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Introduction to the Southwest Oncology Group

The Southwest Oncology Group (SWOG) is a national consortium of institutions and investigators organized for the purpose of improving the survival of cancer patients through clinical research and sponsored by the National Cancer Institute (NCI). The Group began in 1956 as the Southwest Cancer Chemotherapy Study Group; it has expanded to include all modalities of cancer therapy, and institutions in all regions of the country. Most of the studies done by the Group are designed to assess whether a regimen merits further study (Phase II), or to compare two or more regimens (Phase III). The Group is also expanding efforts in multi-center Phase I clinical trials. Studies in cancer control research, including cancer prevention, symptom control and quality of life are conducted in support of the broader mission of reducing the impact of cancer.

The Group is composed of nearly 300 institutions from across the US who enroll patients into Group studies (Figure 1). Of these, 34 are member institutions affiliated with major academic medical centers which formed the original nucleus of the group. There are now 211 affiliate institutions composed of groups of community physicians affiliated with a member institution. Community Clinical Oncology Programs (CCOP) represent another 28 collaborating institutions. These are community hospitals or consortia with a mandate for both clinical and cancer control research. Finally SWOG includes 26 Urologic Cancer Outreach Program (UCOP) institutions, specializing in the treatment of genitourinary cancers. These centers have been important contributors to the prostate cancer prevention work, including the Prostate Cancer Prevention Trial (PCPT) which closed in 2003 and the ongoing Selenium and Vitamin E Trial (SELECT). Sites participating in SELECT are presented in Figure 2.

SWOG studies are typically proposed by disease (organ site) committees, and reviewed internally for scientific merit and feasibility prior to submission to external review by NCI through the Cancer Therapy Evaluation Program (CTEP). The SWOG disease committees (listed in Table 1) represent the primary organizational structure.

In 2006, there were 5,410 patient registrations to SWOG protocols including clinical trials, cancer control studies and ancillary studies. The geographic distribution of patients registered to Group studies in 2006, depicted in Figure 3 based on residential zip codes, indicated representation from all 50 states. Patient registrations, exclusive of the prevention trials over the past six years by study type, committee, and institution type (Table 1) show a steady increase in accrual through 2005, with some contraction in 2006 in response to a directive from NCI based on budget constraints. SWOG also accepts patient registrations from institutions affiliated with other oncology groups, including over 1100 such registrations in 2006. There are currently 93 studies open for accrual.

The Group Headquarters Office is now at the University of Michigan at Ann Arbor, under the direction of Group Chair Laurence H. Baker, D.O. All financial and business operations are coordinated through this office. The Operations Office, with responsibilities for protocol development, membership, data audits and serious adverse event (SAE) reporting, is located at the Cancer Therapy and Research Center in San Antonio, Texas.

The Statistical Center of the Southwest Oncology Group is located at the Fred Hutchinson Cancer Research Center and at Cancer Research And Biostatistics in Seattle, Washington. John Crowley, Ph.D. is the Group Statistician and Director of the Statistical Center. Statistical Center staff have responsibilities for study design and review, data collection and management, randomization procedures, reporting, data analysis and interpretation, data and safety monitoring, quality assurance, training, and computing system development, maintenance and support.
Figure 1
Southwest Oncology Group Institutions
Figure 2
SELECT Study Centers
Figure 3
Southwest Oncology Group 2006 Registrations
Table 1: SWOG Patient Registrations Over 5 Years
(Numbers Exclude Prostate Cancer Prevention Trial and SELECT)

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<tr>
<th></th>
<th>Jan 01-Dec 01</th>
<th>Jan 02-Dec 02</th>
<th>Jan 03-Dec 03</th>
<th>Jan 04-Dec 04</th>
<th>Jan 05-Dec 05</th>
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<td>Other</td>
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<td>0</td>
<td>14</td>
<td>11</td>
<td>9</td>
<td>34</td>
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</table>
Introduction to the Southwest Oncology Group Statistical Center

Primary Mission of the Statistical Center

The primary mission of the Southwest Oncology Group Statistical Center is to reduce the health impact of cancer through clinical research in the treatment and prevention of disease. The mission is accomplished through the design, support, and analysis of multicenter trials designed to address important hypotheses in cancer care, and through translation of biologic concepts to clinical care. Quality research, quality data, and the publication of results are critical to the effort. The Statistical Center contributes through the following:

- **Study Design**
  The Statistical Center has a fundamental role in clarifying study objectives and in designing statistically sound studies to meet those objectives.

- **Protocol Review**
  The Statistical Center reviews all protocols for logical consistency, completeness, and design integrity to assure that study conduct is not compromised through use of an inaccurate protocol document.

- **Data Quality Control and Study Monitoring**
  The Statistical Center enters, manages, reviews, corrects, updates, and stores data from all active Southwest Oncology Group studies, and provides data to Study Coordinators for their review in order that study results not be compromised by flawed data and that studies be appropriately monitored for patient safety.

- **Analysis and Publication**
  The Statistical Center is responsible for statistical analysis and interpretation of all Southwest Oncology Group-coordinated studies and all Southwest Oncology Group database studies.

- **Statistical Research**
  The Statistical Center has an active research program addressing unresolved design and analysis issues important to the conduct of cancer clinical trials and to ancillary biologic studies.

- **Training**
  The Statistical Center plays a key role in the training of new Clinical Research Associates (CRAs) and of Young Investigators in the Group.
Statistical Center Functions and Organization

The Statistical Center of the Southwest Oncology Group is directed by the Group Biostatistician, John J. Crowley, Ph.D., and is located at both the Fred Hutchinson Cancer Research Center (FHCRC) and Cancer Research And Biostatistics (CRAB) in Seattle, Washington. Most doctoral level statisticians also have faculty appointments in the Department of Biostatistics at the University of Washington located approximately three miles from the Statistical Center.

The Statistical Center was moved from the MD Anderson Cancer Center to FHCRC in 1984 under Dr. Crowley’s leadership. For purposes of cost efficiency, in 1997 Dr. Crowley formed CRAB, a non-profit organization, primarily to support the work of the Southwest Oncology Group Statistical Center. Until March 2004, the entire Statistical Center—both at FHCRC and CRAB—were located in the same downtown Seattle building. However, in March 2004, the FHCRC-housed component moved to the new Public Health Sciences building on the FHCRC campus in the South Lake Union area, about a mile distant from CRAB. The two now physically separate staffs are connected electronically. Statisticians are primarily located at FHCRC along with minimal administrative support. All other operations, including data management, software development, and network administration for Southwest Oncology Group Institutions are performed by the Statistical Center housed at CRAB.

The primary work of the Group is accomplished through disease and/or discipline committees. To support this, each committee has at least one statistician and one data coordinator assigned to support scientific activities. Prior to any study initiation, statisticians review the protocol for feasibility, experimental design, and key elements of data collection protocols, define randomization schema and data analysis plans and calculate the appropriate number of patients needed to answer the research objectives. Statisticians also perform analyses of study results for the semi-annual Report of Studies, for the data and safety monitoring committee (where appropriate) and for publications.

Data coordinators review protocols for clarity and consistency, register and randomize patients on protocols, review patient data forms for consistency and completeness, help in study monitoring, oversee mailings to Group participants, and coordinate initial and ongoing training and support for Clinic Research Associates.

Computer programmers maintain the Statistical Center's hardware and software infrastructure and develop new software as needed to accomplish the Statistical Center's objectives. Each staff member at both FHCRC and CRAB has access to the network to carry out all required activities.

Administrative support staff process incoming and outgoing data. Administrative and clerical tasks are carried out by the coordinating center manager, administrative coordinator, administrative assistants, and office workers. Finance oversight is provided by grants and contracts administrators.

The Statistical Center organizational structure is presented in Figure 4, followed by the current staffing (Figures 5 – 7).
Figure 4: SWOG Statistical Center Organizational Chart
**Figure 5: Southwest Oncology Group Statistical Center (FHCRC) Staff**

John Crowley, Ph.D., Director  
Jacqueline Benedetti, Ph.D., Deputy Director  
Catherine Tangen, Dr.P.H., Coordinating Statistician

**Administration**  
Mark Blitzer, B.A., Administrative Coordinator  
Tess Hurley, Finance Administrator

**Behavioral Scientist**  
Carol Moinpour, Ph.D.

**Biostatistics**  
Garnet Anderson, Ph.D.  
Kenneth Kopecky, Ph.D.  
Michael LeBlanc, Ph.D.  
PY Liu, Ph.D.  
Mary Redman, Ph.D.  
Bryan Goldman, M.S.  
Holly Gundacker, M.S.  
Danika Lew, M.A.  
James Moon, M.S.  
Cathryn Rankin, M.S.  
Joseph Unger, M.S.

