National Cancer Institute

Interactive Diet and Activity Tracking in AARP (IDATA)

Polices & Procedures

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1. Background

1.1. The Interactive Diet and Activity Tracking in AARP (IDATA) Study

Scientists have made some notable advances over the last two decades on the impact of changes in nutrition on cancer incidence and mortality. However, there is considerable uncertainty about the structure of dietary and physical activity measurement error which presents a serious challenge to research efforts to assess links between physical activity, diet, and cancer. Such error may lead us to miss important diet- and physical activity-related cancer connections and thereby fail to grasp the extent to which energy intake, dietary change, and increased physical activity could alleviate the burden of malignant disease.

The Interactive Diet and Activity Tracking in AARP (IDATA) was conducted to understand the measurement error properties of both new and conventional diet and physical activity assessment tools against reference biomarkers.

1.2. IDATA Study Participants

IDATA Study participants were recruited from a list of AARP members aged 50-74 years residing in and around Pittsburgh, Pennsylvania. Eligible and consented participants visited the study center three times and also completed assigned activities at home over a 12-month period.

The study recruited 4,967 patients, through the phone and study center screening patients were excluded from study eligibility. The final number of eligible subjects in the CDAS population was 1,082 who were deemed study eligible, had data and had given consent. Participants were assigned to Groups 1, 2, 3, or 4 and followed a specified 12-month assessment protocol. Groups 1 and 3 followed the same assessment schedule whereby reference biomarkers were collected during the first month of assessment. Groups 2 and 4 followed an alternative assessment schedule whereby reference biomarkers were collected during the sixth month of assessment. A subsample of participants (designated by S below; n= 66) were recruited to provide repeated measures of reference biomarkers. For detailed information about study enrollment, including reasons for ineligibility along with charts of which administrations were performed when, please visit the IDATA CDAS site found here: https://cdas.cancer.gov/learn/idata/study-summary/.

1.3. IDATA Study Data and Biospecimen Elements

Data and specimens currently available for research include:

- Demographic and anthropomorphic characteristics
- Physical activity self-report
    - Self-reported 24 hour activity measures
    - Questionnaire for activity over the past 12 months
    - Questionnaire for selected activities over the past 4 weeks
- Physical activity objective monitors
    - Physical activity monitoring measuring acceleration in 3 axis, body position, and ambulation
    - Physical activity log detailing the activities performed while wearing either monitor
- Dietary and Food Frequency Habits
    - Questionnaire detailing food frequency habits for the past 12 months (DHQII)
    - Self-administered 24 hour food recall (ASA24)
    - Food checklist detailing all foods consumed during a 7 day period (7-Day Food Checklist)
- Blood specimens collected from the participants at each of the 2 study center visits
- 24-hour and First Morning Void urine samples collected after each of the 2 study center visits at home
- Saliva samples collected after each of the 2 study center visits at home

The IDATA Biorepository currently stores approximately 130,000 biologic specimens collected from IDATA participants. These specimens and their associated data are available to all qualified researchers through a peer-review process. The scientific utilization of the IDATA Biorepository is actively managed by the NCI, with the goal of maximizing the scientific potential of the resource and meeting strategic priorities.

2. IDATA Biospecimens Resource Descriptions

2.1. Blood Specimens

Blood was drawn from all participants at both study center visits. Two large vials of sodium heparin treated blood were collected. Off of the first, one 1.0 mL vial of whole blood was aliquoted. Then the vials were centrifuged and ultimately divided into four 1.8 mL of plasma, two 1.8 mL vials of red blood cells and two 1.8 mL vials of buffy coat. Serum was also collected and divided into two 1.8 mL vials and one vial with 0.25 mL serum and 1 mL 6% metaphosphoric acid (MPA) (Table 1)

Table 1. Summary of blood specimens

Material	1st Study Center Visit	2nd Study Center Visit
Plasma (1.8 mL)	4	4
Whole Blood (1.0 mL)	1	1
RBC (1.8 mL)	2	2
Buffy Coat (1.8 mL)	2	2
Serum (1.8 mL)	2	2
Serum MPA (0.25 + 1.0 mL)	1	1

2.2. Urine Samples

Participants were asked to collect two first morning void and 24-hour urines, six months apart. At the end of study center visits at months 1, 6, or 12, depending on study group, a 24-urine collection kit that included containers, instructions, and a cooler were given to participants to take home. On urine collection days, which occurred approximately 7-10 days after a study center visit, participants collected 100mL of the first void (FMV) of the morning in a 120mL collection container, and after that began collecting urine for the next 24-hours, including the first void of the next morning and combined this into a 4L collection container that was to be kept refrigerated. They were also asked to take a 100mg para-aminobenzoic acid (PABA) tablet, a marker for completeness of 24-hour urine collection, at breakfast and dinner. Participants were given a urine collection log to report any missed voids and time at which PABA was taken.

