Chapter 2 |

History of Statistical and Data Center



John A. Blessing, PhD, Mark Brady, PhD and Virginia Filiaci, PhD

Overview

When the Gynecologic Oncology Group (GOG) was formed and funded in 1970, its first Chairman, Dr. Myron Hreshchyshyn, established the Statistical Office at Roswell Park Memorial Institute due to its proximity to his office at Buffalo General Hospital in Buffalo, New York. The office was located within the Department of Statistics and was headed by Dr. Nelson Slack. In May 1974, Dr. George Lewis, of Thomas Jefferson University, was elected to serve as the second Group Chairman, effective in July 1975. In September 1974, in anticipation of the relocation of the Statistical Office to Philadelphia, Pennsylvania, upon Dr. Lewis' Chairmanship, Dr. Slack was assigned to different responsibilities, and Dr. John Blessing was hired to "run out the clock" for the next nine months. Due to fortuitous circumstances, Dr. Blessing successfully maintained the Statistical Office at Roswell Park. Since then, the GOG, its Statistical Office (namedthe GOG Statistical and Data Center [SDC]), and Roswell Park (now named Roswell Park Comprehensive Cancer Center) have undergone dramatic changes. In 2011, the GOG agreed to integrate with two other successful National Cancer Institute (NCI) sponsored cooperative groups; the National Surgical Adjuvant Breast and Bowel Project (NSABP) and the Radiation Therapy Oncology Group (RTOG). The new entity, called NRG Oncology, is now a successful component of the NCI National Clinical Trials Network (NCTN). The GOG SDC likewise united with the corresponding NSABP and RTOG statistical and data management centers to form the NRG Oncology Statistical and Data Management Center (SDMC). The SDMC is fully integrated yet distributed across three sites. The Roswell Park component continues to focus on NRG Oncology gynecologic investigations and its dedicated and talented SDC staff remains there. This chapter will attempt to describe the growth, function, and unique innovations of this office. A timeline that underscores significant GOG/SDMC milestones of progress is outlined at the end of this chapter.

The Early Years: 1970-1974

It is important to briefly review the early years of the GOG Statistical Office's existence in order to have a baseline to measure its progress in scope, procedures and responsibilities. In September 1974, there were 21 activated protocols. Data were being submitted, but there were no quality control measures in place. Patient entry took place via sealed envelopes that were maintained in the individual member institutions. All protocols had what was referred to as "source data" coded on one IBM punch card per patient. Most submitted data were merely being filed with very few protocols having any computerized clinical data for analysis. There were pathology and radiotherapy "repositories" maintained in the Group Chairman's office, however there were no eligibility or evaluation measures in place. There were no formal Statistical Reports prepared for semi-annual GOG Meetings; rather there were type-written summaries distributed for selected studies. The staff consisted of Dr. Slack, one programmer, one secretary, one data entry clerk and one clinical data coordinator.

The Lewis Years: 1975-1989

During this period the GOG Statistical Office began to evolve into a viable, interactive participant in all areas of GOG activity. A philosophy of collaboration was initiated, which remains a cornerstone of its success. New initiatives included the creation of the GOG Statistical Report,

which has subsequently been prepared for each GOG Semi-Annual Meeting, the participation in the formation of the GOG Protocol Committee and the development of the corresponding Protocol Procedures Manual. To further enhance scientific interaction, there was a system of Study Chair reviews implemented that featured a team approach to study conduct involving the Study Chair, Statistician, and Clinical Data Coordinator. The Statistical Office enhanced their experience in the investigation of gynecologic malignancies and their ability to make contributions to study design correspondingly increased. As the Statistical Office staff expanded, noteworthy advances in data management, quality control and analytic techniques were evident. Moreover, Dr. Lewis' belief in involving the Statistical Office in all facets of GOG activity enabled its members to make contributions beyond the statistical arena. Finally, during this period, there was a great emphasis placed on modality review and quality control, greatly improving institutional performance, which in turn resulted in dramatic improvement in the quality of submitted data. This section will chronicle these advances.

In May 1974, Dr. Hreshchyshyn hired Ms. Frances Valvo to serve as the first administrative employee to work in the Group Chairman's office. She had previously served as the Group Administrator for the Acute Leukemia Group B (ALGB), the forerunner of today's CALGB, whose Statistical Office had been located at RPMI until May 1974. Coincidently, Dr. Blessing and the Data Entry Clerk had also worked at ALGB. These three individuals attempted to create a GOG Statistical Report for the January 1975 GOG Meeting, using a format modified from their prior experience. Thus, with collegial support from their former ALGB colleagues, the first GOG Statistical Report was prepared.

The next year, GOG Protocol 15, chaired by Dr. George Omura, was approaching maturity. Dr. Omura agreed to collaborate in an attempt to have the Study Chair review the analytical data for each case prior to analysis. A prototype form, called an EVL, to be used for Study Chair review of data as it existed in the computer was developed. Dr. Omura's review enabled questions to be posed to him by the Clinical Data Coordinator, enabled him to raise questions that required follow-up, and provided a record of his review in the patient chart. This review was considered highly successful and innovative. As a result, it was prospectively employed for the next series of studies developed (Protocols 22, 23, 24, and 25.) For these studies, a team consisting of the Study Chair, Statistician, and Clinical Data Coordinator collaborated to determine the "protocol-specific" data which should be prospectively captured and computerized. The success of this expanded use of the Study Chair review provided the rationale for its continued routine use. This process has been modified slightly over the years, but it remains the cornerstone of the GOG quality control review process. In addition to the critical interaction among the collaborating team, it provides an integral component of GOG quality control. It also gives the Study Chair confidence in the data which he or she must ultimately publish.

When Dr. George Lewis became Group Chairman in 1975, he took several steps that had a dramatic impact on the GOG Statistical Office, and the Group as a whole. The first of these was reorganization of the study development process. Prior to 1975, studies were developed during the GOG Semi-Annual Meeting sessions that included all attendees. The discussions were long, and the process was cumbersome. Dr. Lewis named Dr. Tate Thigpen as Chairman of a reorganized version of the GOG Protocol Committee. The Committee composition was structured to include the Chairperson of both Site and Modality Committees to facilitate interaction among the various entities that contributed to sound study design. Equally important was the inclusion of Dr. Blessing as a voting member. Dr. Thigpen had developed a strong working relationship with the Statistical Office, and had an appreciation of the importance of involving it in study development from inception of a concept.

In order to create a set of guidelines for Protocol conduct, Drs. Thigpen and Blessing drafted a Protocol Procedures Manual, which provided timeframes for study development, content, execution, and authorship. This document was then presented to the Protocol Committee, modified, and then adopted. Over the ensuing years, the manual has been further modified and adapted to correspond to the evolution of GOG. The important developments have been formalized and incorporated as part of GOG requirements. For example, early involvement by the Statistical Office to determine feasibility and design issues is mandated. Also, Study Chair review of cases is an expectation for Study Chairs of all prospective studies.

The intimate involvement in the protocol development process mandated by the Protocol Procedures Manual fostered the blending of medical and statistical considerations. Greater familiarity with the medical nuances enabled the Statistical Office to make innovative contributions. The first example involved development of Phase II trials procedures. In 1976, the GOG decided to conduct Phase II trials in six recurrent disease categories: epithelial ovarian carcinoma, squamous cell carcinoma

of the cervix, non-squamous carcinoma of the cervix, adenocarcinoma of the endometrium, mixed mesodermal sarcomas of the uterus, and leiomyosarcoma of the uterus. Each of these disease entities had varying rates of accrual. Additionally, numerous agents were envisioned to be investigated in each category. There was concern that the process was about to become cumbersome to a Group with very limited resources.

Drs. Blessing and Thigpen collaborated to develop a Master Protocol (Protocol 26) that would contain all the required components - other than drug-specific sections - in a standardized format. This would enable rapid development of a specific drug investigation by using the Master Protocol template and incorporating individualized supplementary drug sections. Protocol 26-A (the Master Protocol) contained the generic sections, while the specific drug section being investigated was detailed in a separate protocol. For example, the first drug studied (piperidinedione) was assigned Protocol 26-B, the second (cisplatin) was Protocol 26-C, etc. An investigation into each of the six recurrent disease categories was initiated on Protocol 26-B simultaneously. Accrual was monitored within the Statistical Office for adherence to study design and attainment of targeted accrual goals. At the end of each month, the Statistical Office contacted the Chair of the Developmental Therapeutics Committee to determine the appropriateness of continuing or ceasing accrual for each sub study. If the decision was to cease accrual to a particular sub-study, a replacement investigation would be initiated in the next drug scheduled for study. During the tenure of Protocol 26, 116 studies were conducted involving a total of 34 agents, underscoring the dramatic efficiency of this innovative approach. This is an early predecessor to the contemporary platform or basket trial designs.

