THE SEYCHELLES CHILD DEVELOPMENT STUDY
Resources Sharing Plan

Introduction

The Seychelles Child Development Study (SCDS) in collaboration with the Government of the Republic of Seychelles has developed an extensive database characterizing several participating cohorts. The agreement affirms that the Government of the Republic of Seychelles is a full partner in the research and acknowledg ! ' Sharing Plan to accommodate requests from investigators outside the partnership for access to this d This agreement was designed to facilitate scientific enquiry while assuring that the data are interprete highest scientific standards. The agreement has been subsequently revised for further clarification ab procedures and to be inclusive of additional study partners.

SDCS objectives

The goals of the SCDS are as follows:

1. To delineate normal child development and normal aging in the Seychelles
   postnatal exposure to methylmercury (MeHg)
   and other metals from a fish diet and mercury vapor (Hg^0) from dental amalgams
3. To relate the development of the children to their pre- and postnatal nutritional status
4. To relate the development of the children to maternal and child genetics
5. To relate aging of adult participants to their exposure to MeHg and other metals from a fish diet, as well as their nutritional status and genetics

Definition of “internal partners”

The SCDS Partners were expanded in 1999 to include Ulster University (nutritional expertise) and in 2011 the Karolinska Institute (genetic expertise). For this Resource Sharing Plan, the SCDS partnership includes the following institutions: Government of the Republic of Seychelles, University of Rochester, Ulster University, Karolinska Institute, and Lund University. “Internal partners” are SCDS site Principal Investigators and other scientific leads at partner institutions, and trainees mentored by these individuals.

Definition of “external investigators”

Investigators at partner institutions who are not Principal Investigator or scientific lead, and investigators who are not affiliated with SCDS partner institutions are considered “external investigators”. Investigators at partner institutions who are not affiliated with the SCDS may be invited by site Principal Investigators to join the study as a scientific lead.

Statement of commitment to share data

Within the SCDS partnership, data will be shared if the SCDS study guiding principles and data security are maintained (see Approach to Data Protection and Statistical Analysis for Partners).

The SCDS welcomes collaboration with investigators outside of the partnership. This includes individuals or groups who have expertise and interest in an area which is not the primary focus of the SCDS, but one which the database encompasses. To accomplish the goal of collaboration while maintaining the highest level of scientific integrity and guiding principles of the study, a review committee has been established. The Resources Review Committee (RRC) will consist of the principal investigators/key personnel from the University of Rochester, the Republic of Seychelles, The Karolinska Institute and the University of Ulster. Any investigator who has interest in gaining access to the SCDS data must follow the steps outlined below, beginning by contacting one of the SCDS principal investigators to discuss the proposal. All proposed analysis plans must be based on a plausible biological hypothesis. If the analysis plan involves exposure variables (MeHg, Hg vapor)Hg Â e analysi r) Þ τ ɹ rp o p γ τ ɹ ab s ! . ts
sults will be interpreted jointly by the SCDS Partners and
om the analysis will be the joint responsibility of the SCDS
being jointly determined.

Approach to Data Protection and Statistical Analysis for Partners

This appendix to the Resources Sharing Plan establishes a standard approach to (a) the protection of data, (b) the development of analysis plans, and (c) the process of statistical analysis.

a) Protection of data:

1. Datasets containing mercury levels may only reside on computers that follow strict security protocols. Such protocols will be made available to partners upon request.
2. Datasets containing mercury levels must never be stored on laptops, and they may not be shared with others who do not already have permission to access the data.

b) Availability of data pertaining to SCDS primary objectives:

1. The double-blind nature of the Seychelles study is one of its unique strengths and must be preserved. Mercury data will not be shared with study participants or with study staff who are involved in field work (e.g. recruitment and data collection).
2. Internal partners do not have access to dependent or independent variables that pertain directly to the primary objectives of the SCDS until statistical analyses addressing these objectives for a particular cohort and examination have been carried out and published. Such analyses are to be carried out independently by SCDS biostatisticians. Once the primary objectives have been addressed, these variables (including mercury) will become available to internal partners for secondary analyses.
3. External investigators do not have access to dependent or independent variables that pertain directly to the primary objectives of the SCDS. Such analyses are to be carried out independently by SCDS biostatisticians.

c) Guiding principles for the analysis of SCDS data:

1. All analyses need to be hypothesis driven and based on biological considerations. All analysis plans must begin with a biologically plausible hypothesis.
2. All analyses, including those described in a grant proposal, must begin with an analysis plan. Analysis plans will be specified *a priori,* will be approved by all partners, and will be strictly adhered to. Exploratory analyses will be clearly labeled as such.
3. Primary and exploratory analyses will be transparent and well documented at all analysis stages, reproducible, and documented in partner-authored publications.
4. Dialogue between investigators and biostatisticians at all stages is crucial for the conduct, interpretation, and reporting of analysis results.
5. Papers will continue to be developed jointly among partners and their content agreed upon by each partner participating in the manuscript prior to submission.

d) Development of the statistical analysis plan:

The analysis plan should be formulated along the following lines:

1. The hypothesis should be stated with supporting references.
2. The specific dependent variable(s) to be included in the model(s) should be selected, and the direction of effect (beneficial or adverse) stated. If more than one dependent variable, then they should be prioritized.
3. The covariates to be included in the model should be selected and should be based on biological significance. If a covariate could be coded in different ways, the anticipated coding of the variable and its rationale should be stated, and the meaning of the coding should be stated.
4. If participants are to be excluded from certain models, the rationale for this should be stated.
5. The complete set of models to be used for the analysis should be defined. This should be based on a dialogue between the investigators and biostatisticians.
6. If more than one outcome variable is of interest, and/or more than one set of covariates are to be used, decisions need to be made on the handling of observations which have missing values for r

e) Process of statistical analysis:

Investigators should be familiar with the data to determine and resolve potential data issues before fitting statistical models. Accordingly, prior to fitting models, the following procedures should be followed:

1. Initial data cleaning/checking will identify missing data and implausible values and outliers.
2. Determine available sample size for each model to be run. State for what reason(s) participants are not included, and give the number of participants removed for each reason.
3. Data will be plotted for distributions and key correlations.
    a. Create scatterplots (or boxplots) of the main outcome variable versus any new covariates, and determine the corresponding correlations.
    b. Create scatterplots of key outcome variables versus other outcome variables that may measure similar constructs (if more than one outcome is of interest), and determine the corresponding correlations.
    c. Create scatterplots and determine corresponding correlations between pairs of key covariates (excluding MeHg).
    d. At this stage, prior to fitting models, the findings should be shared with partners (see below).
4. Model assumptions will be checked, and outliers and influential points will be examined in order to determine whether transformations or other procedures are needed to satisfy the model assumptions. If the assumptions are not met, models will be run with changes as suggested based on the nature of the violations. The reasons for making these changes will be documented, and model assumptions will be checked on the final model.
5. Stepwise selection of covariates will not be performed.