The urine samples were returned to the study center in a provided cooler where these samples were aliquoted (Table 2). Each FMV sample was separated into one 4.5mL and five 1.8mL aliquots. Each 24-hour urine sample was weighed and mixed and 500mL was transferred to a container for aliquotting. This sample was then separated into five 4.5mL and five 1.8mL aliquots.

Table 2. Summary of urine specimens

Material	1st Study Center Visit	2nd Study Center Visit
FMV (4.5 mL)	1	1
FMV (1.8 mL)	5	5
24 Hour Urine (4.5 mL)	5	5
24 Hour Urine (1.8 mL)	5	5

2.3. Saliva Samples

Participants were also asked to collect two saliva samples on the same day as the urine collection into two DNA Genotek Omnigene-Discover saliva collection containers. Participants were asked to provide a saliva sample upon waking prior to eating, drinking, smoking or brushing teeth. In the evening, another sample was to be collected at least 30 minutes after eating, drinking, smoking or brushing teeth. If this was not feasible they were asked to rinse thoroughly with water in the mouth at least 5 minutes prior to collecting the sample. Participants were given a saliva collection log to record time of collection along with any antibiotic use that day. Upon return to the study center, each of the samples were separated into two 1.8mL aliquots (Table 3).

Table 3. Summary of saliva specimens

Material	1st Study Center Visit	2nd Study Center Visit
Saliva am (1.8 mL)	2	2
Saliva pm (1.8 mL)	2	2

3. Policies for Access to IDATA Biospecimens and Data

- The IDATA Biospecimen resource is available to the entire scientific community. Access to the biospecimens and associated data is based on a peer review process. Details of the application and review process are described in the next section (The IDATA Application and Review Procedures).

- Only the specimens from subjects who have signed the appropriate consent will be released.

- Once a study is approved, data will be released only as "restricted-use" datasets. No identifying information will be provided in the released data sets.

- Data are non-transferable unless prior authorization by NCI has been granted.

- Recipients of IDATA samples are required to sign and abide by a NCI Material Transfer Agreement (MTA).

- Sample processing (Sample aliquoting, microbiome extraction, QC sample insertion and batching) shall be done at the IDATA central processing laboratories, unless otherwise negotiated during the review and approval process.

- Laboratory analyses shall be conducted in a blinded fashion. The linking of laboratory data with the corresponding individual data shall only be performed by the IDATA coordinating center, and only after generation of the data. Analytic datasets will then be sent to the investigator who generated the data.

- Upon completion and publication of the study, laboratory data and final study results, with an accompanying data dictionary, shall be returned to the IDATA Trial by the investigator.

- IDATA Biospecimen Committee adopts general NIH policies on data sharing, with adaptation to ensure participant privacy consistent with the informed consent. Raw and processed data as well as datasets used in a published and completed study will be made available for other appropriate research after investigators have completed their study aims. Raw and processed data will ultimately be incorporated into the study tracking system and linked to the original study and to the samples. Investigators may also be contacted by other investigators wishing to collaborate prior to completion of their study aims.

- Investigators are encouraged to develop proposals with realistic scope and focused aims, achievable within a reasonable period of time.

- Investigators have up to three years from the proposal approval time to request the shipment of samples and commence activities on the study. Investigators are required to complete annual progress reports, and expected to submit laboratory analysis results within 2 years after receipt of the samples. If an approved study remains inactive for three years, due to lack of funding or other issues, the application will be considered withdrawn. A new application will need to be submitted and reviewed if the investigator wishes to conduct the study again.

4. IDATA Biospecimen Research Priorities

In an effort to improve our knowledge about the structure of measurement error in self-reported dietary assessment tools, studies compare dietary and physical activity assessments to objective biomarkers. However there are a limited number of recovery, predictive, and concentration biomarkers to use as reference measures in assessment and methodology development. This creates a critical need for development and validation of new biomarkers -- physiologic and metabolic markers of intakes and activity. Furthermore, new and alternative methods to measure biomarkers in various types of biospecimens are needed.