Subsequent development of phase II studies further refined the process. In 1994, the single Master Protocol was replaced by individual disease specific protocol queues which facilitate the sequential study of various agents within each targeted disease. In 1996, two-stage sampling designs were incorporated to permit early cessation of accrual for ineffective regimens while protecting Type I and II error probabilities. Other advances included separate development of studies for cytotoxic or cytostatic agents, and for studies with prior treatment or no prior treatment requirements. The underlying principles of successive development and conduct of Phase II trials within individual areas of investigation, close monitoring of accrual, and interaction with the Developmental Therapeutics Committee Chairman continue to this day.

A second example of contribution to design is seen in squamous cell carcinoma of the cervix. An early Phase II trial of cisplatin (the aforementioned Protocol 26-C) in this population resulted in encouraging response rates. As a result, successive Phase III trials of this agent were undertaken (Protocols 43 and 64). Although the response rates observed in these studies failed to reach expectations, most investigators felt that cisplatin should be the first chemotherapeutic attempt. During a semi-annual GOG Meeting, Dr. Blessing met with a group of investigators and suggested that since cisplatin was not the panacea hoped for, perhaps a subgroup of investigators could be identified who would not feel ethically bound to utilize cisplatin and would participate in front-line Phase II investigations of new agents. As a result, Protocol 76 (a series of drug investigations in the treatment of squamous cell carcinoma of the cervix in patients who had not received prior chemotherapy) was developed. The participants were limited to a selected group of GOG members who would participate in this study, rather than the Phase III study in the same population. Of the first twenty investigations completed to date, seven yielded results that were utilized in the development of subsequent Phase III studies, emphasizing the importance of this contribution.

In concert with these progressive innovations, the staff of the GOG Statistical Office, under the direction of Dr. Blessing, gradually began to grow. Ms. Valvo transferred to the Statistical Office in 1975 when Dr. Hreshchyshyn's term as Group Chairman ended. She focused on administrative aspects; initially providing an overall sense of organization and preparing the expanding GOG Statistical Reports for each Group Meeting. However, she also assumed responsibility for manuscript development; one of the unique responsibilities assigned to the Statistical Office.

As early protocols matured and the phase II program was initiated, this aspect became of critical importance. Centralization of this process in the Statistical Office ensured that data were sufficiently mature to warrant analysis and that proper statistical input and interpretation would be inherent in all Group presentations. The Protocol Procedures Manual outlined the steps for manuscript development and the Statistical Office was charged with ensuring that they were implemented.

At the same time, Ms. Bette Stonebraker was employed part-time to participate in the development of a computer-based system for preparing randomization/patient entry systems. Phone randomization replaced the antiquated system of institutional envelopes (Today, all pa-

tient entry is accomplished via the web). During this project, she became familiar with many aspects of GOG activity. She eventually became a full-time employee, assumed the role of Clinical Data Coordinator for all ovarian protocols, helped form the GOG Data Management Subcommittee, and became a member of the Protocol Committee (she later served as Director of Data Management in the restructured GOG Statistical and Data Center).

The evolving GOG Statistical Office philosophy was one based upon scientific interaction involving the entire staff. Interaction between Statistician and Study Chair was essential in designing studies. However, the inclusion of the Clinical Data Coordinator in the team greatly enhanced this professional role within the Group. Study Chair review in the Statistical Office served to enhance the perception of a dedicated staff, committed to GOG research.

It was during this period that several advances in data management occurred. As noted earlier, modality review was non-existent in the first years of the Group's existence. Resolving this deficiency was another of Dr. Lewis' priorities when he became Group Chairman. Due to the backlog of data facing the Statistical Office in 1975, Dr. Lewis placed the responsibility for modality review in the Group Chairman's office in Philadelphia to enable more resources to be quickly applied to these dual challenges. It was determined that all patients entered on GOG studies would have a central review of submitted slides by the GOG Pathology Committee. Likewise, the Gynecologic Oncology Committee would review the surgical aspects for all patients for whom such a review was applicable via submitted operation reports. The Radiation Oncology Committee was charged with reviewing the submitted films, reports, and materials for all atients receiving radiotherapy on GOG studies. Finally, the chemotherapeutic aspects, as well as overall case evaluation, would be accomplished via the evolving system of Study Chair EVL reviews. The individual modality reviews were conducted in the Group Chairman's office, while the Study Chair reviews were the responsibility of the Statistical Office. In 1990, responsibility for all modality review shifted back to the Statistical Office. However, Dr. Lewis' vision in temporarily locating this function in Philadelphia was critical in enabling the GOG to simultaneously address two enormous challenges.

As the initial results of modality review became available, less than optimal eligibility rates in the 80% range were noted, prompting the need to develop measures to increase institutional compliance. To address this issue, the GOG created a Fast Fact Sheet for each protocol consisting of a series of eligibility questions tailored to that study's eligibility criteria. The eligibility questions are asked at entry (via phone or web) to screen prospective patient entries for eligibility. This step has had a pronounced effect; GOG eligibility rates consistently exceed 95%.

Until 1978, Dr. Blessing was the sole statistical resource for GOG. Then in July 1978, Mr. Brian Bundy joined the Statistical Office as a Master's level statistician. Initially, he was assigned two ovarian studies (Protocol 25 and 52) started by Dr. Blessing, and several phase II studies. As Mr. Bundy became familiar with GOG procedures and enhanced his statistical abilities, he was assigned responsibilities for most cervical studies and select ovarian and endometrial studies. He was added to the Cervix and Protocol Committees and became a key asset. In 1987, he obtained his Ph.D. degree. Dr. Bundy continued to work with the GOG, until his departure in 2006. Ms. Barbara Saczynski was hired as a Clinical Data Coordinator for cervical studies in 1978.

In 1982, statisticians at RPMI availed themselves of evolving computer technology and created a generalized database management system called Roswell Park Management Information System or (RPMIS). To verify its utility, it was essential that RPMIS be tested using actual data examples. The Statistical Office collaborated with RPMI in the conduct of a time study which compared the use of RPMIS versus traditional IBM punch cards in the data management of two simultaneous phase II studies. The published results demonstrated the value of RPMIS and led to the conversion of all GOG protocol databases to RPMIS on the Univac 90/80 mainframe computer. A subsequent paper in 1987 documented further successful experience with this system.

Another unique responsibility of the Statistical Office was initiated when the National Cancer Institute (NCI) mandated a program of quality assurance audits to be enacted by each cooperative group in 1983. This program required each participating institution to be visited at least once every three years to verify the accuracy and validity of submitted data via medical source documents; review compliance with regulatory aspects, including IRB processes and informed consent content; and examine drug accountability and security at those sites employing investigational agents. Unlike other groups, the GOG centralized this function within its Statistical Office, since this was the location of the submitted data to be audited (Many other Cooperative Groups have their data management component geographically separate from the

statistical component). This structure has provided many benefits. Of particular note is that this arrangement provides a viable method of incorporating corrections noted during audits into the database. Additionally, the GOG strongly believes that the audit process provides a unique educational opportunity. The interchange has been a two-way proposition; by examining the most frequently occurring errors and misconceptions, the Statistical Office has been able to provide education, protocol clarification and dose calculation tools. This process enhanced the growing portfolio of quality control measures.

In 1986, Mr. Mark Brady joined the Statistical Office as a statistician. Mr. Brady had prior clinical trials experience and was quickly assigned to several ongoing studies. In a short period of time, he was able to assume responsibility for GOG studies in ovarian carcinoma and make valuable contributions. He obtained his PhD in 1999. As will be seen later, he served as Director of Statistics in the restructured GOG Statistical and Data Center.