**Prostate Cancer Prevention Trial**  
Phyllis Goodman, M.S., Lead Statistician  
Susan Carlin, B.A., Project Manager  
Amy Darke, M.S., Statistician  
Katie Arnold, M.S., Statistician

**Data Coordinators:**  
Bernard Moore, B.B.A.  
Roxanne Topacio
Figure 6:
Southwest Oncology Group Statistical Center
Cancer Research and Biostatistics (CRAB) Staff

John Crowley, Ph.D., Director
Evonne Lackey, C.C.R.P., Coordinating Center Manager

Administration
Marcia Foster, B.A., Data Tracking Specialist

Applications Development
Ron Bredehoeft, Director of Applications Development
Angela Smith, B.A., Project Manager
Carlos Marin, Systems Analyst/Programmer
Chris Cook, M.A., Systems Analyst/Supervisor
David Law, B.S., Systems Analyst/Programmer
Darlene Davis, B.S., Systems Analyst/Programmer
Deborah Sopher, M.S., Systems Analyst/Programmer
Keith Hodo, B.A., Software Tester/Programmer
Kelly Balch, B.A., Case Report Forms Programmer
Li Li, M.S., SAS Programmer
Teresa Chern, A.A.S., M.C.S.E., Systems Analyst/Programmer
Rick Mize, Technical Support Analyst
Yoko Rivers, B.A., Software Tester

Biostatistics
William Barlow, Ph.D., Statistician
Antje Hoering, Ph.D., Statistician
Vanessa Bolejack, M.P.H., Statistician

Information Technology
Keith Goodman, M.A., IT Program Director
Patrick Durham, B.S., Senior System Engineer
Anthony McLaughlin, B.A., Network Administrator
Jane Xie, B.A., Database Administrator
Steve Dong, B.A., System Support Specialist
Steven Briggs, B.A., System Support Specialist
Terry Lynch, B.A., Network Administrator

Data Operations Center
Rodney Sutter, Data Operations Manager
Camille White, B.S., C.C.R.P., Data Operations Supervisor
Laura Kingsbury, M.R.T., Quality Assurance Coordinator
Scott Kurruk, B.A., Data Operations Supervisor
Stephanie Edwards, Data Operations Supervisor

Data Coordinators:
Amy Edwards, B.S., B.A.
Brian Zeller
Christine McLeod
Janice Leaman
Jean Barce, B.A.
Jeri Jardine, B.S.
Jennie Barrett
Larry Kaye, B.A.
Lisa Gavigan
Tracy Maher, B.A.

Data Control Technicians:
Iris (Cat) Buchanan

Selenium and Vitamin E Cancer Prevention Trial (SELECT)
Jo Ann Hartline, M.P.H., Project Manager
Phyllis Goodman, M.S., Lead Statistician
Karen Anderson, Retention and Adherence Manager
Monica Yee, B.A., Data Operations Manager
Amy Darke, M.S., Statistician
Katie Arnold, M.S., Statistician
Russell Campbell, M.A., Lead Retention and Adherence Coordinator
Jason Harris-Talley, Retention and Adherence Coordinator
Kathy Weaver, B.A., Administrative/Technical Assistant

Data Coordinators:
Dona Marrah, Data Operations Supervisor
Matthew Scott, A.A.S., Data Coordinator Lead
Diane Liggett, B.S.
Sarah Effert, B.A.
Devin Kearns, B.A.

Data Control Technicians:
Claudia Vio, A.A., A.A.A.S
Ginnie Bauman, A.A.
**Figure 7: Statistical Center Disease and Discipline Committee Teams**

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Main Objectives of the Statistical Center

1. To participate in the development of proposed protocols, particularly as regards experimental design, sample size and feasibility. Biostatisticians work with the study coordinator on the statistical aspects for each protocol, including a specification of the major objectives and the number of patients required to meet those objectives. Data coordinators and biostatisticians comment on concept sheets for proposed studies and work with protocol coordinators in the Operations Office to produce protocols that are concise and clear.

2. To provide for registration of all patients on all studies, and for randomization of patients where appropriate. Registrations for all studies are available by direct Internet Web-based connection to the WebReg program.

3. To develop Web and software technology for paperless submission of data to the Statistical Center.

4. To provide for review and quality control of data collected during studies. Data coordinators screen all incoming data and query institutions regarding any incompleteness or inconsistency. Further range and logical checks are made at data entry. Data are collected on timeliness and accuracy of data submitted by each institution, as part of an effort to improve quality throughout the Group.

5. To provide for data entry, and for computer processing, and storage and retrieval of data. Data entry is performed by trained data control technicians. There are three data entry submission routes: Internet, fax or paper.

6. To work with the Group Chair and other investigators in the Group to improve the quality of clinical trials through the use of improved data forms, uniform and reproducible data definitions and economical data flow, and efficient use of Statistical Center resources.

7. To assist the Group Chair in the administration of the Group.

8. To analyze and publish the results of studies in conjunction with the study coordinators. Improvements are continually being made in the analytic and design tools available to the biostatisticians. The main analytic tool is SAS®, with locally developed software to extract SAS files from Oracle™ and to produce tables and survival curves for the semi-annual Report of Studies and for publication.

9. To use the data collected to try to find new leads regarding prognostic factors and late effects.

10. To perform statistical research on the efficient design, conduct and analysis of cancer clinical trials and cancer control research. In particular, research is being done on the analysis of survival data, on design and analysis strategies for clinical trials, on monitoring strategies for Phase III studies, on analysis of longitudinal data subject to non-ignorable missingness, and on methods for the analysis of high-dimensional cytogenetic, microarray and proteomic data.

11. To educate investigators, nurse oncologists and CRAs in statistical analysis, research design and the utilization of the most advanced scientific and data management strategies.
Major Accomplishments

In fulfilling these objectives, major accomplishments during the years 2001-2006 were:

1. Developed a new Web-based system to allow direct registration by institutions. Expanded this system to allow use by members of other Cooperative Groups, and registration to studies conducted by other Groups.

2. Developed a Web page providing access to the Report of Studies, accrual reports, training manuals and other research information.

3. Offered a training program for experienced clinical research associates on the use of the new Web tools.


5. Contributed to the development and conduct of a Young Investigators Workshop, an intensive training program designed to teach clinical trials principles to new researchers.

6. Revised the program for training new biostatisticians, and instituted a biostatisticians’ meeting to discuss procedures, policies, and methodologic issues.

7. Simplified all forms in response to the need for efficiencies in the clinical trials process.

8. Participated in a national cooperative effort to streamline data collection through the Common Data Element project initiated by the Cooperative Group Chairs and Group Statisticians, and supported by the NCI.

9. Served on external committees in the form of faculty participation on data monitoring committees, NIH review panels, American Joint Commission on Cancer task forces, development of CTC and RECIST definitions, editorial boards, etc.

10. Developed an electronic patient chart system.

11. Developed an on-line study coordinator evaluation system which allows the primary physician in charge of a particular study to access patient information via the internet, and electronically review and send feedback to the Statistical Center.

12. For intergroup communication, initiated collaboration with other cooperative group statistical centers to allow direct data submission on intergroup trials. Worked with CTSU on regulatory and data submission procedures.

13. Continued participation in the Intergroup Remote Data Entry (RDE) effort which will result in all the Groups adopting the same system for online data submission.

14. Revised guidelines for the design and assessment of quality of life on Southwest Oncology Group studies.
15. Continued development of the database management system, including more flexibility in handling multiple registrations, cycle-specific data collection, extensive additional logic checks at the time of entry of patient evaluations, and enhanced capability for managing double blind studies in anticipation of planned prevention studies.

16. Met responsibilities with respect to the conduct, design, and analysis of Southwest Oncology Group studies.

17. Made advances in statistical methods for therapeutic and prevention trials, for quality of life studies, and for the analysis of high-dimensional data, as evidenced by presentations at national meetings and publications. Developed and improved tools for the design of trials and made them available on the Web.

18. Continued the development of analytic software, including the Statistician's Report Worksheet (SRW) for producing the Report of Studies, and programs for exploratory and longitudinal data analysis.

19. Managed follow up of multiple large intergroup trials, including SWOG 8814, 8897, 9346, 9304 and 9916. Managed a number of successful Phase III trials, including an intergroup sarcoma trial, S0033, testing two doses of Gleevac in GIST tumors.

20. Completed accrual to a large chemoprevention study, the Prostate Cancer Prevention Trial (PCPT). Study results were published in the New England Journal of Medicine in July 2003.

21. Opened a second cancer prevention study, the Selenium and Vitamin E Cancer Prevention Trial (SELECT), which accrued a total of 35,534 men between activation in August 2001 and the end of accrual in June 2004.

22. Established SELECT as a model for large-scale prevention trials, with all trial communication and data management conducted electronically.


25. Joined a consortium of SWOG researchers in the development of an Early Therapeutic Program for the Group. Developed a new Web program to allow rapid data transmission for this initiative.

26. In conjunction with the Group Operations Office, expanded the Web security systems to require individual password access to the Group Web site, thus allowing more detailed Web-based communications between institutions and the statistical center.

27. Information Technology introduced virtual server technology from VMWare® ESX Server to streamline server deployment and management and to enhance backup and disaster recovery. Continued ongoing enhancement of best practices for security and systems management including additional monitoring of servers and services.

28. Initiated development of a tracking system for use by institutions and off-site laboratories for the shipment and tracking of specimens.
29. Moved the cytogenetics business office to the Statistical Center and created a new cytogenetics application.

30. Developed an internal Quality Assurance program to audit the data coding quality of Data Coordinators, and to provide continuing education as needed.

31. Established a correlative sciences statistical team to support the increasingly complex analyses involving high dimensional data.

32. Managed 25,000 new therapeutic registrations and 24,000 therapeutic patients in follow-up.
Computing Infrastructure

Information Technology Environment

The Statistical Center computing resources are based on the Microsoft® Windows Server® 2003 network operating system. The key services include the patient databases, E-mail, WEB, application and file sharing, electronic document and image management, Cardiff Teleform® data forms design and submission, batch application processing, disaster recovery, virus protection services, Citrix-based terminal services, remote access, desktop configuration and network monitoring/management.

Desktop Systems and Network

Each staff at FHCRC and CRAB has an Intel Pentium III or higher system. Each desktop PC runs Microsoft® Windows® XP Professional. Over 35 desktop applications are supported. All workstations access the Statistical Center servers and the Internet. The Statistical Center database, WEB, file and related services are housed at CRAB. Statistical Center staff at FHCRC access CRAB resources (over a dedicated network connection to improve performance and security) using Citrix terminal services and Internet Explorer. Sensitive information is transmitted using encryption. In addition to the dedicated network link between CRAB and FHCRC, each organization has independent connection to the Internet.