IDATA study provides unique resources to explore a wide range of topics related to diet and physical activity -- not only individual components of a diet and but also overall patterns of diet and activity. The IDATA study welcomes innovative and thoughtful proposals from well-qualified and experienced investigators who wish to use specimens to conduct research on the areas mentioned above, as long as the use of such samples is appropriately justified. Studies that do not directly address measurement error or biomarkers related to diet or activity will be considered, but such studies should have potential to significantly contribute to advancing our understanding of nutrition and/or physical activity in health and disease.

4.1. Biospecimens Research

IDATA strives to adapt to the NCI Best Practices and to improve management practices to ensure quality control/quality assurance of the biospecimens.

Consistent with the goals for evidence-based best practices, IDATA will support limited pilot studies to assess quality of the IDATA specimens or suitability of certain assays (note that an IDATA biospecimen application is required for all pilot studies). Specifically IDATA may consider the use of certain IDATA specimens (as specified in the Specimen Use Guidelines) to systematically evaluate the quality of the IDATA samples with regard to:

- Assay reproducibility
- Long-term intra-individual variation in analyte levels
- Effects of long-term storage on certain analytes or assays
- Effects of different sample processing methods on certain analytes or assays

5. IDATA Biospecimen Application and Review Procedures

A goal of the IDATA Biospecimen application and review process is to ensure fair, equitable access to IDATA resources based on scientific merit and NCI priorities. Preliminary applications for access to the IDATA biospecimens are accepted year round. Upon receipt, proposals are reviewed for feasibility by IDATA Biospecimen Committee. The purpose of this initial review is to ensure sample availability and concordance with IDATA Biospecimen scientific objectives and priorities. Upon acceptance of the preliminary application, a final application may be submitted twice yearly in March/April and September/October.

Final proposals are reviewed by the IDATA Biospecimen Committee Review Panel (see Section 7) for scientific merit. The IDATA Biospecimen Steering Committee (see Section 7) makes the final decisions based on the Panel review results and recommendations. Final decisions are communicated in writing to the applicants along with reviewers' written critiques. The current turnaround time is about 4-6 months.

Application materials and all other relevant IDATA Biospecimen documents are posted on the Cancer Data Access System (CDAS) website https://cdas.cancer.gov/. Information on the specimens is also available on that website. Announcement of the upcoming open review cycle is emailed to prospective applicants on the IDATA Biospecimen mailing list about two months before the submission deadline; it is also posted on the above-mentioned IDATA website.

6. IDATA Biospecimen Proposal Evaluation Criteria and Considerations

Due to the exhaustible nature of the biospecimens, stringent evaluation criteria apply to the selection of proposal applications. In addition to the overall scientific and technical merits, a research proposal must demonstrate the need and suitability to use IDATA specimens. Parsimonious use of the samples is a must. Additional programmatic and resource management considerations will also be used to evaluate and prioritize research projects.

The below sections describe in more detail some of the specific requirements that are of particular importance.

6.1. Scientific and Technical Merit

6.1.1. Overall Study Design

Study design must be consistent with study aims, including appropriate choice of study subjects, assays, statistical methods, study power, and must address potential confounders and biases. Because of the importance of assay operating characteristics in the laboratory being used for a study, pilot studies may be needed to address inter- and intra-batch variability and inter- and intra-person variability, with the intraclass correlation coefficient (ICC) being a key parameter in determining the adequacy of approach. For high-dimensional data, a plan for independent validation should be included. Since some of the IDATA samples have been stored for many years, potential analyte degradation needs to be considered. Multiplex assay approaches that minimize volume requirements are preferred.

Laboratory discovery of new biomarkers may be supported on a case-by-case basis. Additional criteria may include, but are not limited to:

- Public health needs
- No other suitable resources are available
- Overall excellence in study design and data analysis plan
- Use of proven, matured technologies
- Parsimonious use of samples

6.1.2. Statistical Methods

Applications should include an analytic plan and a statistical methods section. It is also recommended that a biostatistician be included as a co-investigator. They should also include a proposed sample size and provide the estimated statistical power for the analysis. For studies with a large number of analytes, statistical adjustment for multiple comparisons must be used.

6.2. IDATA Biospecimen Programmatic Considerations

6.2.1. Collaboration & Coordination

Investigators not familiar with the IDATA trial and the IDATA biospecimens resource are particularly encouraged to seek collaborations or feedback. Duplicate or highly similar efforts are not supported in general. Investigators with similar ideas and approaches are usually asked to develop a collaborative project.