Due to continuing workload growth, the acquisition of additional data management resources was essential. Accordingly, two individuals were promoted from within the organization, based upon their demonstrated growth in entry level positions. In 1987, Ms. Angie Saxer was promoted to Clinical Data Coordinator for endometrial studies. In 1986, Ms. Patricia Brehm was promoted to Clinical Data Coordinator for Phase II studies, and subsequently in 2000 assumed that role for endometrial studies upon Ms. Saxer's departure. Each of these actions was based upon the ability of these individuals to accurately process a large volume of data, interact with investigators and representatives of member institutions, and represent the GOG in a professional manner. The ability of Statistical Office staff to understand the nuances of varied aspects of GOG activities and mechanisms has always fostered the ability to grow within the organization. This in turn has tended to promote a high level of dedication and longevity of staff. In keeping with the Statistical Office philosophy of inclusion, the Clinical Data Coordinators became members of the relevant disease committees, which further enhanced their ability to participate in GOG science.

During this period, several analytic advances occurred. In 1984, procedures were developed for designing studies with a time-to-failure endpoint, which estimated the time required for study maturity and completion. Also, experimentation was initiated with the use of personal desktop computers in study development and management. The following year RPMI statisticians developed the FREND procedure for calculating Kaplan-Meier estimates and performing proportional hazards modeling in SPSS. Additionally, in 1989 the Statistical Office began using commercial software on PC's including SAS, SPSS and BMDP for statistical analyses. A Novell local area network (10 MB/sec) was established to permit intra-office file, printer and software sharing. Since an electronic infrastructure was not available, establishing the intra-office network required the statistical office staff to physically run wires and modify their own computers.

From the outset, Dr. Lewis recognized the importance of involving the Statistical Office in all aspects of Group activity, both scientific and administrative. Accordingly, Dr. Blessing was named as a member of the Executive, Protocol and Membership Committees. This policy continued as the Statistical Office expanded its staff and as the Group broadened its scope. This allowed Statistical Office staff to make significant contributions and enabled new initiatives to be fully incorporated into the GOG structure.

One example is the evaluation of member institutions by the GOG Membership Committee. Initially, the performance of member institutions was primarily gauged by their accrual. As quality control measures evolved, patient eligibility monitoring was incorporated. It was no longer sufficient to enroll cases, it was important that they be eligible as well. Accordingly, the Statistical Office was able to provide critical data to the GOG Membership Committee regarding institutional eligibility rates and timeliness of data submission for its use in evaluating member performance. Also, a program of Data Assistance Reviews was initiated to enhance the educational component of this evaluation. At the discretion of the Membership Committee, the GOG Statistical Office would organize and conduct an onsite review of an institution to address problem areas. At least one representative of another institution with demonstrated proficiency in the problem area would participate in an effort to interact with investigators to develop procedures to avoid such problems in the future. This notion of an initial attempt to address and correct deficiencies before any punitive action was taken became an integral part of GOG philosophy.

A second example of the important Group-wide role of the Statistical Office was seen in the development of GOG's innovative "per capita" reimbursement system in 1988. In this instance, the Statistical and Administrative Offices collaborated to poll all members for fiscal data that was then used to determine the average cost per patient across the entire Group. This simple, yet comprehensive formulation served as the rationale that

supported the sole request made by NCI for all institutional funding. Therefore, it was extremely important that this presentation be supported by data and be logically convincing. As a result of the adoption of per capita reimbursement, institutions were no longer required to prepare grant applications to participate, and the GOG was no longer burdened with review of these grant applications. The success of this mechanism of funding has led to its continued use for 25 years.

During Dr. Lewis' tenure as Group Chairman, the GOG Statistical Office staff grew in number, expertise and responsibility. It developed an underlying philosophy of total involvement and commitment, and it contributed greatly to the GOG's emergence from a Group with potential to be one of the premier cooperative groups.

The Park Years: 1989-2002

By the time Dr. Robert Park became Group Chairman in 1989, the GOG Statistical Office had assembled a staff of talented individuals who possessed significant expertise and experience in clinical trials research in gynecologic cancer. The Statisticians and Clinical Data Coordinators had been involved for many years and were well-integrated into all facets of GOG activities. During Dr. Park's tenure, previous modality and quality control initiatives were enhanced, a formalized Quality Assurance Audit Committee was created, and a focus on medical ethics emerged. The GOG expanded its clinical trials emphasis to include basic science, quality of life, and cancer prevention and control research. To support these endeavors, the GOG Statistical Office expanded its expertise via a consulting component to address these areas. Based upon the growth and expansion of both staff and responsibilities, the GOG Statistical Office was formally reorganized. The resulting GOG Statistical and Data Center (SDC) featured continued excellence in statistics and data management and fostered the development of strong translational research and information technology components. The latter component emerged to provide state-of-the-art technologic advances not only to the SDC, but also to the entire GOG. This section expounds upon these significant accomplishments.

GOG quality control mechanisms continued to grow and, in 1990, further refinement of data timeliness was addressed. To this point, the Statistical Office had monitored data timeliness via a Delinquency List provided to member institutions. This list provided a catalog of all forms and materials that were overdue. While this was a valuable aid in the retrospective effort to retrieve missing data, it was not preventive. Accordingly, a Forms Due List was developed to supplement the Delinquency List. This led to an improvement in data submission timeliness since the proactive informing institutions of upcoming form submission deadlines enhanced their ability to avoid delinquencies. This is but one example of the Statistical Office philosophy of working with participants to determine their needs and be responsive to them.

As previously mentioned, responsibility for all modality review was transferred from the Group Chairman's office to the Statistical Office in 1990. Prior to that time, the responsibility for all modality review had been vested in one staff member in the Group Chairman's office. To expedite the processing of results and enhance the scientific involvement, the Statistical Office subdivided modality review responsibilities among three Clinical Data Coordinators. Each assumed the added responsibility for the modality review, which was most relevant to her experience. Surgical review conducted by the Gynecologic Oncology Committee was assigned to Ms. Stonebraker, who had been the Clinical Data Coordinator for several surgical staging protocols. Ms. Saczynski, who was the Clinical Data Coordinator for all cervical studies, was assigned responsibility for review of radio therapy due to its obvious connection in that disease site. Pathology review was ultimately assigned to Ms. Janis Barnes.

There continued to be important additions to the GOG Statistical Office staff in the early 1990's. Based upon the growth in protocols investigating epithelial ovarian cancer, Ms. Suzanne Baskerville was added to the Data Management staff as a Clinical Research Coordinator. As a result of a dramatic increase in computer-related activities, Mr. Joe Jelonek joined Ms. Karen Puehn to provide programming support. Ms. Laura Porter was hired to perform data entry functions due to an ever-increasing volume of data. She later assumed the role of Forms Tracking Coordinator as GOG quality control measures were expanded. Ms. Amy Speaker was hired in a clerical role and was subsequently assigned responsibility for overseeing the randomization/patient registration process and assisted with quality-of-life data. She later assisted Ms. Barnes and assumed the responsibility for GOG pathology review upon Ms. Barnes retirement in 2008. Ms. Kathy Ker was employed to process radiotherapy materials. Subsequently, she assumed the role of Administrative Assistant upon Ms. Valvo's retirement. Her responsibilities included preparation of grants and semi-annual GOG Statistical Reports. She excelled in this capacity until her untimely death in 2002.

Based upon its continued growth, in 1991 the GOG Statistical Office, having grown from the initial five to 18 staff members, was formally recognized as an independent

department within RPMI, with Dr. Blessing as its Department Chairman. This recognition by RPMI was indicative of the level of respect accorded to this group based upon their demonstrated accomplishments. Commensurate with the resulting increased administrative responsibilities, Ms. Mary Ann Kuczmarski, Administrative Assistant, was hired to support these functions.

In 1992, Dr. Park requested that the Statistical Office form a Quality of Life (QoL) working group. Ms. Karen Iseminger was hired as a Cancer Research Scientist with a focus on QoL and quality assurance audits. She and Dr. Brady were original members of the GOG Quality of Life Committee when GOG formalized that area of research in 1993. Subsequently, she received a PhD in Medical Ethics and was named to the GOG Protocol Committee as a medical ethicist. Her unique perspective has enabled her to participate in many areas of GOG activity such as the GOG Data Monitoring Committee, Data Safety Monitoring Board, and Human Research Committee. In 1994, Ms. Virginia Filiaci assumed the role of statistician for GOG studies in endometrial carcinoma and uterine sarcoma. She quickly adapted to that role and became a member of both the Corpus and Protocol Committees. In 2010, she obtained her PhD and Dr. Filiaci was named Associate Director of the SDC Biostatistics and Science Division.