MS Windows Servers

The Southwest Oncology Group Statistical Center uses a modified, distributed architecture with the majority of its MS 2003 Servers, i.e. different servers perform different functions. The introduction of virtual server technology, using VMWare® ESX Server, continues to support this distributed architecture while making more efficient use of hardware resources with multiple virtual Windows servers on each physical machine. There are over 50 network servers including a small number of development and test servers. Production servers are Pentium III or higher servers with multiple processors, a minimum of 1 Gigabyte (GB) of memory, have fault-tolerant disk subsystems and carry on-site maintenance. Several tape library systems are used for backup.

Key network server services offered at the Statistical Center include:

- Oracle® Database
- Microsoft® SQL Server
- Microsoft® Exchanger Post Office
- Microsoft® IIS WEB Servers (Internet and Intranet)
- Lyris™ Listserv
- Ecora® Auditor
- TNT® ELM Event Monitoring
- Cardiff™ Teleform®
- Citrix® Terminal Services
- Camellia® C/S Batch Services
- Symantec™ Backup Exec Enterprise
- Trend Micro™ Virus Protection
- Symantec™ Ghost Enterprise and WinInstall
- Microsoft® System Management Services
- SAS® and Splus® Statistical Packages
Data Security and Disaster Recovery

Data Security and Disaster Recovery is based on what are often referred to as “best practices” in electronic computing and networking. CRAB Network Administrators periodically review and compare current network and security best practices with existing CRAB policies and procedures. Outside professional reviews and audits also provide critical information. Updates to policies, procedures and training are incorporated as appropriate.

A summary of key Statistical Center network policies and procedures requirements are:

Contingency Plans

All servers are backed up to tape (full and incremental). Backup Media are transferred to secure fireproof cabinets daily and transported to and from a bonded, secure off-site storage facility (vault) on a weekly basis. The most recent, and critical backups are stored in a fireproof safe with combination lock. Original software, media, and directions are stored in centralized fireproof cabinets.

Servers are configured using fault tolerant disk subsystems. Special disk imaging and file recovery applications are used to speed up restoration on key file servers including database systems. Not only has this process been tested, it is used as a part of normal server construction and upgrades.

Emergency mode plans cover varying levels of disaster recovery developed to address the severity and extent of disaster. This may include a combination of manual and electronic replacement systems until such time critical network services can be re-instated to a fully working level.

Information Access Control

Supervisors submit Employee Action Forms (EAF) to key account management staff for all employee hires, terminations, or job function changes for staff. User accounts are user-based. Individually identifiable patient data, collected only at the time of registration, are stored in a secure table where read and write access is highly restricted and requires prior approval of the Group Statistician, based on demonstration of the user’s “need to know” to perform their job functions. All accounts have controlled access to resources based on individual user account definitions.

The highest-level account for network administration is renamed/changed periodically to increase security. For network and database accounts, all staff are required to use “strong” passwords (those with a combination of lower and upper case alphabetic characters, numbers and special characters) to reduce the risk of password cracking. Passwords are aged and staff are required to change them on a regular basis. Passwords are not transmitted via E-mail or over the Internet.

The CRAB firewall utilizes Check Point® firewall security to provide restricted access to and from resources. The firewall and other border security is monitored 7 X 24. Secure Socket Layer
(SSL) encryption is used on Web and E-mail servers. Secure File Transfer Protocol (SFTP) is used for the file transfer with remote clients.

Information Technology Security and Monitoring

The CRAB Security and Disaster Recovery Handbook along with the Information Technology Standard Operating Procedures define overall electronic security policies and procedures for the Statistical Center Resources.

Senior level Information Technology staff at CRAB are responsible for monitoring and addressing network security and host/server resources, including the patient database. All Information Technology support staff have appropriate levels of supervision.

Network administrators review network and server event, security and application logs and other reports on a daily basis to monitor login, file access, security incidents and the status of hardware and services. Notification software is configured to provide immediate notification (paging and E-mail) to network administrators for unexpected network and server events.

Servers and workstations are proactively updated with security patches as well as OS and application updates. Network Administrators subscribe to notification lists to stay on top of emerging problems and corresponding updates or fixes.

All desktop computers, servers and the E-mail post office have active, real-time virus protection. Virus protection software is automatically pushed to the CRAB network and subsequently updated on each system.

Computer equipment (including equipment checked out to staff) is logged and tracked in an online inventory database including location and user (for individual desktops).

Identified real or suspected security incidents are logged, addressed and reported to and/or by senior network administrators and the Director of Information Technology. Problems are in turn reported and/or escalated to the appropriate governing body such as CRAB Executive Officers and/or SWOG Headquarters and Operations Office.

Senior management including senior network administrators perform risk assessment on new systems and events to define the cost and benefits of different solutions and the solution impact on: Confidentiality, Integrity and Accessibility.

Media Controls

All software media and licensing are filed in fireproof file cabinets and restricted areas. Only authorized personnel may access original software media and licensing. All software upgrades to workstations, servers or other systems are done by Information Technology staff or by explicit permission of the Information Technology Director (in very rare situations, some users may install specified software licensing).

All on-site backup media are stored in either a fireproof safe or fireproof cabinet located in restricted access areas where only authorized staff may enter. All off-site backup media are stored in a secure, bonded, protected vault at professional facilities.

All old server and PC disk drives, CDs, portable media and other storage material are destroyed by a bonded, professional media destruction company.

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All server rooms, server configuration areas and media storage are in restricted access locations. Signs are clearly posted on restricted areas noting that they are restricted. Only a limited number of authorized staff may enter restricted areas. All server rooms and server configuration areas have security cameras, which record 7 X 24 hours per week. All servers have screen/keyboard locks. All vendors or other third party visitors accessing restricted areas are logged into an electronic file and escorted by authorized staff.

Information Technology Resource Access Policies

All staff are required to read and sign software, network, computer and data protection policies. These policies clearly outline and define proper use of desktop computers, E-mail, access to other network services, software usage, protection of patient information and other related practices. Operating System policies may further restrict staff from inappropriate computer or software usage. Network software monitoring applications track software use by user and workstation. All users must have valid accounts and passwords. Logon sessions have enforced password protected screen savers that lock the systems after 30 minutes of inactivity. Staff workstations are located in specific work areas that are locked after normal business hours. Remote and local users must maintain integrity and confidentiality when accessing CRAB resources.

Data Authentication and Encryption

The use of encryption (VPN, SSL and SFTP) reduces the risk of alteration or easily viewing of Internet traffic (packets) containing sensitive information. Operating system and database controls restrict inappropriate access privileges to data, files and other objects that require protection from modification.

Software

The operation of the Southwest Oncology Group Statistical Center depends on six major classes of software: database management, statistical analysis, desktop applications, network services, report processing, and data management.

Database Management

The database management software used is Oracle, one of the major commercially marketed systems. Oracle is based on the relational model of database management and is built around the industry-standard SQL language. The Statistical Center's data management operation is built around Oracle's capability for multiple users to manage simultaneous database modifications. In addition to the core relational database management module, Oracle has components for ad hoc queries, report writing, generation of screen-based data maintenance applications, interfacing to high-level languages (C++ or Visual Basic, for example), and database administration and tuning.

Statistical Analysis

The main statistical package used is SAS. Several in-house programs have been written using SAS and Splus to perform tasks such as Cox regression diagnostics, Kaplan-Meier survival curves, sample size computations, exact methods, recursive partitioning, and longitudinal data analysis. The Center has recently acquired licenses for GenePlus and Insightful ArrayAnalyzer software for the analysis of microarray data.
Desktop Applications

Several Microsoft desktop applications are used by staff including Office Professional (Word, Excel, PowerPoint and Access), Visio and Project. Another key application is Adobe Acrobat.

Network Services

Electronic mail is used extensively for communication within the Statistical Center as well as with the Operations Office and with other Group members. CRAB and FHCRC staff access respective Microsoft Exchange Post Offices with MS Outlook and Outlook Web Access (OWA). The Statistical Center uses MS Internet Information Server (IIS) for Web services. Cardiff Teleform® is used for forms design, data submission and data entry.

The Southwest Oncology Group Home page can be found at http://swog.org. This site is maintained at the Operations Office in San Antonio. The swog.org website has links to the Statistical Center’s services.

Report Processing

The Statistical Center Report of Studies is created using an application developed at the Statistical Center (Statisticians’ Report Worksheet, or SRW) incorporating a web-based interface, creation of a SAS data set from Oracle, and the word processing tools of Microsoft Word.

SRW is based on a “thin” Client/Server (C/S) model using Web publishing technology. Web pages are driven from two primary database sources: Oracle and SAS data sets. MS Internet Explorer provides a program interface for input of textual and study parameters needed to define and set up charts, tables, graphs, and descriptive information. SAS extracts the data from the patient database via Open Database Connectivity to create a SAS data set, i.e., a "snapshot" of the patient data. Study chapter generation is done on a Web server based on input from the SAS data sets, study information defined in the Oracle database and end user input (such as text, label definitions, and table format information).

Users are able to view and output the study/chapter results in three ways:

1. As Web pages for preliminary browsing/viewing of the document.
2. As Web pages for final publication.
3. As formal output to a printer, a postscript file, and other file format, e.g., MS Word or Portable Data Format (PDF), for professional printing of the Report of Studies. PDF copies of the Report of Studies are available on the SWOG Home page (http://swog.org).

Hyper Text Markup Language (HTML) templates represent the various tables/charts. Microsoft's IIS Web Server and some of its key components are used to provide Web and final publication. A program process fills in much of the templates based on the SAS data sets and other stored database information, in order to generate more complete HTML documents. Additional programming filters further refine the Web pages, and the formal output of the Report of Studies (ROS) is an executed "object linking and embedded-enabled document production manager", as the final ROS requires more extensive formatting (headers, footers, page numbers) compared to the Web pages.