Programmatic and logistic coordination may be beneficial when multiple studies are ongoing and addressing related scientific questions. Use of a common sample and data set facilitates direct comparison or integration of data across studies. In addition, it is often necessary to coordinate among multiple studies so that the samples can be aliquoted at once, minimizing freeze/thaw cycles and saving labor cost. These considerations were key points in becoming involved in large consortial efforts to enlarge sample size.

Developing the most effective approaches for sample management is an on-going process and may evolve rapidly. The IDATA Biospecimen Committee does consider requests on a case-by-case basis, with application of the above described principles.

6.2.2. Balancing Current & Future Needs

Management of the biologic sample resources requires judicious balancing of the need to further the NCI goals in the short-term *versus* preserving samples for unforeseen future uses. The IDATA leadership takes stewardship of the resource most seriously, and decision rules, documented in the IDATA Biospecimen Use Guidelines, have been established to assure maintenance of critical levels of the samples for future studies for all study subjects.

Demands for samples will certainly increase with advances in the science, but time may also work in our favor, with advanced technologies tending to require less and less sample. For example, the serum requirements for protein based multiplex assays have fallen over the years. The urine specimens for IDATA should be adequate for most foreseen studies, while the serum and plasma and saliva resources are more susceptible to depletion. However, the material from the saliva, whole blood and serum MPA is far more limited and thus more precious.

6.2.3. Quality Control

Certain quality control measures should be incorporated into proposed assays. Pilot studies will be required for new assays to establish assay reproducibility. A pilot study typically involves a small number of samples, with the assays done laboratory-blinded and in repeat samples. Data from a pilot study must be evaluated and approved by the IDATA Biospecimen Committee before full analytic samples can be released.

Systematic blinded QC sample insertion in the full analytic batch is necessary for monitoring assay quality. This is particularly important when samples are being assayed over an extended period of time. To minimize sample deterioration, thawing of samples will be coordinated to the extent possible at the IDATA processing lab. Aliquots of various sizes will be made at the first thawing of the samples to reduce freeze/thaw cycles.

6.2.4. Parsimonious use of samples

Regardless of study types, parsimonious use of the samples is a must, as IDATA samples are precious and depletable. To ensure that no amount of the biospecimens will be wasted, investigators must provide detailed justifications for the amount of samples requested. Investigators may be asked to list the exact amount of samples needed for each assay or laboratory method.

7. IDATA Biospecimen Management Infrastructure

The NCI Division of Cancer Prevention (DCP) oversees the management of the IDATA Biospecimen program. The division is committed to supporting the IDATA Biospecimen infrastructure, providing extensive capabilities in biospecimens management and tracking, as well as scientific coordination, administration and strategic planning.

7.1. IDATA Biospecimen Steering Committee

NCI guidance and oversight of the management of the IDATA Biospecimen is carried out by the IDATA Biospecimen Steering Committee (SC). The SC develops management policies and procedures, provides oversight and direction to the day-to-day management of the studies, and resolves conflicts over management and policy issues. The SC is composed of NCI staff from the Division of Cancer Prevention (DCP). All decisions of the SC are subject to review and approval by the DCP director.

7.2. IDATA Biospecimen Review Panel

The IDATA Biospecimen Review Panel is responsible for the peer-review of proposals submitted to the IDATA Biospecimen program. The panel is comprised of intramural scientists from within NCI, biostatisticians (academic or NCI) and extramural sceintists. If needed, *ad hoc* reviewers may also be chosen for specialized areas of expertise. The Panel makes recommendations to the IDATA Biospecimen Steering Committee based on scientific and technical merits of each proposal.

Each panel member serves a 3 year term, with some exceptions. Although panel members are allowed to submit an IDATA Biospecimen application, or to be a co-investigator on an IDATA Biospecimen application during their term, they must recuse themselves from evaluating or discussing these applications. They are required to acknowledge any potential conflict of interest as soon as they are aware of such.

7.3. Contract Support

Contract support coordinates the IDATA Biospecimen application and review processes including the IDATA Biospecimen Committee panel review meeting, and monitors progress and tracks status of all approved studies. Contractor also provides support for day-to-day biospecimens management actives, and the post-approval sample requisition process.