Since the inception of the NCI-mandated Quality Assurance Audit Program in 1983, all aspects of this function were centralized in the Statistical Office. In 1992, Dr. Park formalized this process by forming a Quality Assurance Audit Committee. In recognition of their inherent role in managing this process, three members of the Statistical Office were named to this four-person committee. Their participation in on-site reviews, coupled with their familiarity with GOG data management requirements, enhanced quality control, and simultaneously provided on-site educational opportunities for institutional staff. In 1994, Dr. Blessing collaborated with members of the newly formed NCI Clinical Trials Monitoring Branch (CTMB) in the development of Common Cooperative Group Guidelines for quality assurance audits and the Statistical Office helped pilot the interactive programs developed for scheduling and reporting. The uniformity of evaluation inherent in the Quality Assurance Audit Committee review of all audits enabled the GOG Membership Committee to incorporate the results of audits into its criteria for evaluating parent institutions. Due to the continued expansion of the GOG parent institutions, affiliates, and CCOP's,

Ms. Carol Mullins was named Quality Assurance Audit Assistant within the Administrative Division of the Statistical Office, with responsibility for the interactive scheduling of audits and preparation of reports. She served in that capacity until her departure in January 2013. Additionally, the Statistical Office initiated periodic workshops to provide audit training, education, and improve performance.

The breadth of GOG science and the corresponding responsibilities of the GOG Statistical Office changed markedly in 1993. Quality of life research was added to the GOG research portfolio and a Tumor Biology and Applied Science Committee was formed to develop translational research studies. In 1995, the Cancer Prevention and Control Committee was created to undertake research in these emerging scientific areas. Each of these initiatives individually constituted a significant challenge. Moreover, the combined effect of the three endeavors was a monumental undertaking. Accordingly, the GOG Statistical Office initiated a program of obtaining the services of consultant statisticians to provide expertise in each area. Dr. Richard Kryscio, Chairman of the Biostatistics Consulting Lab at the University of Kentucky, agreed to participate in translational research, bringing noteworthy expertise in applying translational research to gynecologic oncology investigations. Dr. Howard Thaler, of Memorial Sloan-Kettering, joined as a researcher in quality of life; he too had considerable experience with the investigation of quality of life in gynecologic malignancies. Dr. Roger Priore, former Chairman of Biomathematics at Roswell Park and member of the Department of Social and Preventive Medicine at the University of Buffalo, agreed to participate in the epidemiologic studies being developed by the Cancer Prevention and Control Committee. Each of these talented professionals provided a significant time commitment to GOG, attended GOG meetings, and served on relevant committees. They helped develop funding applications, participated in protocol design, and co-authored GOG manuscripts.

As the Group approached its 30th Anniversary in 1999, Drs. Park and Blessing discussed the nature of the GOG Statistical Office and reached two conclusions that have had significant positive implications. First, it was decided that the name of the office implied a much more limited scope of responsibility than the office bore. Unlike the statistical centers for most cooperative groups, the GOG Statistical Office also had responsibilities for all aspects of data collection and processing, information technology, quality control, publications, quality assurance audits, etc. Consequently, it was decided to rename the office as the GOG Statistical and Data Center (SDC) to

better reflect these responsibilities. Secondly, the increase in staff size, responsibilities and complexity warranted a more formalized office structure that would continue under Dr. Blessing's overall leadership, but create three divisions (Statistics, Data Management, and Information Technology) with individual Directors and Associate Directors (where appropriate). Initially, Dr. Eugene Sobel was named Director of Statistics and Dr. Brady served as Associate Director. Dr. Brady assumed the role of Director in 2003 upon Dr. Sobel's resignation. Ms. Bette Stonebraker was named Director of Data Management, formalizing a role she had played for many years. Mr. William Elgie was hired to serve as Director of Information Technology (IT) in 2000; he had considerable cooperative group experience that would prove vital in establishing an IT division.

Under this reorganization, Dr. Blessing continued to have overall responsibility for the SDC, but delegated individual leadership roles to the Directors. Moreover, Dr. Blessing and these individuals developed a series of meetings to enable all to have a voice in charting direction and focus. This format has fostered increased organization and provided a critical forum to allow joint decisions to be made on issues with implications for multiple divisions.

In 2000, Kathleen Darcy, PhD, accepted a position in the SDC and her expertise in translational research quickly led to her reclassification as a Translational Research Scientist, supporting the GOG's increased effort in basic science research. Shortly thereafter, Dr. Zoe Miner joined Dr. Darcy in this effort. As a result, the expertise and resources dedicated to translational research available within the SDC increased substantially. Both Drs. Darcy and Miner became members of the GOG Committee on Experimental Medicine (CEM) and played integral roles in the incorporation of translational research components into clinical studies, as well as in enhancing the SDC interaction with the GOG Tissue Bank in the procurement and tracking of biologic specimens.

The GOG continued to enjoy significant growth. During the period between 1999 and 2003, accrual grew by 43%, and Phase III accrual grew by 49 percent. Additionally, GOG protocols grew in complexity with the advent of translational research, quality of life, and cancer prevention and control components. Accordingly, it became essential for the Statistics Division of the SDC to acquire new staff. Dr. Michael Sill brought his expertise to the growing portfolio of Phase II studies involving cytostatic agents. Ms. Marion Piedmonte and Mr. Jim Kauderer were hired to provide statistical support for studies funded by the Cancer Control grant. Ms. Helen Huang was employed to specialize in quality-of-life investigations while Mr. Chunqiao Tian, and later Mr. Jim Java, came onboard to focus on ancillary data projects. Mr. Shamshad Ali has assumed responsibility for GOG cervical studies. All became acclimated to GOG procedures in a remarkably short period of time and complemented the longstanding experience of existing scientists.

Likewise, this period saw a comparable expansion in the Data Management Division. Corresponding to the growth in patient accrual, the volume of submitted case report forms grew by 68 percent. Coupled with the increased complexity of protocols, this created the need to hire additional Clinical Data Coordinators. Ms. Sandra Dascomb was assigned responsibility for the management of Phase II study data, Ms. Linda Gedeon for a large-scale Cancer Prevention and Control study, and Ms. Angela Vazquez for cervical studies. Case report form processing, data entry, clerical, and receptionist functions were performed by a talented group which included Ms. Rachelle Dutka and Ms. Lois Newman.

The creation of the IT division initiated a dramatic growth in technologic capabilities. Prior to 1999, the GOG had been well-served by two excellent programmers, Mr. Jelonek and Ms. Puehn. However, their primary responsibilities had been to accomplish the required programming needs of the Statistical Office. They spearheaded the progression from the original use of punch cards to the development of individual computer terminals, the incorporation of statistical packages, etc. In 1990, for example, Mr. Jelonek completed all required programming to allow the GOG to create a dedicated computer facility and become independent from the Roswell Park computer system. However, due to the limited staff, the programmers had been put in the position of reacting to requests that were based upon current needs.

Within six months of the IT division's inception, its staff had grown to include Mr. Michael Calanan, a Systems Analyst, and Mr. Scott Gould, a Network and Systems Analyst, in addition to Mr. Elgie, Mr. Jelonek and Ms. Puehn. The following year, Mr. Edward Kopek, a User Support Specialist, and Ms. Florence Vecchione, a Technical Writer, were added to the team. Shortly thereafter, Mr. Quang Le and Ms. Susan Klier came on board as Programmer/Analysts, after successfully completing IT internships within the SDC.

The IT staff was positioned to fully participate in GOG activities, not merely respond to requests. Moreover, through their inclusion in SDC leadership, the IT division

had the opportunity to participate more fully in GOG activities and offer prospective suggestions for computer-related advances. In 2001, all SDC IT members were named to the Medical Informatics Committee and in 2003, Mr. Elgie was named Co-Chairman. A commitment was made to have IT staff attend GOG Meetings. This change has enabled them to staff a Resource Room at all meetings that offers wireless internet access in all meeting rooms, provide access to workstations, offer one-on-one technical advice and present training sessions on new GOG IT initiatives. Within a brief period, the dedicated GOG computer system was completely overhauled and expanded to foster future growth and an emergency back-up system was implemented.

Prior to 2001, the GOG had a significant presence on the internet. Dr. Michael Bookman had secured industry support to establish a website for the Administrative Office. In 2001, the SDC in collaboration with Dr. Bookman, fostered electronic communication for the entire GOG via the establishment of a user-friendly, interactive web site. These endeavors resulted in the creation of an SDC website which offers a variety of reporting and data submission tools to assist staff at participating institutions in their day-to-day activities.