The study chapters are made available as static publications based on the "snapshot" data sets. Data sets, other interim priority documents and the final chapter output are archived for future retrieval and reference. Since this model is a mix of “thin” C/S and Web publication with some
portions being batched off to back-end Windows servers, it works well for both Local Area Network and Remote Access clients.

Security is built into the systems: correct user account information and password protection are required for accessing these services and firewalls are used to audit and restrict access.

Other in-house reports are created using SQL queries and Microsoft Active Server Pages (ASP) technologies to provide dynamic links to the Oracle database. Production reports and other documents are created using Microsoft Word, PCTex and Scientific Workplace.

Data Management

The main data management systems have been written in-house and consist of the patient/participant registration and randomization system (WebReg), the patient evaluation system (EVE), and Chart Manager, for the creation, manipulation and viewing of electronic patient charts.

**WebReg (Patient Registration)**

The patient registration and randomization program is very complex, since it is a generalized program that facilitates study set-up and patient registration. It is designed to handle the wide variety of requirements for SWOG studies. It is a thin client application designed to be used in-house or via the Internet by a CRA. It is a web-based application written in Microsoft VB.NET and interfaces with the Oracle database. Randomization is typically accomplished using a dynamic balancing algorithm, which uses current accrual counts by stratification variables directly from the database.

**EVE (Patient Evaluation System)**

The patient evaluation system allows data coordinators to update derived data about treatment and response, with comprehensive cross-field edit checks. The data coordinator also uses EVE to write queries, manage expectations, and indicate which cases are ready for study coordinator review. This system is written in Visual Basic and runs on Windows.

**Chart Manager (Image Management)**

Several years ago, the Statistical Center made the decision to move towards electronic data image management for our therapeutic studies. Because we did not want to maintain both paper and electronic systems into the future, we undertook the scanning of 80,000 paper charts (2.2 million images), now completed. We now create, maintain and view electronic charts using an in-house application (Chart Manager), a web-based application that interfaces with Oracle. All Teleform® patient file images and future data entry documents are included in the document management system (as TIFFs).

All SWOG data coordinators have client query tools for viewing patient charts, query and annotation utilities, and redaction (for HIPAA compliance). WebReg and EVE integrate directly with Chart Manager. Future enhancements will include the ability to view electronic data in other than TIFF format, as was developed for the Selenium and Vitamin E Cancer Prevention Trial (SELECT).
The Southwest Oncology Group Statistical Center manages its database using Oracle®, a relational database management system. There is a production database that stores data that are reflective of real events, and a test database that is used for ongoing development and testing of applications. Each database is organized into two schemas, one for staging tables and one for active tables. Active tables hold data that are included in evaluations and analysis. Staging tables are used to store submission attempts from electronic data entry (EDC) applications, attempts that may violate pre-determined business rules. Once the business rules are cleared, data from the staging tables are promoted to the active tables.

The table structure in each database is organized into five main components:

1. **Common Patient**: This component contains patient-related data items, which are common to all Group studies including patient characteristics; identification of investigators and institutions to which a patient is associated; registration date; stratification; treatment; common evaluation items; and adverse events. Many of these items are accessed frequently in the day-to-day operations of the Statistical Center. One of the largest tables in the database stores over 2 million reported adverse events.

2. **Study Characteristics**: These describe the Group studies and are available to the data operations software, which must modify its behavior depending on the study being processed.

   At present (May 2007), SWOG holds data for over 180,000 patients with over 250,000 registrations to over 1000 studies we coordinate or participate on (including those with multiple registration steps).

3. **Membership**: The membership component describes the investigators, clinical research associates, institutions, pharmacies, labs, radiation therapy facilities, bone marrow transplant facilities, and the relationships between people and sites. We further describe members by the web site and registration permissions they have for each site affiliation.

   Counting both past and present members, SWOG has membership records on over 27,000 investigators and staff as well as information about 3600 institutions.

4. **Detailed Patient**: Detailed committee or study specific patient data items are regarded as a separate database component. These are not accessed as frequently as the common patient data items.

5. **Quality Control**: A major aspect of quality control data is our generalized tracking system, which stores data expectations, and tracks submission of the required study information. Over 6 million expectations have been posted for scheduled data submission. We also maintain data from various review processes (pathology, surgery and radiation therapy). In addition, the data submission software forces quality control standards and collects quality control data.

**AUDIT TRAIL**

In October 2000, a comprehensive audit trail was implemented for the entire production database. Every insert, update, and deletion of data from the production database is recorded in the audit...
trail. The audit trail records the user name, terminal name, date and time of the change, table name, unique identifier for the row, column name, and the old and new value.
Data Operations

Patient Registration

All patients are registered using a computer program (WebReg), which interacts with the database during the registration. Registrations are performed either directly via the Web by institutional CRAs or by data operations staff using WebReg during the telephone conversation with the representative from the institution registering the patient. The main advantage of using WebReg is that the registration procedures are strictly enforced in a uniform manner for all registrations. Manual registration procedures are available for those times when the computer system is not available. Some of the other advantages and features of WebReg include:

1. The database is instantaneously updated with each registration.

2. The approval status of the investigator and institution registering the patient is validated as well as that of the facility to perform radiation therapy, if applicable.

3. There is a review of previous registrations in cases where the patient is being registered to additional protocols or subsequent parts of a protocol.

4. Blinded treatment assignment is possible.

5. Registrations requiring randomization are dynamically balanced using the current database stratification counts. Post-registration modifications to stratification data instantaneously adjust the dynamic balancing algorithm.

6. Relevant study characteristics and special notes about the study, including stratum or treatment specific notes, are automatically presented during the registration.

7. A confirmation of registration is generated with copies for all relevant study participants. This confirmation includes a summary of the registration along with a list of expectations for forms submission.

WebReg is driven by a study description file (SDF), which contains the information needed to control the registration process and to load the database study description tables. There are one or more SDFs for each study. These are prepared by the data coordinator for that study with the consultation of the data coordinator’s supervisor, the study statistician, and discipline data coordinators and biostatisticians when applicable.

Flow of Data

All newly activated trials use data capture forms which can be submitted electronically via the web. All SWOG members have mandatory data submission on the web for all but selected data (operative and pathology reports, quality of life instruments). Institutions participating on SWOG coordinated trials via the Cancer Trials Support Unit (CTSU) submit data either by fax or by mail. Other Groups participating on SWOG trials submit data via fax. For non-SWOG coordinated intergroup studies, institutions submit data directly to that coordinating statistical center. Data forms are processed according to the following conventions:
Submissions by fax or mail lacking required identifiers or other required information are returned to the institution. Completed forms are routed to the data control technicians for processing.

Slide and/or block information (as applicable) for pathology reviews are entered into the database by the registering institution using the Specimen Tracking program. Materials are tracked in the database through the review process. All results (eligibility and detailed review results) are also entered in the database.

Complete sets of radiation therapy materials are sent either directly to the Quality Assurance Review Center or to the central RT reviewer. The review results are entered into the database by the discipline coordinator at the SWOG Data Operations Center.

Surgical summary forms (as applicable) are forwarded to the surgery study coordinator, along with operative records and pathology review forms.

Upon completion of data entry, all forms are routed directly to the electronic patient chart. The disease site data coordinator is then responsible for quality control review.

Data Entry

All trials activated after August 14, 2006 use data capture forms which can be submitted electronically via the web. Extensive range and logical error checks are incorporated.

Exceptions to web-based data submissions are allowed for selected forms (pathology reports, operative reports, and patient completed forms), for data submitted through the CTSU or for other Cooperative Group data. These data are submitted by mail or fax. Most of these data forms were created using the commercial product Teleform®, which produces forms that can be scanned directly into the database. Entry of data submitted in formats other than Teleforms is also done through the Teleform® software. Updates of last contact date, status, off-treatment date and expectation resolution are done through a separate in-house Visual Basic application. Data is sent to the database and a TIFF image of the form is then sent to the electronic patient chart.

Electronic File Organization

The Statistical Center organizes files so that all data for a patient are located in one electronic file. Data within patients’ charts are maintained with the most recent data at the top or on the left-hand side of Chart Manager as an incoming document. Electronic records are saved in a back-up database each evening. Security for these files is detailed under data security and disaster recovery in the computing infrastructure section. The electronic filing system of data is stored by patient-specific numbers, then under study identification.
Quality Control

Quality control occurs on every level: the scientific review of new protocols, the design of new forms, review of data by study coordinators, training of study staff, review of each submitted data form for consistency and completeness, and at creation and analysis of final analytic data files.

Protocol Development and Review

The first step to ensure quality control in clinical trials is to develop protocols that are clearly stated and exhaustively inclusive of all criteria and procedures necessary for conduct of the study. The protocols are the standard against which the Group measures the conformance of the investigators. Most importantly, protocols reflect the scientific direction and standards of the group.

The Statistical Center is intimately involved in the development of protocols, from the capsule stage through to activation. The Committee Statistician works closely with the Study Coordinator(s), the Disease Chair, and the Protocol Coordinators to develop the protocol design. Statisticians collaborate with their medical colleagues to determine appropriate scientific questions, correct endpoints, and feasible accrual goals. During the protocol development, the Data Coordinator for each committee may provide critiques and recommendations to eliminate ambiguities. Each protocol is reviewed for protocol consistency via a Protocol Review Committee in the Statistical Center and a Protocol Consistency Checklist in the Operations Office.

Several aspects of each protocol have been designed to enhance the quality of the data.

