

The Selenium and Vitamin E Cancer Prevention Trial (SELECT)

Overview

The Selenium and Vitamin E Cancer Prevention Trial (SELECT) (S0000) is a Phase III, randomized, double blind, placebo-controlled trial to prevent prostate cancer. SELECT was designed to accrue 32,400 healthy men, ages 55 years and older (African American men ages 50 years and older), with 20% (6,480) of the study participants to be African American. The efficacy of selenium and vitamin E, as single agents and in combination, on reduction of prostate cancer incidence, will be tested in a statistically highly powered 2 x 2 factorial trial design. The planned total study period is 14 years, including 1 year pre-study for ramp-up to accrual (completed), 5 years for accrual, 7 to 12 years of treatment, and 1 year post-study for analyses and publication of results. Participants will be followed twice per year (four times in the first year after randomization) to monitor general health, prostate health, and adherence to the study supplements.

In addition to primary and prespecified secondary endpoints, the SELECT will examine many important tertiary/ancillary endpoints, including dietary/nutrient assessments, pathology and molecular/cellular biomarkers, quality of life, and molecular epidemiology. Development and monitoring of the trial involves the input and scientific expertise of a panel of experts representing several cooperative groups.

The study opened for recruitment on July 25, 2001. Randomizations began on August 22, 2001. The trial was closed to accrual on June 24, 2004 at which point 35,534 participants were randomized to the trial, 15% of whom are African American, at 427 different study sites across the United States, Puerto Rico and Canada.

Role of the Statistical Center

The Statistical Center is responsible for data management for the trial, described in detail below:

1) Study Design and Analysis

The Statistical Center develops methods for analysis of study data, evaluates and modifies the study design as needed, analyzes study data, and provides reports to the Data and Safety Monitoring Committee and to the Steering Committee and its subcommittees.

2) SELECT Workbench

The SELECT Workbench is a secure Web site located on the World Wide Web, administered by the SELECT Statistical Center. The Workbench contains the SELECT protocol, Study Manual, and a variety of materials to assist sites in performing all activities associated with randomization, participant follow-up, and study administration. Regular review of the effectiveness of the Workbench and updates to its content are ongoing.

3) SELECT Study Manual

Version 1.0 of the SELECT Study Manual was released in November 2000. Since that time, numerous revisions have been released. The Study Manual contains procedures and guidelines to augment the protocol. All sections of the Study Manual have been released and undergo regular review and revision as necessary.

4) Study Site Staff Training

Study Site staff members receive training on SELECT procedures at the semi-annual SWOG Group Meetings. This training consists of presentations, small group breakout sessions on specialized topics of interest, and poster sessions. A special session is held for staff members who are new to the trial.

5) Communications

The Statistical Center is available Monday through Friday 7:00 AM PST through 4:00 PM PST for telephone queries. In addition, Study Site staff members are contacted as necessary by their assigned Data Coordinator to resolve recurrent problems in data management or study administration. A Helpdesk function is also available, by both voice and e-mail, for Study Sites to call for assistance with a wide range of study management issues.

6) Document Management and Quality Assurance

Participants were randomized by Study Site staff using Web-based (html) data collection and transmission. Data collection is done using Cardiff™ Teleform®, an electronic document management system featuring both Web-based and fax transmissions. Data collection is also done using Web-based (html) transmission. The Statistical Center provides a dedicated toll-free number for faxed data transmission from the Study Sites. Data are validated by data operations staff and stored in a relational database; electronic documents and digitized images of forms are archived in a disk storage system.

a. Electronic Document Management Update

The electronic document management system is operated by Data Control Technicians and Data Coordinators and is maintained by programming staff. Data Control Technicians initially review each page of faxed data for completeness prior to entry to the database. Data Coordinators also assist with this review at a secondary level. Subsequent data review is also completed by the Data Coordinators. This includes evaluating routine data forms and data from narrative summaries for accuracy, completeness, consistency, and compliance to data collection requirements and follow-up procedures. The results of these reviews are noted in an evaluation program.

b. Data Collection Forms

The forms developed for this protocol have been designed to optimize their processing and management using an electronic document management system that features both Web-based and fax transmissions of data from the Study Sites. In general, forms that are completed by the participant are faxed to the Statistical Center; CRA completed forms are submitted via the SELECT Workbench web data entry process.

With the exception of the 17-page Dietary Supplement and Food Questionnaire, which is available in three languages, the Study Sites download data collection forms from the Sta-

tistical Center via the SELECT Workbench. A set of reference forms, with instructions for the completion of each form, is included as part of the Study Manual.

c. Routine Reports

Study Sites have the ability to access a variety of reports via the SELECT Workbench. These reports are developed and maintained by the Statistical Center and are available to assist with identifying time requirements of individual participant follow-up activities, provide updated accrual and data collection and submission information for each Study Site.

d. Quality Control

The Southwest Oncology Group Operations Office conducts Study Site Quality Assurance Audits. The Statistical Center provides data reports for the audit team.

Quality control review begins with the initial review of each incoming electronic document for data entry errors (e.g., missing data items, illegible entries) including those resulting from inaccuracies in image-to-data translation. Translation errors are corrected at this time. Other errors are annotated for correction or clarification; these notes are included in query reports accessible to the Study Sites dynamically on the SELECT Workbench.

Quality control review is completed by the Data Coordinators. This includes evaluating routine data forms for accuracy (the correct form was used to document a specific protocol requirement); completeness (all required data items have been addressed); consistency (data recorded on one form is supported by and/or matches that recorded on another form); and with protocol requirements (all required study parameters have been addressed and documented within the specified time frames).

A system of edit checks implemented at the time of Web-based data transmission from the Study Sites and during review at the Statistical Center contributes to the overall quality control review. All deficiencies, discrepancies, and other quality-related problems identified by the Statistical Center staff are included in the query reports. Study Sites are directed to correct or clarify data items in response to the Statistical Center's requests, and resubmit the amended version of the original document. The results of these reviews are noted in an evaluation program.

All electronic documents received are logged into generalized tracking system (Expectation System) designed to identify those documents not received and participant follow-up not completed per protocol requirements. Reports listing these missing documents and instances of incomplete participant follow-up are available to the Study Sites via the SELECT Workbench

Following study completion each Study Site will be expected to archive the materials collected during the study for storage for a minimum of 5 years.

e. Institutional Performance Review: Monitoring Study Center Performance

Data submission by the Study Centers is monitored monthly, using a number of specific Institutional Performance Review (IPR) measures. These measures include the timeliness of follow-up and the completeness of annual visit data. IPR reports for all SELECT Study Centers are posted to the Workbench.

Any Study Center with a rating of 10% or greater in any measure will be strongly encouraged to take actions to move into compliance. To help an institution improve its IPR rating,

the Statistical Center will schedule a mentoring visit, by members of the Statistical Center staff and/or a CRA, to the Study Center. The mentoring visit is designed to provide a spectrum of techniques, tools and procedures that can be implemented to develop a system that will help a SELECT institution meet the follow-up and documentation requirements of the SELECT.