In 2001, with annual accrual exceeding 3,000 patients, the SDC began to replace the antiquated phone/fax-based patient registration system with a web-based patient registration/randomization system that is heavily utilized by the GOG to enroll patients. Initially, this was accomplished on selected studies, and has been continually expanded so that virtually all patients registered to GOG protocols are entered via the web.

These IT initiatives exemplified two key points. First was the enhanced technological ability of the SDC. Second was that these projects illustrated the success of the restructured SDC in achieving its goals. Interaction among the Directors was essential in developing and achieving each plan of action. For example, both the Data Management and IT divisions had to collaborate and coordinate to ensure that the critical eligibility screening component of phone-based patient entry was retained in the new web-based patient registration system. Subsequently, testing and then gradual conversion was achieved without disruption. Progress was monitored and discussed during routine Directors' Meetings.

Dr. Park's tenure as Group Chairman witnessed a dramatic growth into new areas of scientific investigation. In a similar fashion, the GOG Statistical and Data Center evolved to encompass new expertise, create an academic environment, and promote technologic advances.

The DiSaia Years: 2002 - 2017

When Dr. Philip DiSaia assumed the GOG Chairmanship in 2002, the restructured SDC was poised to take on many new initiatives due to both the stability and long-standing commitment of SDC staff, as well as the infusion of additional expertise acquired via newly acquired members. Of note, a scientific liaison was established with the newly created Department of Biostatistics at the University at Buffalo. Moreover, as initial studies involving translational research and quality of life matured, procedures were developed to ensure the timely and efficient preparation of the increased number and more complex nature of manuscripts. In the current era of reduced federal support, the GOG embarked upon numerous collaborative ventures with industry resulting in the preparation of an increasing number of grant applications and the need to efficiently manage resulting funding. These expanding responsibilities and a desire to enhance efficiency warranted the expansion of the SDC structure to include a formal Administrative Division. Web-based data entry was accomplished via the development of the SDC Electronic Data Entry System (SEDES) and the electronic management of biologic materials via the Bioinformatic and Specimen Tracking (BAST) system was initiated. More recently, NCI initiatives such as migration to the Oncology Patient Enrollment System (OPEN) and a common remote data entry system (Medidata Rave) have created new technologic challenges that have been successfully addressed. Finally, the decision to create NRG Oncology has initiated exciting new collaborative possibilities. The SDMC continues to be inherently involved in the planning, evaluation, and development of procedures in preparation for the inception of this venture. This section details these innovations.

In 1999, Dr. Blessing and Dr. Maurizio Trevisan, Chairman of the Department of Social and Preventative Medicine (SPM) at the University at Buffalo (UB), had initiated a formal relationship between the SDC and SPM. This constituted the onset of a formal academic relationship. In 2002, Dr. Alan Hutson was recruited to chair a newly created Department of Biostatistics at UB. Subsequently, because of this fortuitous development, Drs. Hutson and Blessing initiated a symbiotic collaboration that has paid impressive dividends. Drs. Blessing, Brady and Sill all have academic appointments at UB, while Dr. Hutson, Dr. Randy Carter, Associate Chairman of the Biostatistics Department, Dr. Jeff Miecznikowski, Dr. David Tritchler, and Dr. Lori Sheperd of the UB faculty became valuable GOG staff members. Dr. Hutson served on the GOG Protocol Committee as well as the Committee on

Experimental Medicine. Dr. Carter was a member of the Cancer Prevention and Control Committee and Drs. Miecznikowski, Tritchler, and Shepherd further expanded the SDC expertise in translational research. As a result of this alliance, a program was initiated whereby UB students were able to do internships within GOG and/or have joint appointments. Mr. William Brady (2006), Mr. Austin Miller (2006), and Ms. Wei Deng (2010) became valued additions to the GOG Division of Biostatistics and Science while pursuing advanced degrees at UB. All three successfully completed their PhD programs and took on significant GOG responsibilities in Rare Tumors (Brady), phase II trials (Deng), and Ancillary Data studies (Miller). Virginia Filiaci also achieved her doctorate and was promoted to the role of GOG Associate Director of Biostatistics and Science. She and Dr. Brady collaborated to provide outstanding statistical leadership and mentoring to a well-respected cadre of SDC biostatisticians and scientists who are fully integrated into GOG science. In 2009, James Java was hired to focus on ancillary data investigations. Dr. Heather Lankes was hired in 2008 as a Translational Research scientist and has interacted with the Committee on Experimental Medicine to greatly enhance the coordination of translational research investigations. Mr. Brandon Marzullo joined her in 2010 to round out the current TR staff upon the departure of Dr. Darcy. Both have contributed to the increased efficiency of the Committee on Experimental Medicine and the GOG Tissue Bank. The infusion of academia-based expertise and the careful recruitment of staff has enhanced the SDC's ability to meet the growing scientific diversity of the GOG and positions it to anticipate and proactively address future challenges.

Based on the expanded administrative functions of the SDC, the Administration Division was formally created in 2003 with Ms. Sally Bially as its Director. This division encompassed fiscal management, manuscript preparation, all quality assurance audit functions, and the production of the semi-annual GOG Statistical Report, as well as administrative functions necessary for a department in excess of 50 staff members. The resulting constituency of the SDC Directors represents every aspect of SDC activity and further enhances efficiency.

Substantial progress was also evident in the preparation of GOG manuscripts for publication. This process, which had been centralized in the GOG SDC and governed by the GOG Protocol Procedures Manual, requires timely development of a first draft by the primary Study Chair, collaborating Statistician and Clinical Trials Editorial Associate. Subsequent steps involve review by co-authors, the GOG Publications Subcommittee, and journal reviewers. Manuscripts at each of these stages typically require revision and circulation. Following a 2002 GOG Retreat conducted by Dr. DiSaia, an increased emphasis was placed upon manuscript development. Accordingly, the SDC hired Ms. Anne Reardon (2003) and Ms. Kim Blaser (2006) as Clinical Trials Editorial Associates to guide each manuscript through the various stages of manuscript development. Also, working closely with Dr. George Omura, Mr. Frederick Stehman, former Chairs of the Publications Subcommittee, and the GOG Operations Committee, Ms. Baily developed a system to set, monitor and enforce deadlines for each stage of manuscript development. The efficiency of this process was documented in an investigation1 comparing the development time for phase II trials during 2003-6 vs 2007-10.

For many years, the GOG, and subsequently NRG Oncology, received "flat" federal funding at best, and in some instances reduced levels of funding. As a result, NCI funding for the SDC grant was less in 2010 than it had been in 2000. This circumstance is compounded by the increased complexity and commensurate workload mandated by current research studies. To ensure the continued high quality of GOG investigations, it has been necessary to explore avenues of supplementary funding. Under Dr. DiSaia's leadership, the GOG embarked upon numerous liaisons with industry. Scientific development of protocols has become increasingly complex and labor intensive, as agreement among the GOG, the NCI, the corporate collaborator, and frequently the Food and Drug Administration must be negotiated. This impacts study design, content of data forms, toxicity reporting, etc. Additionally, the Administration Division of the SDC was charged with the preparation and oversight of numerous contracts and/or applications for funding. As a result, the SDC has successfully assumed considerable additional fiscal responsibility to develop budgets, review contracts, manage funding, and ensure fulfillment of contractual obligations. In 2002, the SDC managed three modest sources of funding in addition to its primary NCI grant funding; by 2005, there were 47 additional awards, contracts, or applications for supplementary funding being managed.

In 2008, Ms. Jennifer Delair was hired as Grants, Fiscal, and Personnel Administrator to manage fiscal processes. With the advent of GOG Partners, the fiscal responsibilities multiplied as it is essential to disburse funds for NCI and non-NCI projects commensurate with the effort required for each. Of note, an electronic mechanism was created to fine tune budget requirements for each individual task associated with the development, conduct, data capture, quality control, analysis, and pub-

lication of any concept initiated through the Partners mechanism[2]. This allows the SDC to function as a contract research organization (CRO) in GOG collaborations with industry. The first such effort, Protocol 3003, was initiated using this process.