1. The eligibility section, which assures eligibility of all patients at the time of registration, must be confirmed by the physician and the clinical research associate prior to the placement of the registration call to the Statistical Center.

2. The study parameter calendar for each arm of a study, details the data to be collected at each patient encounter, and treatments to be delivered at each treatment visit. This is not only essential at the institution level to assure conformance to standards, but is useful in quality control review of the submitted record.

3. Study data collection forms are designed to provide efficient data collection and study analysis.

Eligibility and Initial Treatment Review

Initial forms required by the protocol are reviewed by the data coordinator to ensure protocol compliance. All data are assessed to confirm that prestudy information pertaining to stratification variables is the same as that given at registration; that the patient's body surface is calculated correctly; that the required protocol tests were performed; and that initial treatment was given as per the protocol. Results of quality control are communicated to the registering institution via an evaluation status report. If a documentation error or discrepancy is noted, the institution may correct the error by submitting the appropriate amended form. Evaluation status reports are mailed to institutions regardless of the quality control outcome.
Patient Evaluations

All patient evaluation data is provided to the study coordinator for review and evaluation via the online Study Coordinator Evaluation program. This program includes preliminary evaluation information entered by the Statistical Center data coordinator on eligibility, protocol deviations, toxicity grades, and response. These judgments are preliminary until reviewed and confirmed by the study coordinator. In the case of a disagreement, the disease committee statistician may become involved. Continuing disagreements are adjudicated by the disease committee chair or in rare instances, the Group Chair.

Data Coordinator Quality Assurance (DCQA)

The DCQA program was implemented in August 2000 as an internal audit mechanism to monitor and maintain the quality of data evaluations conducted by data coordinators. Each data coordinator is audited twice per year by the quality assurance coordinator, with respect to coding of: eligibility; disease status, treatment; reason off treatment, toxicity; notes; other (second primaries, etc). If necessary, further instruction and education is provided to the data coordinator to ensure that errors are not repeated.

Study Coordinator Evaluation Monitoring System

Study Coordinator Evaluation Forms (SCEFs), are electronically generated by the disease site data coordinator at certain key points after patient registration to a Southwest Oncology Group protocol, e.g., following completion of treatment, relapse, and death. For some protocols, it may be appropriate for the study coordinator to evaluate patient data every three months or more often during treatment.

The Evaluation Monitoring System tracks all SCEFs generated after June 1995. Each time a SCEF is electronically generated, the patient number, study number, registration type, and date of generation are automatically recorded as a row in the SCEVAL database table. This row also includes fields indicating the SCEF returned status and the study coordinator evaluation date (generally the date the study coordinator completes and submits the form). Upon electronic submission of each SCEF from the study coordinator, any coding changes made by the study coordinator are entered into the database by the data coordinator.

A Study Coordinator Evaluation Report is generated and sent to the Group Chair, the disease committee chairs, and to individual study coordinators. This report contains information on the number of evaluations generated for a particular study, the number of evaluations submitted, and the length of time since outstanding evaluations were generated. These and other reports are used to monitor study coordinator workload and to evaluate compliance with study coordinator responsibilities.

Expectation System

The Statistical Center expectation system provides the structure within which quality control functions are implemented. The primary focus is data submission timeliness. The expectation system notifies institutional clinical research associates when specific submissions or tasks are due; when a submission becomes overdue, the notifications become insistent. The expectation system also generates timeliness data on each institution, which can then be used to provide feedback on performance.
Expectations are entered into the Study Description File (SDF) and are posted automatically at the conclusion of the registration process. Expectations are highly study dependent and may additionally depend on registration-specific factors such as treatment assigned, applicable stratum, registering institution, type of institution, prior treatment, and/or prior pathology reviews. Expectations are defined in the SDF corresponding to that study registration using a simple procedural language to implement the logic necessary for deciding whether an expectation of a specific type is to be posted. For example, SWOG 9917 is a placebo-controlled study of L-Selenium based chemoprevention of prostate cancer among men with high grade prostatic intraepithelial neoplasia. The study requires a repeat biopsy only for those patients whose initial biopsy included fewer than 10 cores or was performed more than six months prior to registration. Materials from the repeat biopsy, if required, must be submitted for central review within 14 days of the repeat biopsy to confirm absence of cancer prior to randomization. Therefore, pathology submission expectations associated with the repeat biopsy are posted only for a subset of patients.

An expectation is resolved when the Statistical Center has received the data or has been provided evidence that the task has been performed. In most cases, the resolution of an expectation is an automatic process resulting from data entry of the submission. Remote data entry for forms submitted on-line automatically resolves the data expectation item. Lists of expectations are posted monthly for the institutions on the CRA Workbench. In addition to the monthly expectation postings, a current expectation report can be run on-demand and is also available on the CRA Workbench.

Institutional Performance Review (IPR)

In conjunction with the monthly expectation report, the Southwest Oncology Group summarizes monthly statistics to assess institutional performance. These standards assess timeliness of data submission in three categories: initial forms sets; follow-up for alive patients on protocol treatment, and follow-up of patients who are no longer on protocol treatment. Data items that are overdue on any of these categories are starred on the institutions’ expectation reports, to aid in identification of cases requiring immediate attention. The monthly IPR statistics are reported to the institutions, and monitored at the Statistical Center by the Deputy Director. Institutions that are out of compliance for two months in a row receive a warning letter. Any institution that is out of compliance with the standards of the Group for three months in a row lose registration privileges until the deficiencies are corrected.

Serious Adverse Event (SAE) Reporting System

Serious adverse events are reported in several ways. If an SAE occurs that is reportable per protocol, investigators are expected to call the Operations Office to report it and/or enter it immediately into NCI’s AdEERS (Adverse Event Expedited Reporting System). Certain adverse events, including fatal toxicities for all treatments and life threatening non-hematologic toxicities for investigational treatments, are subject to an automatic Serious Adverse Events Reporting System.

Toxicities for treatment studies are entered into the SWOG database via adverse event forms submitted by institutions. If a Grade 5 (fatal) toxicity occurring within 30 days of last protocol treatment is entered for any patient or if a Grade 4 (life threatening) toxicity is entered for patients receiving investigational treatment, the computerized Serious Adverse Events Reporting System checks the database to determine if the event has been reported as an SAE. If the event has been previously reported, no further action is taken. If the event has not been previously reported, the patient number, study number and registration type will appear on a report that is
routed to the statistical center SAE coordinator and to the Operations Office SAE manager. This allows the Ops SAE manager to contact the institution to ask that the event be reported.

Serious adverse events reported to the Operations Office in any of above ways receive an SAE number and are entered into the tracking system by the Ops SAE manager. Once the SAE has been evaluated to determine whether it is attributable to protocol treatment, the toxicity is copied into the AE database for the affected patient.
Discipline Committees

The Statistical Center provides considerable support to three Southwest Oncology Group active discipline committees: pathology, surgery, and radiation therapy. These committees require two kinds of support from the Statistical Center: (1) processing the results from the data reviews performed by the members of these committees, and (2) providing statistical design and analysis services in support of their scientific activities.

The review functions performed by the discipline committees are designed to answer questions of protocol eligibility (pathology and surgery) or protocol compliance (surgery and radiation therapy). The summary data, which result from these reviews, are an important part of the Group patient data evaluation system and are integrated into the patient evaluation forms along with other eligibility and compliance data. In addition, the review processes yield important detailed data regarding pre-treatment status (pathology), procedures performed (surgery and radiation therapy), or outcome (pathology and surgery). The study coordinators are provided with copies of these detailed data forms.

The specific elements of the Statistical Center data operations that are relevant to the support of these discipline committee functions include the following.

1. A master’s level biostatistician is assigned as the statistical liaison to each discipline committee. This biostatistician is responsible for seeing that the review processing requirements of the assigned committee are implemented and functioning.

2. The discipline coordinator supports each discipline committee through a variety of functions, depending on the needs of each discipline committee. These include patient registration, data entry management, forms tracking, quality control, protocol compliance enforcement, protocol setup, and review of protocols with respect to discipline committee data processing.

3. The study description file (SDF) corresponding to each study registration that involves discipline committee participation specifies the various review committee options. Most of these are processing steps to be executed at the time of patient registration; others cause flags to be set in the database. The processing steps might include request for additional information, display of special notes, creation of expectations, validation of special eligibility requirements, etc. The database flags include indications that the patient is registered to a study involving one or more review processes, and the setting of these flags may depend on the treatment assigned.

4. The expectation system notifies institutions of the need to submit pathology and surgery materials and/or forms required by the discipline review processes, and tracks the submission of the materials or forms. The system also provides timeliness data for the institutions. Pathology expectations are resolved when the required materials are logged into the specimen tracking system. Surgery expectations are resolved by the study data coordinator as the forms or materials arrive at the Statistical Center.

5. The primary returns from a review process are the summary results, that is, an indication of eligibility (pathology and surgery) or protocol compliance (surgery). The data are entered as soon as the review is completed and returned by the respective reviewer. The summary data are scanned into the database from the teleform review forms. Some
surgical data are entered by the Statistical Center data coordinator. The input procedures are highly structured and include the creation of notification of changes in eligibility status, automatic update of overall eligibility (if applicable), and the ability to make annotations.

6. Summaries of the pathology and surgery results of the discipline review, including annotations, are reported to the study coordinators in the evaluation forms sent to them for patient evaluation data review.

7. For each Group Meeting reports may be prepared for the Pathology and Surgery discipline committees on the results of the review processing for that cycle. These reports include information on institutional timeliness, review-specific eligibility/deviation rates, review process timeliness, review process volume, etc.

8. The Statistical Center also provides support for the entry of whatever other discipline review committee data are generated.

