JHS contract-derived data can be contributed. Additionally, there may be limitations on data sharing based on participant consent. The Ancillary Study staff (jhsanc@umc.edu) can provide guidance about consortium involvement.

7. Closing an approved ancillary study

A funded ancillary study will be closed after data collection has been completed and all data or new variables generated by the ancillary study have been returned to the JHS Coordinating Center.

Ancillary studies that have been approved and are pursuing funding will have 2 years from the study approval date to obtain funding. If funding is not obtained within the 2-year timeline, the ancillary study will be closed. A new ancillary study application with all necessary study reviews will be required for a new grant submission.

8. Appendices

Appendix 1 – Overview of Submission and Review Process

Appendix 2 – Ancillary Studies Committee Meeting Schedule

Appendix 3 – Ancillary Study Proposal Form Template

Appendix 1. Overview of Submission and Review Process

1. Investigators wishing to propose ancillary studies are required to discuss their proposed studies with the Ancillary Study staff (jhsanc@umc.edu) before formally submitting a proposal to the JHS Ancillary Studies Committee. **Ancillary study proposals submitted without this initial contact will be administratively withdrawn.**

    a. The Ancillary Study Staff will review the planned proposal and discuss with the Ancillary Study PI to determine involvement of JHS Field Center, Coordinating Center, Central Lab and/or Reading Centers, and potential overlap.

    b. The Ancillary Study Staff will assist the Ancillary Study PI with identifying a Field Center and/or Coordinating Center-affiliated investigator for the ancillary study.

2. The Ancillary Study PI will share their proposal with the Field Center or Coordinating Center designee, and after their initial review, use the online portal to submit the ancillary study proposal.

3. Ancillary study proposals will be reviewed by the Ancillary Studies committee. The committee meets monthly to review complete proposals (i.e., those that have all required documents submitted and any queries addressed). The ancillary study proposal must be approved by the Ancillary Studies committee before obtaining other study approvals.

    a. If the Ancillary Studies Committee requires revisions to the ancillary study proposal, the review comments are sent to the Ancillary Study PI. The PI must address these comments in a memo that accompanies the revised proposal (tracked and clean copies) and submit to the Ancillary Studies Staff (jhsanc@umc.edu). The revised ancillary study proposal will be reviewed by the Ancillary Studies committee.

    b. If the ancillary study is not approved by the Ancillary Studies committee, no additional study reviews will occur and the application will be closed.

    c. If the ancillary study is approved by the Ancillary Studies committee, the ancillary study proposal will be sent to the JHS Steering Committee for review and approval. The Steering Committee meets monthly.

    d. *For proposals that are approved by the Steering Committee and involve participant contact or use of biospecimens*, the proposals are sent to the NHLBI Project Officer and OSMB Executive Secretary. The OSMB review period is 2-3 weeks. The results of the OSMB review are communicated by formal letter to the PI by the OSMB Executive Secretary (with copies to the Chairs of the Steering Committee/Ancillary Studies Committee, and NHLBI Project Officer).

Appendix 2. Ancillary Studies Committee Meeting Schedule

MEETING DATES: (2ND THURSDAY)	SUBMISSION DEADLINES: (ALL DEADLINES ARE NOON CT)
JANUARY 9, 2025	December 30, 2024
FEBRUARY 13, 2025	February 1, 2025
MARCH 13, 2025	March 1, 2025
APRIL 10, 2025	April 1, 2025
MAY 8, 2025	May 1, 2025
JUNE 12, 2025	June 1, 2025
JULY 10, 2025	July 1, 2025
AUGUST 14, 2025	August 1, 2025
SEPTEMBER 11, 2025	September 1, 2025
OCTOBER 9, 2025	October 1, 2025
NOVEMBER 13, 2025	November 1, 2025
DECEMBER 11, 2025	December 1, 2025

Appendix 3. Ancillary Study Proposal Form Template

JACKSON HEART STUDY ANCILLARY STUDY PROPOSAL FORM

PART 1: Basic Study Information and Projected Impact on JHS

1) Date:

2) Title of study:

3) Keywords:

4) Ancillary Study Principal Investigator(s):
    a. Name:
    b. Institutional affiliation:
    c. Address:
    d. Phone number:
    e. E-mail address:

5) JHS Field Center or Coordinating Center Representative:
    a. Name:
    b. Institutional affiliation:
    c. Address:
    d. Phone Number:
    e. E-mail address:

6) Other Ancillary Study Co-investigators:

Co-Investigator (Last name, First name)	**Institution Affiliation**	**Phone number & E-mail address**	**Responsibility**	**Percent Effort**

7) **Are there any potential areas of overlap?** Please contact the JHS ancillary study staff and JHS Field Center or Coordinating Center representative to confirm. If there are potential areas of overlap, please state how this will be addressed.