Between 1993 and 2003, the number of CRF's received annually in the SDC rose from approximately 40,000 to 70,000 forms. As a result, the SDC developed methodology for a web-based data entry system, SDC Electronic Data Entry System (SEDES), that allows for the intermediate submission of patient data over a highly secure internet connection. This project underscores the efficiency of the current office structure. The initial step in web-based data entry was the development of Case Report Forms (CRF's). This required collaboration involving statistical, data management, and IT staff to develop the design and content of each CRF and assure compliance with NCI Common Data Elements. Subsequent steps included range and logic testing for each question, form testing, and activation. Initially, web-based versions of individual forms were made available across all protocols. With the knowledge and feedback obtained from this process, the SDC initiated total web-based data entry for phase III Protocols 197, 204, 209, and 210. Based upon the initial success and institutional feedback, the SDC convinced the GOG leadership to mandate web-based data entry for Protocol 212 prior to its activation in 2005. The database for this investigation, and that for Protocol 218 were used to collect data for regulatory review and possible drug approval. Upon receipt of the final database for the latter study in 2010, the sponsor remarked "…the database was inherently very clean … very unusual and impressive for a cooperative group." This reflected the thoughtfulness of the design, functionality of SEDES, and the thoroughness of the Clinical Data Coordinators.
In a similar fashion, this type of interaction was vital in the development of an electronic system to provide a bioinformatics platform that allows the efficient and accurate integration of clinical, patient consent, and specimen information with data generated from high through-put laboratory testing procedures. The Bioinformatics and Specimen Tracking (BAST) system consists of a series of interrelated databases and processes which facilitate the combination of clinical and translational data. It enables the tracking of the quality and utilization of GOG collected specimens and contains laboratory assay results and controls collected from approved testing labs. The creation of BAST was of paramount importance to efficiently accommodate the rapid expansion of translational research in GOG Protocols.

The Information Technology staff was augmented by the addition of Mr. Josh Killion (2005) and Mr. Kareem Kouis (2009) as programmer/analysts, and Mr. Justin Dittmar (2007) as a technical writer/support specialist.

The NCI mandated that all Cooperative Groups transition to a common electronic data entry system, Medidata Rave, in 2013. The SDC IT staff became fully engaged in workshops, training sessions, webinars, etc., to be in the forefront of the Rave EDC adoption. The past Group-wide acceptance of and praise for the in-house accomplishments of SEDES and BAST provide every confidence that this hard-working group will make this transition as seamless as possible.

The technological advances, increased protocol complexity, volume of protocols, and exceptional Group-wide accrual prompted significant changes within the Data Management Division. In 2007, Ms. Angela Kuras was named Associate Director of Data Management. Her ability to interact closely with IT was of great significance in fostering the continued evolution of GOG systems. To ensure the uninterrupted high level of expertise of the Senior Clinical Data Coordinators, the SDC instituted a program of having each one mentor new Clinical Data Coordinators. This resulted in the reassignment of Rachelle Dutka (2009) and Melissa Leventhal (2010) and the addition of Kristin Engel (2007), Randy Vogt (2009), Jill Evans (2010), and Jessalyn Reboy (2010). The foresight of this initiative was seen in 2009 when Patricia Brehm (Corpus) and Suzanne Baskerville (Ovary), two outstanding Senior Clinical Data Coordinators decided to retire. Ms. Engel and Ms. Dutka were then promoted to assume these responsibilities. Typical of the long-term commitment that SDC members have had to GOG, both Ms. Brehm and Ms. Baskerville returned briefly on a part-time basis. New additions to the Data Management staff include Sharon Desabrais (2007), Tracy Flick (2007), Mary Kaletta (2009), and Kristina Klausen (2009). Ms. Desabrais subsequently was switched to receptionist responsibilities in the Administration Division.

Innovation not only is critical for efficiency improvements recognized by end users and developers but also for maintaining talent locally. The SDC maintains a culture of innovation for staff engagement and retention, to strive for quality improvement and contribute to trial reliability, safety, and integrity through increased efficiency. Innovations supporting NCI funded clinical trials developed by SDC staff at Roswell Park cover areas of operational efficiency, quality assurance, statistical design, Medidata Rave study build and quality control tools. Many of these accomplishments have been featured in peer reviewed manuscripts and abstracts involving all divisions.

This served to demonstrate their research prowess, present innovative initiatives, and underscore efficiency. Biostatistics and Science research includes methodology for phase II trials with co-primary endpoints (Sill)[3]. The results of this research have been incorporated into the design of several Phase II GOG studies: drop-the-loser approach for designing multi-arm studies and proposed methods for reducing the bias in the estimated treatment effects and controlling type I error (Sill)[4,5]; a biomarker based adaptive design two-stage randomized phase II study design (Filiaci)[6]; a permutation based approach to phase II historical control trials (Hutson)[7]; response as a surrogate endpoint for survival in endometrial cancer (Filiaci)[8]; and a comparison of weighted log rank procedures and a time-dependent Cox model (Brady)[9] .

Administrative Division efforts to enhance efficiency and education have been featured in both manuscripts and abstracts on topics which include: the value of the assignment, monitoring, and enforcement of deadlines in reducing the time to manuscript submission (Bialy)[1]; initiatives for improvement resulting from an analysis of GOG Quality Assurance Audit results (Blessing)[10]; efficient management of diversified funding (Bialy)[2]; creation of a digital library for GOG manuscripts utilizing information technology infrastructure (Leventhal)[11].

Ms. Kuras presented Data Management Division innovations before the Society for Clinical Trials on the quality control of electronically captured data[12] and the ability to conduct remote paper-less study chair reviews of data[13]. IT presentations covered: online application for the tracking and implementing specimen consent choices (Elgie)[14]; electronic submission of paper based clinical reports, such as pathology and operative reports (Elgie)[15]; web-based management of phase I trials with multiple institution participation (Elgie)[16]; automated drug ordering in a cooperative group setting (Elgie)[17]; the secure exchange of electronic data (Gould)[18,19]; and the creation of web-based teleforms (Puehn)[20].

The accomplishments achieved during this period relied heavily on the strong foundation built during the previous eras. Dr. DiSaia continued the GOG tradition of including the SDC in all facets of GOG investigative activities. He fully endorsed SDC initiatives and developed innovative alternative funding mechanisms to ensure stability and growth in a difficult fiscal climate. His guidance and support enabled the SDC to anticipate and meet the scientific, technologic, and financial challenges associated with GOG research. Beyond the development, conduct and reporting of GOG led clinical trials, these accomplishments further supported the Group's contribution to the regulatory approval of treatment for women with gynecologic malignancies as outlined in Table 1.

Table 1.

Contributions to regulatory approvals from NCI funded clinical trials

1. 1990 Paclitaxel for advanced ovarian cancer (GOG-0111)
2. 2006 Topotecan for advanced cervix cancer (GOG-0179)
3. 2014 Bevacizumab for advanced cervix cancer (GOG-0240)
4. 2016 Bevacizumab recurrent ovarian cancer (GOG-0213)
5. 2018 Bevacizumab with chemotherapy for ovarian cancer following initial surgery

NRG Oncology

With the alliance of the National Surgical Adjuvant Breast and Bowel Project (NSABP), the Radiation Therapy Oncology Group (RTOG) and GOG to form NRG Oncology, the combined resources of the new entity are outstanding. This is particularly true for the NRG Oncology Statistical and Data Management Center (SDMC). As co-Executive Directors, John Blessing, PhD (GOG), Joseph Costantino, DrPH (NSABP), and James Dignam, PhD (RTOG), jointly governed this integrated entity distributed among the three present locations (Buffalo, Pittsburgh, and Philadelphia). Leadership representation from all three legacy groups ensures that the SDMC would be poised to take advantage of the best practices that each individual group had to offer to integrate multiple systems and processes into a cohesive unit. A strong collegial relationship and friendship among the three Co-Executive Directors preceded NRG Oncology. Likewise, the division directors from each legacy group had worked together on numerous NCI projects, intergroup studies, and scientific collaborations. The daunting process of developing the SDMC grant application required significant interaction: familiarization with one another's standard operating procedures and policies (SOPs); discussion to identify areas of commonality and differences; development of NRG Oncology procedures, etc. In the end, a comprehensive, cohesive plan that retained expertise, yet would operate as one entity was developed. Moreover, the reinforcement of the

collaborative nature and willingness to compromise to achieve a common goal reflected very positively on all participants. This positive outcome was mirrored during the inaugural grant period, in the governance plan, and in all decision-making policies. Ultimately, the approved grant named Joseph Costantino as Group statistician and Drs. Dignam and Blessing as Co-Principal Investigators.