Cytogenetics

The Southwest Oncology Group Cytogenetics Business Office was relocated from City of Hope National Medical Center to the SWOG Statistical Center in June 2002. The Business Office is staffed by one data coordinator and one statistician. Responsibilities of the SWOG Cytogenetics Business Office include coordinating the application and approval process for new cytogenetics laboratories and data entry of cytogenetics forms. The data coordinator and biostatistician coordinate Cytogenetics Committee meetings, prepare patient files for central reviews held at each semi-annual Group meeting, and assist committee members as necessary during the central review process. Database queries are generated and submitted as requested by the Cytogenetics Committee Chair and other members of the committee. A future goal for the Cytogenetics Business Office is to allow participating laboratories to remotely submit cytogenetics data directly into the database. There are currently 5,540 cases in the cytogenetics database from 50 different SWOG trials. SWOG receives an average of 30 cases per month.

Radiation Therapy (RT)

Rapid review of radiation therapy for SWOG studies, previously performed by the SWOG Quality Assurance Center located at Wayne State University in Michigan, was transferred to the Quality Assurance Review Center (QARC) in Providence, Rhode Island, in January, 2003. Other aspects of radiation therapy review that were previously handled by the SWOG Statistical Center were also transferred to QARC. The RT biostatistician notifies QARC of each new registration to a study that included RT review, and QARC is responsible for notifying institutions of the need to submit materials and/or forms required by the review process.

On-study (“rapid”) RT reviews are performed by radiation oncologists and dosimetrist at QARC, while end-of-study RT reviews are performed by the SWOG radiation oncologist designated as the RT Study Coordinator for a specific study. The RT Study Coordinator travels to QARC to perform the reviews in one or more batch review sessions, and QARC maintains the review results. The summary data are sent to the Statistical Center on a quarterly basis, or other specified schedule for individual protocols. QARC prepares reports for the Group meeting, including information on the number of reviews performed for specific protocols.
Training Programs

Clinical Trials Training Course (CTTC)

The Data Operations Department at the Statistical Center, along with assistance from the Operations Office staff and experienced clinical research associates, conducts a one and a half day training course for new clinical research associates. This training course is held prior to each Southwest Oncology Group Meeting. Seventy-four clinical research associates from throughout the Southwest Oncology Group participated in the Spring 2007 course.

The training course provides an overview of the Southwest Oncology Group as well as information pertaining to topics such as the explanation of clinical trials, phases of studies, quality control, quality assurance, ethics and quality of life. Familiarization with the Southwest Oncology Group registration process, forms, and office procedures is also included. A practicum round-table discussion provides clinical research associates with practice of forms completion, adverse event grading, response assessments, and calculating laboratory values.

An explanation of data flow, the expectation system, patient follow-up, and adverse events are other topics discussed in the training. The Clinical Research Manual (CRA Manual), which details the administrative procedures of the Group and the forms and coding guidelines of each disease committee, is available via the internet at swog.org. CTTC participants are oriented to the web-based manual during the training course.

Study Coordinators Workshop

Members of the Statistical Center staff, in conjunction with Operations Office staff have designed an on-line training course for physician investigators who have never served as a SWOG national study coordinator and who wish to coordinate a Group protocol. The workshop's primary objective is to provide the foundation necessary to perform the responsibilities of a SWOG study coordinator. The course is located on the Study Coordinator Workbench on the SWOG website. Participants must complete the full course, as evidenced by completion of the test questions at the end of all presentations, to receive approval to develop and coordinate a SWOG research trial.

The course provides training in the responsibilities of a Study Coordinator, and of the coordinated efforts of the Statistical Center and Operations Office. There are presentations on ethics, protocol development, clinical trials design, the evaluation process and study coordinator responsibilities during development, during study accrual and during manuscript preparation.

Investigators Training Course

The Young Investigators Training Course is an intensive 3-day workshop held annually to develop a cadre of experts able to quickly and efficiently develop priority studies. For the purposes of this training, young investigators are defined as oncology fellows in training or assistant professor equivalents affiliated with Group institutions or otherwise eligible for Group membership. The course primarily focuses on protocol development, maintenance, and administration.

These young investigators are asked to produce a concept for a Southwest Oncology Group Phase II or Phase III protocol and follow this idea through an intensive simulation of the protocol
development process. A panel including Group leadership and the Chair of the applicable Disease Committee reviews each application package and chooses attendees for each training course. At the end of the course, the investigators' ideas are presented to the respective disease committee chairs for consideration of activation within the Group. While no guarantee is given that these particular ideas will be pursued within the Group, it is hoped that the principles learned through this workshop will produce attractive protocols that will be of great interest within the committees.
Interacting with Other Cooperative Groups

The Southwest Oncology Group participates in NCI-sponsored intergroup protocols. These are protocols in which more than one cooperative group participates. The protocol is coordinated by only one of these groups. The three types of participation are as follows.

Other Group-Coordinated Protocols Not Conducted Through the Cancer Trials Support Unit

For non-SWOG intergroup treatment trials that are not conducted through the NCI funded Cancer Trials Support Unit (CTSU), the Southwest Oncology Group primarily participates by contributing towards the accrual of patients onto the protocol. Currently, the Southwest Oncology Group participates in 10 of these intergroup protocols. The Statistical Center’s responsibilities for all of these trials include cooperating with the coordinating group’s statistical center and operations office by performing data monitoring and follow-up tasks as required.

For trials coordinated by another Cooperative Group, a Direct Data Submission Initiative has been piloted and proven successful for expedient data transfer to the coordinating group. Via this direct data submission initiative, data are submitted by the institution directly to the coordinating group, bypassing the participating group’s data operations center. A nightly secure ftp database transfer from the coordinating group to the participating group updates the patient’s survival and last contact information as it is processed by the coordinating group.

The Statistical Center is responsible for conducting patient registrations for intergroup/non-CTSU trials. For these registrations, a data operations staff member contacts the other Cooperative Group Statistical Center and obtains treatment assignment and patient identification numbers. The staff member is then responsible for completing the registration by calling the SWOG CRA and relaying the treatment assignment and patient identifiers as indicated by the protocol.

The Statistical Center facilitates its participation in non-CTSU intergroup protocols managed by other groups by recording in the Southwest Oncology Group database the patient number assigned to Southwest Oncology Group patients by other groups.

Other Group-Coordinated Trials Conducted Through the Cancer Trials Support Unit

The Statistical Center’s responsibilities for non-SWOG trials conducted through the CTSU differ in that patient enrollment is routed from the institution directly to CTSU and to the coordinating group. The direct data submission initiative has also been implemented for these registrations. Registration information is relayed to the SWOG Statistical Center for recording (for those CTSU studies endorsed by SWOG).

Southwest Oncology Group-Coordinated Protocols

The Southwest Oncology Group currently coordinates 10 open intergroup treatment protocols. These studies are available to non-SWOG participants either via the CTSU menu, or directly with specific cooperative groups. For these protocols, a number of innovations have been implemented.
1. The computerized registration system recognizes intergroup protocols. When the registering institution is from another group, the program follows special instructions with respect to identification of the registering investigator and institution, dynamically balanced treatment assignment, the expectation list, and specific notes directed to the registering groups.

2. The database maintains the investigator and institution associated with each patient to support requests for follow-up data sent to other statistical centers.

3. The expectation reports and requests for follow-up sent to other group statistical centers are specifically designed to facilitate communication with their institutions, and are therefore different in style and content from the analogous reports sent to institutions in the Southwest Oncology Group.

4. Reports were designed specifically to facilitate the monitoring of intergroup studies. These reports are for monitoring accrual (by group) and identifying data submission or follow-up problems.

5. Procedures are being developed to allow participation with collaborators from Europe and Asia.
Statistical Designs and Study Monitoring Policy

The Statistical Center guidelines for the design and monitoring of clinical trials encourage consistent designs that are similar across disease committees, but allow flexibility to accommodate individual study needs. Consistency is promoted through use of common statistical design tools, and a multi-level review process.

All Southwest Oncology Group Phase III trials have a named faculty level statistician who oversees the statistical development of the protocol including refining the hypotheses as needed, defining data collection protocols, specifying randomization details, defining the data analysis and data monitoring plan and determining the target sample size. To provide for a comprehensive and definitive test of a novel regimen relative to a standard treatment, Phase III SWOG trials are typically designed to have close to 90% power to detect moderate improvements in a survival-based endpoint based on a two-sided 0.05-level test. Occasionally multiple arms will be tested in the same trial, either in parallel or as a factorial design. Such trials are rare because of the practical challenges in mounting such efforts. Non-inferiority trials may also be conducted in SWOG, using principles outlined in Kopecky and Green (2006). Power calculations are generally made using tools available on the Statistics Workbench on the Statistical Center website. For survival, these calculations are based on Bernstein and Lagakos (1978).

All Phase III studies managed by the Southwest Oncology Group are designed with formal stopping rules in the protocol and are reviewed by a single Data and Safety Monitoring Committee (DSMC). This committee consists of three members of the Group, a patient advocate, two clinicians and a statistician not involved with the Group, two non-voting representatives from the NCI, and the Group statistician (also non-voting). Detailed interim results are generated at the Statistical Center and are presented only to this DSMC. The DSMC decides when to close the study and when to report the results, using the stopping rules in the protocol as a guideline.

Stopping rules are based on group sequential designs, which preserve the overall error rates but allow for early stopping if extreme results are observed. In addition to the usual specification of Type I and Type II errors, a typical design for a Phase III study would call for specification of the number of analyses (generally 3 or 4) and of a small probability of terminating at each interim analysis if the null hypothesis is true. A one-sided test can be supplemented with a similar early stopping rule based on testing the alternative hypothesis. The result is a procedure with virtually the same power and level as the fixed sample size procedure, but one that allows for early termination and permits a final analysis at close to traditional levels (Crowley, Green, Liu and Wolf, 1994; Fleming, Green, and Harrington, 1984).