8) **Collaboration approval:** Does this ancillary study use data from or rely on the use of data from another approved ancillary study? Yes □ No □

   If yes, please provide the Ancillary Study name and number.

9) **Funding:**

   a) Source:
      - If NIH, specify funding mechanism:
      - Note: If direct costs ≥ $500K in any year, prior approval from NIH is required. Additional time for ancillary study review will be needed to meet the required milestones for seeking and obtaining NIH prior approval.
   b) Grant due date:
   c) Proposed grant start date:
   d) Proposed grant end date:
   e) Does this study involve the support or collaboration of a for-profit entity?
      Note: For-profit involvement requires that participants who did not consent to their data being used by private companies be excluded.

10) **Sample Size:** Explicitly state the size and any special characteristics of the participant sample.

   a) Proposed sample size
   b) Proposed inclusion criteria
   c) Proposed exclusion criteria

11) **Participant involvement:** Will participants be contacted, interviewed, or examined?
   Yes □ No □

   If yes, please list participant involvement and estimate the time required for each measure (e.g., questionnaire, specimen collection, physical measurement) in the table below. *Note: Each questionnaire must be listed separately in the table and uploaded with this application.*

Measure	Contact Type Required	Estimated Time	If questionnaire, is it validated?	If questionnaire, is permission to use or a license agreement required?	If questionnaire, provide reference for its development and scoring.
e.g., CES-D 20-item scale	In-person or phone	15 minutes	Yes	No permission to use is required. Available in public domain.	Radloff, L. S. (1977). The CES-D Scale: A self-report depression scale for research in the general population. Applied Psychological Measurement, 1(3), 385–401.

12) **Biological Specimens:** Do you propose to use stored specimens or collect new samples?
Yes □ No □

If yes, please list the proposed analyte, specimen type required for each analyte (serum, plasma, citrate, urine, DNA), volume of specimen, exam cycle and numbers of participants.

Analyte	Type of specimen	Exam Cycle	Amount of specimen	Number of participants

a) Total volume of each sample type you would like sent: _____

b) Do you propose to request a total sample volume that exceeds 250 microliters (µl) and/or samples from Exam 1 (baseline)? Yes □ No □
If yes, please provide justification.

c) Are re-frozen samples acceptable? Yes □ No □
If yes, please indicate whether there are any limits on the number of freeze-thaw cycles.

d) Laboratory performing analysis:
   I. Lab Investigator Name:
   II. Lab Institutional affiliation, if any:
   III. Address:
   IV. Phone number:
   V. E-mail address:
   VI. Means of specimen delivery to the laboratory:
   VII. Storage resources (e.g., emergency power for freezers:
   VIII. Bar code reader available: Yes □ No □

e) List method of analyses for each analyte requested in the table below.

Test	Assay	Method of Analysis (e.g., ELISA, HPLC) (include manufacturer)	Lower Limit	Upper Limit	Low CV	High CV

f) If a proposed assay or kit is not well-validated or relatively unknown, specify additional details here:
    a. Name of test:
    b. What is the test for and what does it provide for the JHS?
    c. References for method:
    d. Kind of specimen required:

g) Projected timeline for:
    a. Pulling and shipping samples:
    b. Sample analysis:
    c. Return of samples to lab:
    d. Have you corresponded with the JHS core lab about this ancillary study?
    Yes □ No □

h) Please specify plans for disposition of any residual specimen.

13) **Images:** Do you propose to have access to images such as CT scans, ECG, MRI, ultrasound?
Yes □ No □

If yes, describe imaging materials requested in table below.

Image Type	Exam Cycle	Format requested	Additional information?

14) Does your study require raw data files from the parent study or data that is access-restricted (e.g., CMS data)? Yes □ No □
If yes, specify and provide justification.

15) **JHS Coordinating Center Involvement:** Describe the estimated effort and time required of JHS Coordinating Center staff for the proposed ancillary study activities in the table below.

Activity	Estimated effort or time	Comments
Local regulatory approvals (e.g., IRB) and required study reporting		
Sample selection and coordination with central biorepository		
Data collection forms review		
Create and test data collection project		
Quality assurance and quality control		

De-identified data set preparation		
Statistical analysis		
Data management and integration into parent study dataset		
Other (Specify:)		
Other (Specify:)		

16) **JHS Field Center Involvement:** Describe the estimated effort and time required of JHS Field Center staff for the proposed ancillary study activities in the table below.