Since the decision to form this alliance, leaders of each division of the SDMC were involved in numerous working groups to create the structure (Transition Steering, Administrative Transition, Communications, Grant Writing, Membership, Website) and develop common procedures (Audit, Publications, Biostatistics, Data Management, Modality, Outcomes, Scientific Agenda, Information Technology). Intense participation in meetings and/or conference calls ensured that common procedures were in place upon the formal initiation of NRG Oncology on March 1, 2014. Indeed, many of the resulting SOPs were immediately utilized in the Legacy Groups where possible. The challenge to accomplish these tasks in such a short time was formidable. Nonetheless, the GOG SDMC members and their colleagues in NSABP at the University of Pittsburgh and in RTOG at the American College of Radiology and the University of Chicago accomplished a great deal in a short time.

During the early years of NRG Oncology, the Buffalo office of the NRG Oncology SDMC continued to develop innovations that helped create operational efficiencies for a distributed workforce committed to NRG Oncology clinical trials. Recognizing the need for access to important documentation and training, a low-cost, proprietary online SOP system was developed to manage documents, online authoring, and training. This system has been used for NRG Oncology SDMC SOP management and for other projects handled locally by the Buffalo office. Prior to assimilation into the NRG Oncology audit program, the Buffalo SDMC auditors pioneered pre-site visit reverse review of regulatory and drug accountability records which increased on-site auditor time for concentration on patient chart review. This strategy was adopted as a best practice by the NRG Oncology audit harmonization working group and has become an essential procedure used to increase the level of efficiency required to manage a workload growing in both volume and complexity; this has become best practice within the NCTN and NCORP. Through a collaboration with the Gynecologic Cancer Committee Chair, Carol Aghajanian, MD, simple reusable tools such as Excel spreadsheets were implemented to aid site staff in scheduling important or critical protocol assessments; an important tool for maintaining compliance. A web-based publications system was developed to efficiently track and report on the publication life cycle of GOG and NRG Oncology. This includes a database and tracking of publication assignments, co-authorship, intellectual property review and deadlines starting with the final analysis.

With the mandate to use Medidata Rave for all NCTN trials, it was recognized that the system siloed each study and did not include a clinical trial management system. New architecture was needed to link data in the Rave EDC across studies to efficiently manage a portfolio of studies. Expertise in the utilization of Medidata Rave to its fullest is evident via the Buffalo SDMC office's development of Rave innovations and solutions recognized by the NCI's Clinical Trial Support Unit (CTSU) and implemented across Lead Protocol Organizations. Rave functionality improvements developed to streamline data collection and management for complex trials include:

- Integration of a translational research transmittal form within the Rave EDC gave site users an efficient, lone source to enter patient data and generate transmittal forms for shipment to a biobank or laboratory reducing the risk of transcription errors.

- A generalized, reusable, remote review tool was developed to support study chair data reviews for NRG Oncology and GOG Foundation trials that utilize Rave as an EDC system. The review tool architecture is designed in a way to allow for other types of reviews to be built within the system, requiring no additional software development effort. For example, a safety review system for Phase I trials and safety lead in trial components has been integrated into this system.

- Collaboration with CTSU, providing guidance and feedback in the development of the eventual serious adverse event (SAE) Rave integration architecture, including the utilization of a central study to support maintainability.

- Development of Data Summaries for data captured in Rave is used to support efficient data management and review activities using a framework that is available freely with existing software.

- Development of Date Query Free functionality for NRG and shared with CTSU and Medidata and consequently implemented across the lead protocol organizations. This functionality supported forms tracking and delinquency monitoring.

- The ability to track a new set of baseline measure-

ments for response evaluation criteria in solid tumor (RECIST) response evaluations after the first progression on study was developed for studies that mandate treatment crossover.

- A copy forward function was created to copy select CRF content forward to subsequent visit forms. This feature reduced the amount of data entry required for sites reporting unresolved adverse events and concomitant medications.

- Dynamic and configurable study event roll-out functionality was developed and first used to support the capture of solid tumor and quality of life data using an advanced form and folder roll-out.

- Patient reported outcome form advanced notice and schedule was piloted in Rave for two large studies with the aim of positively impacting compliance.

Several gynecologic oncology studies have been initiated under the newly formed National Clinical Trials Network (NCTN) and NCORP in the consolidated NRG Rave instance. At least three of these were developed prospectively for potentially seeking regulatory approval; NRG-GY004, NRG-GY005 and GY018. Such studies require close monitoring and auditing. At this time the NCI began to support furthering these efforts. One of these initiatives involved Site Audit Reporting (SAR) using Medidata Rave efforts for NCI. Buffalo SDMC auditors piloted this system. Since then, SAR has been put into production, and is currently being used routinely by Buffalo lead auditors who conduct CTMB audits. In addition, a team comprised of audit, data management, and IT staff led the way in the implementation of remote/virtual monitoring for two NCI sponsored FDA registration trials; GY004 and GY005. Since the initiation of remote/virtual monitoring of these two registration trials in 2016, source documents have been uploaded into Rave from hundreds of research institutions, queries have been processed within the application to resolve data inconsistencies, and reporting modules have been used to monitor progress and provide information to NCI. With monitoring and auditing processes being parallel paradigms, this developmental work and experience formed a solid foundation to accelerate development of the infrastructure required to perform remote/virtual audits. The ability to perform remote/virtual audits became important during the period of the COVID-19 pandemic starting in March 2020.

In the new NCTN, funding levels were reduced with fewer studies being approved than were across three independent groups; even though the studies were increasingly complex and new responsibilities were added. Initial efforts to consolidate SDMC areas of responsibility across offices for efficiency and reduce duplicative work and resources down the road started with utilizing a single Medidata Rave URL. Later, a single NRG Randomization Node was established; NRG-GY012 was the first gynecologic oncology study to utilize this centralized NRG application. Specifications of the node were developed collaboratively across the offices.

Eventually, hard choices were necessary and work force consolidation was required. Unfortunately, numerous staff across the offices were let go. Dr. Costantino transitioned data management study build, clinical data quality control review, query management, and PRO collection responsibilities for gynecologic studies to the Pittsburgh Office starting in 2015 under the direction of Mary Jo Antonelli. NRG-GY006 was the first new NRG gynecologic study to be taken on by her team. Eventually these responsibilities included legacy studies as well. Since systems could not be transferred, data remained in Buffalo but access to data was provided to the new data managers. The audit program leadership was also transitioned to the Pittsburgh Office. Fortunately, the Buffalo NRG SDMC office staff continued to audit sites and maintained data management responsibilities for studies operating under contracts with Pharma partners and continued to partner with GOG Foundation on studies initiated through their Partners division.

SDMC Reorganization at Roswell Park

In October 2016, after 42 years of dedication and service and 25 years as the Chair of a Roswell Park Department, Dr. Blessing retired, and the Buffalo SDMC underwent a major reorganization. The SDMC was moved into the Department of Biostatistics and Bioinformatics under its Chair, Dr. Alan Hutson. Dr. Hutson took over as the Buffalo site PI for the NRG SDMC. In addition to Dr. Blessing, Dr. Brady, Bette Stonebraker and Sally Bialy also retired shortly thereafter but all these veteran members continued to contribute to the SDMC even after retirement. Dr. Hutson promoted key individuals into leadership roles, including Angela Kuras as Director of Clinical Trial Management, Dr. William Brady as Director of Biostatistics and Statistical Programming, Scott Gould as the Director of IT Infrastructure and Strategies, Josh Killion as Director of Software Systems and Implementation and Dr. Virginia Filiaci as the Chief. The newly formed division of Biostatistics and Bioinformatics was rebranded as the Clinical Trial Development Division (CTDD). Following her official retirement, Ms. Bialy returned as the Director of Quality Assurance and Reporting completing the reorganization.

The Copeland and Mannel Years: 2017 - Present

The GOG Foundation underwent some planned leadership changes in 2017 with Dr. Copeland taking over Dr. DiSaia's role as the leader of the GOG Foundation, and Dr. Mannel taking over Dr. DiSaia's role as an NRG Oncology PI. Along with the leadership change, the GOG Foundation also was undergoing a transformation. With the support of Dr. Copeland, Drs. Hutson and Filiaci and Josh Killion were all invited to participate in a strategic retreat to help reorganize the GOG Foundation to strengthen its foundation for the future.