All Phase II studies have a faculty level or master’s level statistician assigned to fulfill design, implementation, analysis and reporting functions described above. The standard Southwest Oncology Group approach to Phase II designs is based on a single arm test of the null hypothesis that the response probability is \( p_O \), too low to be of interest, vs. the alternative that is \( p_A \), sufficiently high to warrant further study, at a level approximately .05 and power close to .9. In some circumstances, randomized Phase II studies are designed and in those instances, selection designs are preferred (Liu, Moon and LeBlanc, 2006).

Phase II studies involving investigational new agents are generally designed with two-stage stopping rules, and protocols are temporarily closed at the end of the first stage to assess response rates. Reporting of early results for Phase II studies is restricted, subject to the discretion of the study coordinator, statistician, and disease committee chair, to avoid informal closing due to premature judgments based on small numbers. Studies are stopped early if the alternative hypothesis is rejected at the .02 level after the first stage of accrual. Otherwise,
accreditation is completed and the agent is judged promising if the null hypothesis is rejected. This approach has good statistical characteristics and is easily adaptable to the typical case in which the actual attained sample size differs from the planned sample size at the first stage or at the second stage (Green and Dahlberg, 1992).

Phase II trial monitoring is the responsibility of the study coordinator, the study statistician and the disease committee chair. Response monitoring is done by the study statistician and study coordinator. Toxicity and accrual monitoring are done routinely by the study coordinator, study statistician, by the disease committee chair. In addition, the Statistical Center, Serious Adverse Event Coordinator at the Operations Office, and the Executive Officer monitor toxicities on an ongoing basis.
Data Analyses and Reporting

Data Reporting

All open and most recently closed studies are described in the semi-annual Report of Studies, which forms the basis for much of the discussion in the Disease Committees at the Group meeting. Data are as current as possible, subject to printing deadlines and the need for data review by the study coordinators. A patient-driven evaluation system is utilized to smooth the workflow, rather than relying on batching the reviews every six months. The description of each study includes a summary face sheet, schema, accrual information by arm and by institution, stratification and description factors and toxicity information. Response and survival comparisons are presented only when approved by the Data and Safety Monitoring Committee.

Standard report modules extract data from the database and create these tables and a computerized worksheet program helps keep track of the Report contents. The Report of Studies includes chapters for each disease committee, and the Cancer Control Research committee. An additional section contains information on accrual to all Group studies by institution and study type; data on institutional performance regarding timeliness and completeness of forms is also included.

Analysis of Studies

Additional analyses, generally using SAS after data have been extracted from the database, are typically necessary before a study can be published. A program to extract data from the Oracle® database and create a SAS data set was written to assist in this process. SAS procedure LIFETEST is used for log rank and stratified log rank tests, and the procedure PHREG is used for proportional hazards regression and testing alternative hypotheses. Dichotomous data are analyzed using the procedures FREQ and LOGISTIC. Locally developed analysis software is used when necessary, especially for Cox regression diagnostics and for recursive partitioning. In addition, faculty statisticians are involved in ongoing methodologic research for more efficient trials designs, and improved analytic techniques.
Prostate Cancer Prevention Trial (PCPT)

Overview

The Prostate Cancer Prevention Trial (PCPT) was a Phase III, randomized, double-blind, placebo-controlled trial of finasteride for the prevention of carcinoma of the prostate. The primary objective of the PCPT was to test the difference in the histologically proven prevalence of carcinoma of the prostate between these two groups of randomized participants. Other objectives included assessment of the effect of finasteride on the stage and grade of carcinoma at the time of diagnosis, and estimation of the difference between the two groups in (1) total and prostate cancer-specific mortality and (2) the incidence and severity of benign prostatic hyperplasia (BPH). A total of 18,882 essentially healthy men, aged 55 and older, were randomized to receive finasteride (5 mg daily) or placebo for seven years. At the end of seven years, all participants not previously diagnosed with prostate cancer were asked to undergo a prostate biopsy.

The PCPT was an intergroup study with participation from 213 study sites in the United States and Canada. The trial was activated on October 13, 1993 and closed to enrollment on December 6, 1996; the last participant was randomized on May 16, 1997.

Results

The PCPT was closed early on June 24, 2003 based on an independent Data and Safety Monitoring Committee recommendation. The study results were published in the online version of the New England Journal of Medicine and appeared in the print journal on July 17, 2003. The analysis of the data revealed that men in the finasteride group who were evaluated were 24.8% less likely to develop prostate cancer when compared to the men evaluated who were in the placebo group. Although the men taking finasteride had fewer prostate cancers, they had an increased number of high-grade prostate cancers. In the entire group of men assigned to finasteride who were evaluated, 6.4% had high-grade cancers while 5.1% of the men evaluated in the placebo had high-grade cancers.

Several manuscripts have been published since the closure of the PCPT. Publication topics have included the effect of finasteride on the pathology of prostate cancer, prostate specific antigen (PSA), digital rectal exams and the detection of prostate cancer, the assessment of prostate cancer risk, finasteride and prostatic intraepithelial neoplasia (PIN), the effect of lifestyle characteristics on PSA, erectile dysfunction and subsequent cardiovascular disease and the design, biases and interpretation of the PCPT study results. Analyses of PCPT data are ongoing and future publications of interest will focus on important topics such as benign prostatic hyperplasia (BPH) and prostate cancer, the side-effects of finasteride related to treatment efficacy as well as additional quality of life and urologic issues associated with this study. Lastly, a comprehensive statistical model will be developed that will take into account a number of known and hypothesized biases (PSA, DRE, prostate volume, biopsy compliance) that may confound the observed relationship of finasteride and risk of prostate cancer and high-grade disease.
New Studies

A program project (P01) was initiated in 2005 to make use of a specific set of specimens collected during the course of the PCPT (serum, white blood cells, prostate biopsy tissue). This program project is a multi-institutional study and is investigating various areas of research including:

- Androgen metabolism in the PCPT (Reichardt, University of Sydney)
- Diet and diet-related factors (Kristal, Fred Hutchinson Cancer Research Center)
- Insulin-like growth factor axis and insulin resistance (Pollack, McGill)
- Genotypic and phenotypic studies of inflammation (Platz, Johns Hopkins)
- Oxidative damage and DNA repair (Santella, Columbia)

The goal of this program project is to study the genetic, metabolic and environmental factors associated with the risks of prostate cancer and high grade prostate cancer, to investigate the effects of these factors on the efficacy of the study agent, finasteride, and to understand the mechanisms underlying the risk-factor associations. In addition to individual project aims, there are cross-project aims to investigate the joint effects of the biologic markers. Finally, traditional and newer innovative statistical methods will be used to develop prognostic groups based on the combined results from each of the projects.

In addition to the program project (P01), the PCPT Long Term Follow-up (LTFU) protocol S0437 was activated in September 2005. This study was developed to follow the men randomized in the PCPT who were diagnosed with prostate cancer on or before December 31, 2003. The primary objective of the LTFU study is to estimate the time-to-metastasis for those in the finasteride group compared to the placebo group. Additional objectives include estimating the difference in time to secondary therapy after definitive therapy with radiotherapy or radical prostatectomy, estimating the difference in all-cause and prostate cancer mortality and the final secondary objective is to assess the predictive value of a panel of prognostic biomarkers performed on the PCPT program project (P01), on the risk of metastatic disease. This study is expected to enroll and follow participants through 2013. Nearly 2,400 men are eligible for this study. Upon enrollment, a comprehensive medical and treatment history is obtained and the men are followed twice yearly by telephone contact. Currently 90 sites have received IRB approval to enroll participants in the LTFU study. Eight of these sites have been designated as “Regional Sites” and are accepting participants from sites who are unable to participate in the study.

Role of the Statistical Center

The primary role of the Statistical Center in the PCPT and its related studies is to ensure the successful implementation of the trial design through effective study design and implementation, training and support of study site personnel, data management, data analysis and overall trial management.

The biostatisticians continue to work with study investigators to analyze the clinical and pathologic data from the PCPT as well as quality of life and adherence measures. In addition, the biostatisticians produce routine and special reports describing the status of the studies and set the priorities for Statistical Center data management activities to support statistical analyses.

The data operations staff at the Statistical Center is responsible for the review and evaluation of the data received for the PCPT and LTFU studies including the quality control activities and special projects required to support data analyses and publications. In addition to data management, the data operations staff are the sites’ primary contact and reference resource for questions related to the PCPT and LTFU studies. Annually, the data operations staff conduct
PCPT LTFU Study Workshops and provide presentations regarding updates and training to site staff at the SWOG meetings.

Throughout the course of the PCPT, the data management system used was DataFax™, an integrated image management and database system which used optical character recognition (OCR) technology. Following the closure of the PCPT, the study data were transferred into Oracle database tables and the images were converted into TIF files for long-term access and storage. This data management system integrates image management with an Oracle database and utilizes HTML forms and .net technology.

The PCPT LTFU study uses a web-based technology for nearly all tasks associated with study administration, enrollment and follow-up. The PCPT Workbench was developed specifically for this study and is located on the swog.org website. The PCPT Workbench is password-protected and site staff must be granted permission to access the website. The website is administered and maintained by the Statistical Center.
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 prostate cancer prevention trial. 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 the reduction of prostate cancer incidence, will be tested in a statistically highly powered trial design. The planned total study period is 14 years, including one year pre-study for ramp-up to accrual, five years for accrual, 7 to 12 years of treatment, and one 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 pre-specified secondary endpoints, SELECT will examine many important tertiary/ancillary endpoints, including dietary/nutrient assessments, pathology and molecular/cellular biomarkers and quality of life. Development and monitoring of the trial involve 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% African Americans) at 427 different study sites across the United States, Puerto Rico and Canada.