7.4. Study Management and Tracking

The Cancer Data Access System (CDAS) is developed and maintained by a contractor. All completed and on-going studies are stored in the database, including proposal abstracts and annual progress status. Prospective investigators can search for past and current research activities that may be related to proposed studies, thereby avoiding duplicate effort. The IDATA Biospecimen proposal review process is also managed and tracked by this database system.

7.5. Biospecimens Use Guidelines

A separate document entitled “Biospecimens Use Guidelines” has been developed to provide specific guidelines for each material type. The goal of the guidelines is to prevent sample depletion, and to ensure appropriate use of the samples, including quality controls. Sample selection must be based on the guidelines. Sample requests that violate the guidelines must be approved by the IDATA Biospecimen Committee.

8. IDATA Biospecimen Appeal Process

If an applicant has concerns about an IDATA Biospecimen Panel review and wishes to appeal the review outcome, he/she must submit a formal appeal letter within 30 days of the date on the final decision letter. An appeal letter must describe specific issues with the review. Appeals based solely on differences of scientific opinion will not be accepted. The IDATA Biospecimen Steering Committee will conduct the initial review of the appeal and make recommendations to the NCI Division Director (Division of Cancer Prevention). The Division Director will make the final decision. There are three possible outcomes: 1) the appeal has merit and the application is approved, with or without certain conditions; 2) the appeal has merit and the application will be re-reviewed in the next round; and 3) the appeal has no merit and is rejected. The outcome of an appeal is final and cannot be appealed again.

9. IDATA Biospecimen Policy on Addenda

Certain circumstances may merit an addendum request to an approved on-going IDATA Biospecimen study. The addendum process is intended, in general, for small scale extension of an existing IDATA Biospecimen project. Requests of no more than 10% of the original request, either sample size or amount of the materials, are considered suitable for an addendum. Requests larger than 10% of the original approved requests, or limited expansion of scientific scope or aims, may be considered on a case-by-case basis by the IDATA Biospecimen Steering Committee. In general, no more than 3 addenda should be submitted per study (an addendum that does not involve new biospecimens, such as adding a PI or changing PI institution, is not counted toward the allowance).

Addenda that substantially expand the scope of the project—for example, examining a different class of markers, a different technology of assessment, or a different endpoint,

will not be approved. These require a new application. The IDATA Biospecimen Steering Committee will make final decisions to accept or deny addendum requests.

10. IDATA Biospecimen Data Return and Data Sharing Policy

Laboratory-generated data on IDATA samples through an IDATA Biospecimen study must be returned to the IDATA database.

As described above, blinded samples are shipped to the investigator-designated laboratory. Investigators must submit the laboratory generated data and data dictionary to IDATA staff in order to receive an un-masked analytic dataset from which to perform their analysis.

Upon publication of the study, the raw laboratory generated data, a cleaned version of the data, final study results, and an accompanying data dictionary shall be returned to the IDATA Trial by the investigator.

Below is the list of data elements and other information that must be submitted to IDATA.

Assay data (Format: Excel or SAS)
For each sample provide the
following:

1. Sample ID (provided by IDATA)
2. Marker name(s) (include full protein name, gene symbol and aliases so that there is no ambiguity in the marker identity)
3. Marker measurement(s) (specify unit of measurement, assay batch number)
4. Name of the assay platform
5. Date and time assay performed
6. Reagent lot/batch number
7. Operator(s)
8. Instrument(s) and calibration
9. Any QC data on the IDATA samples (as an example, PH level)
10. All other QC data
11. Missing value indicator and reason(s) for the missing value
12. If applicable, case/control predictions

Descriptive information

1. Name of the laboratory that performed the assay measurements
2. Name of the Principal Investigator responsible for the data submitted/Owner of the data
3. Study ID (IDATA Biospecimen XXXX-XXXXX) and title
4. Technical description of the assay platform(s)
5. Detailed assay protocol, including specimen preparation method
6. Description of method for normalization of marker measurements if applicable

Decision rule for classifying samples (if applicable)

1. Name of a point-of-contact for the classification rule submitted
2. Detailed description of the classification rule for classifying subjects as cases or controls. If the classification rule is based on a propensity score, provide a detailed technical description of how that score is determined.

These laboratory data will be made available to other investigators who request them after the data have been published. Investigators may request published study data online via the Cancer Data Access System (CDAS) (https://cdas.cancer.gov/). Prior to releasing published study data to other investigators, The IDATA Biospecimen Committee will contact the original study investigator (s) to confirm that the data are indeed published and that the proposed research does not overlap with an in progress research aim that was previously approved by IDATA.