Activity	**Estimated effort or time**	**Comments**
Participant recruitment		
Administer interviews		
Conduct measurements		
Collect blood or urine specimens		
Prepare and disseminate participant results letters		
Medical records review or abstraction		
Other (Specify:)		
Other (Specify:)		

17) **Genetic Information**: Does your proposal plan to use genetic data (defined as any data from participant's DNA)?
Yes □ No □

If yes, please answer the following items.

a) What gene(s) will be investigated?
b) Will genetic information be used to address a primary aim or secondary aim of the JHS?
□ Primary aim (heart and vascular disease)
□ Secondary aim (other health conditions)
c) Should genetic results be reported to participant's physicians? Base your response on your knowledge of existing literature and current practices regarding increased risk and availability of treatment for adverse outcomes associated with the gene mutations to be studied. Describe the plan for addressing any relevant clinical or other (ethical, legal, or social) implications of the findings.
d) If your proposal requires genetic informed consent, provide the estimated number of participants who have the appropriate consent.

18) **Clinical Implications**: Will the findings have clinical implications? If so, describe the plan for reporting results to participants and providing recommendations for follow-up.

19) **Quality Control**: If new data is being collected or new variables being generated, describe the quality control process that will be implemented.

20) **Patent Intent**: Do you intend to use the data to patent any process, aspect or outcome of the analysis?

21) **Rationale and Impact:** What is the advantage of conducting this ancillary study with the JHS cohort (versus other cohorts)?

22) **Assurances:** Please provide the following assurances (check each):

☐ Confidentiality of JHS participants will be maintained.

☐ The Ancillary Study PI will abide by all JHS policies and procedures.

☐ The Ancillary Study PI will report progress of the study as requested.

☐ The Ancillary Study PI will develop and submit a manual of procedures, if required, and quality control plans for their ancillary study.

☐ Data collected by the Ancillary Study, with complete documentation, will be provided to the JHS Coordinating Center for review. This submission will include newly generated data with clear labels, units (if applicable), documentation of methods, guidance for using the data in analyses, and programming code for checking and verifying any calculated or derived variables. After the submission has been reviewed and passes data quality checks, the Ancillary Study Investigators will receive an integrated file containing data from the parent study. The ancillary study PI is given the first and exclusive opportunity to analyze, present and publish data collected by the ancillary study. The JHS Coordinating Center will make ancillary study data available for use by other investigators in accordance with the timelines and conditions outlined by the parent study contract and NHLBI. Collaboration with ancillary study investigators who collected the data will be encouraged. An ancillary study PI who wishes to extend the period of protected use must send a written request with justification to the Steering Committee for review.
https://www.nhlbi.nih.gov/grants-and-training/policies-and-guidelines/nhlbi-policy-for-data-sharing-from-clinical-trials-and-epidemiological-studies

Part 2: Description of the Proposed Ancillary Study

Please provide a research narrative (maximum 5 pages not including references) for the proposed study, and include the following:

a) Abstract (maximum 1 page)
Summarize background information and literature, and state how they lead to the questions(s) of interest. Include a concise justification and explanation of the research question(s) to be addressed. Conclude by stating the aim of the ancillary study and summarizing the method(s) that will be used to address the question(s).

b) Specific Aims (maximum 1 page)
Identify the research questions or hypotheses to be addressed by the ancillary study.

c) Significance
Explain in detail, the significance of the planned work. Explain why this information is lacking with regard to the ancillary study question(s), and how the proposed study will address that gap. Finally, explain how the methods and/or information from the JHS will address the ancillary study question(s). Acknowledge any limitations or concerns related to the proposed methods, and explain how they have been or will be dealt with.

d) Approach
1. Study population – Describe the sample of interest (e.g., the entire JHS cohort or subgroups). Include the anticipated time frame of participant involvement (if any).

2. Methods – Describe information to be collected and any methods or equipment to be used. Included detailed explanations and protocols for each method used. Explain how the information from the method or equipment will address the question(s). Describe data needed from JHS parent study and how defined (e.g., exposure, outcomes, covariates).

3. Statistical Analysis – Explain how each study hypothesis will be analyzed. Include any current hypotheses or information that might influence the approach to the analysis or the question.

4. Power Calculations

e) References