Role of the Statistical Center

The Statistical Center is responsible for a number of aspects of the trial, described below:

1) Study Design and Analysis

The Statistical Center developed the original trial design, evaluates and modifies the study design assumptions as needed, analyzes study data, and provides reports to the Steering Committee, its subcommittees and the Data and Safety Monitoring Committee.

2) SELECT Workbench

The SELECT Workbench is a secure internet site, 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. There is ongoing review of the effectiveness of the Workbench and updates to its content.
3) SELECT Study Manual

The Study Manual contains procedures and guidelines to augment the protocol. The Study Manual was released in November 2000 and undergoes 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 or need a refresher on study procedures.

5) Communications

The Statistical Center is available Monday through Friday 7:00 AM - 4:00 PM PT for 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. All data collection is done using Web-based transmissions. Data are reviewed by Data Operations staff and stored in a relational database. Electronic documents and digitized images of forms submitted by fax earlier in the trial 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 performed initial review of all data submitted by fax. Data Coordinators evaluate data for accuracy, completeness, consistency, and compliance with data collection requirements and follow-up procedures. Data problems requiring additional follow-up are logged into a query system into which Study Site staff enter the results of their follow-up. The results of data review and follow-up are noted in an evaluation program.

b. Data Collection Forms

The forms developed for this protocol were designed to optimize their processing and management using an electronic document management system. Although some data were initially submitted by fax, Study Sites now submit all data via the Workbench. A set of reference forms, with instructions for the completion of each form, and example source documentation are maintained on the Workbench. Confirmation of biologic specimen collection and shipment is logged into a Web-based Specimen Tracking System.

c. Routine Reports

Study Sites have the ability to access a variety of reports via the SELECT Workbench. These reports, developed and maintained by the Statistical Center, assist Study Sites to conduct timely participant follow-up, ascertain participant adherence, maintain compliance with participant contact schedules and data submission requirements, monitor Study Supplement distribution and track biologic specimens.
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 is largely event-driven and 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 (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 a 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 three years after the trial is completed.

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, the completeness of annual visit data, and attendance at required training workshops. IPR reports for all SELECT Study Centers are posted on the Workbench. Statistical Center staff, SWOG auditors, and members of the Sites at Risk Subcommittee and the Retention and Adherence Committee regularly monitor IPR data and take action if a Study Center’s performance is poor.

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 or telephone call, to be conducted by members of the Statistical Center staff and/or a CRA. The mentoring program 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 SELECT.
Statistical Applications and Research

Statistical Center faculty participate in scholarly activities that are not directly related to a specific protocol or which reflect research efforts not directly evaluating interventions. In particular, several faculty statisticians pursue statistical methods research for a fraction of their time on an R01, Statistical Methods for Clinical Studies (PI, Dr. Michael LeBlanc). The emphases currently are design and analysis strategies for Phase III trials and survival analysis (particularly graphical and other exploratory methods). Other efforts are devoted toward improving other aspects of multicenter clinical trials. Publications highlighting the breadth of Statistical Cancer research activities are listed below.

2007


2006


2005


2003


2002


2001


Leadership and Service in Cancer Research, Clinical Trials, and Statistics

Southwest Oncology Group statisticians provide leadership and expertise on the national and international level to other research and professional organizations through service that in turn enriches and strengthens the activities at the Statistical Center. Recent examples of these activities are:

Review / Advisory panels
2007 – present, Member, External Advisory Committee, Cancer Prevention Trials Unit, Cancer Research UK (J Crowley)
2007 – 2010, Member NIH Health Services Organization and Delivery Study Section (W Barlow)
2007 Reviewer, NIH, Subcommittee F - Manpower & Training (M LeBlanc)
2007 – present, Member, Symptom Management and Health-Related Quality of Life Steering Committee, National Cancer Institute Clinical Trials Restructuring Initiatives (J Moinpour)
2006 Member, VA cooperative Studies Program (J Crowley)
2006 – present, Member, International Myeloma Foundation Scientific Advisory Board (J Crowley)
2006 – present, Member, NCI Subcommittee H, Cooperative Groups (J Benedetti)
2006 – 2010, Member, Advisory Board, FHCRC Survivorship Center, Lance Armstrong Foundation Network of Survivorship Center (J Moinpour)
2006 Member, Cardiovascular Strategic Planning Level 1, Clinical Trial Design, NHLBI (G Anderson)
2006 – 2009 Member, International Society for Quality of Life Board of Directors (J Moinpour)
2006 Chair, Quality of Life Science Advisory Committee, American Cancer Society (J Moinpour)
2006 Member, External Advisory Board, MD Anderson Community Clinical Oncology Program Research Base (J Moinpour)
2005 Member, Subcommittee on Acute Leukemia in the Elderly, ASH/FDA Workshop on Endpoints in Hematologic Malignancies (K Kopecky)
2005 Member, International Agency for Research on Cancer (IARC) Working Group on Oestrogen-progestogen Replacement Therapy and Combined Oral Contraceptives (G Anderson)
2004 Reviewer, NCI Subcommittee D, Clinical Studies (PY Liu)
2004 Member, Institute of Medicine Committee on the Review of National Immunization Program’s Research Procedures and Data Sharing Program (G Anderson)
2003 Member CDC Ovarian Cancer Workshop Expert Panel (G Anderson)
2002 NCI Special Emphasis Panel, SPORES in Gynecologic Cancers (G Anderson)
2001 – present, Member, University of California at Davis Cancer Center External Advisory Committee (J Crowley)
2001 Member, International Working Group to Standardize Response Criteria in AML (K Kopecky)
2000 – present, Member, NexCura Medical Advisory Board (J Crowley)
2000 – present, Member, Clinical Significance Consensus Meeting Group, Assessing Clinical Significance for Oncology QOL Assessment (J Moinpour)
2000 – present, Member, Cancer Outcomes Measurement Working Group, Outcomes Research Branch, Division of Cancer Control and Population Sciences, National Cancer Institute, December (J Moinpour)
NCI Service:
2004 – present, Member, Breast Cancer Intergroup Committee (W Barlow)
2004 – present, Member, Breast Cancer Intergroup Translational Medicine Committee (W Barlow)
2006 – present, Member, Breast Cancer Datamart Committee (W Barlow)
Alternate Statistical Member, Gastrointestinal Steering Committee (J Benedetti)
Member, Gastrointestinal Task Forces (Colon and Neuroendocrine) (J Benedetti)
2006 – present, Member, Group Banking Committee Steering Committee (and Information Technology Subcommittee) (K Kopecky)
2002 Member, Common Data Elements Committee – Lymphoma (K Kopecky)
2001 – 2002, Member, Common Data Elements Committee – Leukemia Pathology (K Kopecky)
2001 – 2002, Member, Common Data Elements Committee – Pediatric Leukemia (K Kopecky)
2001 – 2002, Gynecologic Cancer Progress Review Group (G Anderson)
2000 – 2002, Chair, Common Data Elements Committee – Leukemia (K Kopecky)

Data and Safety Monitoring Committees
2007 – present, Effects of Aspirin in Gestation and Reproduction (G Anderson)
2006 – present, Member, Independent Data Monitoring Committee for MD Anderson Cancer Center (M LeBlanc)
2006 – present, Early Detection Research Network, Validation of Serum Markers for the Early Detection of Hepatocellular Carcinoma (DCP) (J Benedetti)
2006 A Phase III Multicenter Study of Valganciclovir for the Prevention of Late Cytomegalovirus Infection after Bone Marrow Transplantation (J Benedetti)
2005 – present, Member Southwest Oncology Group DSMC (C Tangen)
2004 – 2007, Member, DSMC for study Pharmion AZA PH GL 2003 CL 001 (K Kopecky)
2002 – present, Member, DSMB for Trials to Address Disparities in Children’s Oral Health, School of Dentistry, UCSF (C Tangen)
1999 – 2004, American College of Surgeons Oncology Group (PY Liu)
Chair, DSMB, Ethiopia Trachoma Monitoring Study (NEI) (W Barlow)
2005 – present, Member, Multicenter Uveitis Steroid Treatment Trial (NEI) (W Barlow)

Professional Societies
2006 – 2008, Member, ASCO Education Committee (J Crowley)
2006 – present, Statistical Editor, Journal of Thoracic Oncology (J Crowley)
2006 – present, Member AJCC Committee to Develop Version 7 Coding Guidelines (and Associated Task Forces) (J Benedetti)
2006 – present, Member Program for Assessment of Clinical Cancer Tests Strategy Group (J Benedetti)
2006 – present, Secretary/Correspondent, Western North American Region of the Biometrics Society (A Hoering)
2005 – 2007, Member, Scientific Program Committee of the American Society of Clinical Oncology (M LeBlanc)
2005 – 2006, Member, ASCO Program Committee (C Tangen)
2005 – 2006, Society for Clinical Trials Working Group on Data Monitoring (C Tangen)
2005 Member, Subcommittee on Acute Leukemia in the Elderly, ASH/FDA Workshop on Endpoints in Hematologic Malignancies (K Kopecky)
2004 – 2010, Associate Editor, Quality of Life Research (C Moinpour)
2002 Member, 3rd International Consultation on Prostate Cancer New Treatment Modalities (C Tangen)
2001 – 2007, Member, American Urologic Association Local Prostate Cancer Treatment Guidelines Panel (C Tangen)

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2006 – present, Member, Statistical and Lymphoma Committee, American Joint Committee on Cancer, American Cancer Society and American College of Surgeons (M LeBlanc)
2004 – present, Treasurer, Western North American Region (WNAR) of the International Biometric Society (K Kopecky)
Literature Cited