With fewer gynecologic oncology treatment studies being approved by the NCTN, GOG Foundation began to expand their portfolio of studies with industry partners. The newly branded CTDD was successful in gaining sponsor approval to take on data management, as well as statistical, quality assurance, and/or DMC management roles for several trials; some with a regulatory approval pathway. The CTDD successfully completed collaboration on the first of these studies, GOG-3003 in 2017. Since then, additional studies with CTDD collaboration have been completed: GOG-3008, GOG-3009, and GOG-3016. A few studies are ongoing, such as investigator-initiated trials GOG-3007, GOG-3026, and GOG-3039, and a registration-intent trial, GOG-3018 (publicly reported as not reaching its primary endpoint). In addition, we have collaborated on other studies such as GOG-3028 and some that are currently under development. With each of these collaborations, CTDD expanded their capabilities and helped to facilitate or take on responsibilities for the Sponsor. A few notable examples include the collaborative development and implementation of an SAE portal in the SEDES system. This was done rapidly with close collaboration with GOG Partners leadership and staff to help facilitate pharmacovigilance by GOG Partners. This was later translated to integrate with Medidata Rave by GOG Partners. Other examples include developing formal procedures to set up and manage a DMC, to incorporate a blinded and unblinded statistician for randomized trials monitored by a DMC and to create and validate statistical deliverables such as tables, listings, and figures to support development of a clinical study report or other statistical analysis reports included in FDA submissions.

In 2017, CDISC data submission requirements were formalized by the FDA. Use of CDISC standard data sets defined by SDTM and ADaM for regulatory submissions were required for new studies; CDASH compliant forms were also needed to enable mapping data to these dataset standards. In advance of this requirement, training in CDISC standards had been initiated by Josh Killion and Jim Kauderer but in 2019 NCI also planned for adopting use of CDISC standards. Subsequently, in 2019 all data managers, statisticians, programmers, and study builders received CDASH training, and the statisticians and programmers completed SDTM and ADaM training in 2020. With this training, use of CDASH compliant forms was initiated across all studies. While somewhat different, the GOG SDC had historically developed and implemented their own standards for collection and dataset creation. For now, these requirements have been adopted for studies seeking regulatory approval. Adoption of these new standards across studies, whether regulatory approval is sought or not, has been partially implemented.

In 2017, Dr. Virginia Filiaci took over as the site PI for the Buffalo Office and she, along with Kathryn Winter, were named as Deputy Directors. In 2019, Dr. Joseph Costantino retired, and Dr. James Dignam officially became the NRG Oncology Group Statistician.

In mid-2018, Dr. Bill Brady left for a position with a CRO and Dr. Austin Miller was promoted to the position of Director of Biostatistics and Statistical Programming. Angela Kuras' leadership and dedication during this period earned her a role as Associate Director of CTDD. Additionally, Jon Kiddy was hired to replace Josh Killion after taking a role with GOG Foundation (GOG-Partners). Soon after, Jon Kiddy was promoted to Director of CTDD IT Operations.

Starting in 2018, the NCI began several new initiatives aimed at furthering the research output of important trials with both data and biospecimen collections, NCTN Navigator and NCTN/NCORP Data Archive. NCTN Navigator is a mechanism for sharing annotated specimens collected on phase III and tissue banking trials across the oncology research community. Since its adoption, 25 legacy trials and one NRG gynecologic trial have been added to Navigator as sources of biospecimens with clinical data. The Buffalo NRG SDMC has evaluated nearly 30 letters of intent for feasibility and have been asked to collaborate on proposals. Several of these collaborations have been approved by the NCTN Core Correlative Sciences Committee and are seeking or have received funding. To complement the specimen sharing through Navigator, clinical data contained in analysis datasets from published phase III trials are also uploaded into the NCTN/NCORP Data archive. A unique and random identifier is used to link data and specimens to allow efficient linking of data and biospecimen outputs. One additional NCI Cancer Moonshot℠-funded program, Molecular Profiling to Predict Response to Treatment (MP2PRT), allows

the NCTN groups to apply for sequencing of valuable annotated tissues collected on NCTN trials to investigate prediction of response to treatment based on sequencing output from normal and tumor specimens. The program was announced in late 2019 and again in 2020. The Buffalo NRG SDMC has participated in three submissions with two approvals. Specimens from GOG-0240 have been sequenced and specimens from GOG-0210 are approved for sequencing. This is an important collaboration between NRG Investigators and statisticians, NRG Biorepository investigators, Leidos, bio informaticists and genomics experts that will yield critical information for expanding our understanding of the gynecologic malignancy genetic landscape and planning future targeted therapies aimed at cervix and endometrial cancer.

Precision medicine has been an important focus for the NCI. One major component of the NCI Precision Medicine Program has been the evaluation of single and combination therapies aimed at actionable targets of solid tumors through Molecular Analysis for Therapy Choice (MATCH) and ComboMATCH. NRG Oncology is an active participant in ComboMATCH, and in 2021 was the first to get a study approved, with Dr. Austin Miller responsible for its statistical design.

Starting in 2020, the Coronavirus (also referred to as COVID-19) pandemic created a great challenge for conducting clinical trials. Immunocompromised cancer patients were at elevated risk of contracting and dying from COVID-19 infection. Out of concern for the safety of cancer patients and staff, SDMC staff transitioned to work from home. The switch was completed over a two-day period and resulted in little downtime. SDMC productivity remained high and, in some cases, increased. The use of virtual meetings led to increased communication and progress on activating and conducting trials. Study accrual slowed slightly in the first few months, but rebounded; close monitoring continues. Some study designs required thoughtful consideration and amendment to minimize COVID-19 risks. For example, accrual was suspended to amend the maintenance treatment in NRG-GY018, which included a placebo-only arm.

The SDMC staff with its current leadership, structure, wealth of experience, gynecologic oncology trial expertise, academic affiliation, and collaborative arrangements (with the University of Chicago/Dignam, University of Pittsburgh/NSABP, and the American College of Radiology/RTOG) is uniquely poised to contribute to GOG Foundation's ability to maintain the highest standards of clinical trials development, execution, analysis, and dissemination of results.

GOG/SDC Milestones of Progress

1970 The "Cooperative Gynecology Oncology Group" involving ten institutions is founded and is later constituted as the "Gynecologic Oncology Group" (GOG). Dr. Myron Hreshchyshyn is elected Group Chairman. The Group Chairman's office is located at the Buffalo General Hospital and consists of a central endocrine laboratory and a pathology and radiation therapy repository. Drs. Irwin Bross and Nelson Slack established the GOG Statistical Office at Roswell Park Memorial Institute (RPMI).

1971 Dr. Slack is appointed Group Statistician. Fifteen institutions participate in five GOG studies and enroll 49 patients.

1974 Dr. George Lewis is elected Group Chairman, effective July 1975. Dr. John Blessing replaces Dr. Slack as Group Statistician. The Statistical Office consists of Dr. Blessing and four staff members.

1975 The Group Chairman's office is relocated to Philadelphia. The first formal GOG Statistical Report was prepared and distributed at the January GOG Meeting. The first Study Chair review is performed. The GOG Protocol Committee is established to coordinate protocol development and manage ongoing studies. The GOG Protocol Procedures Manual was created to regulate these processes. The 2,500th patient is registered onto a GOG study.

1976 Standardized Phase II study queues are implemented to facilitate protocol development and accelerate drug evaluation.

1977 The GOG Data Safety Monitoring Board (DSMB) is created to review treatment related deaths and unexpected toxicities.

1978 The Statistical Office utilizes Mag Card equipment to prepare documents electronically.

1981 GOG and RPMI statisticians begin to develop a library of in-house generalizable computer programs for designing clinical trials, generating graphical presentations, and performing data analyses on a mainframe computer.

1983 The Statistical Office initiates a program of institutional quality assurance audits in accordance with NCI mandate. GOG clinical trials data are converted to a generalized database management system called RPMIS, developed at Roswell Park to run

on the Univac 90/80 mainframe computer. The ASCII terminals permit real-time data management through acoustic couplers over the phone line at 150 characters per second.

1984 Procedures for designing studies with a time-to-failure endpoint are developed which estimate the time required for study maturity and completion. Experimentation with the use of personal desktop computers in study development and management is initiated.

1985 RPMI statisticians develop the FREND procedure for performing Kaplan-Meier and proportional hazards modeling in SPSS. The first treatment study incorporating a measure of each patient's self-assessed quality of life (Protocol 97) is initiated. The 10,000th patient is registered onto a GOG study.

1986 The Statistical Office joins RPMI's Corvus (1 Mbit/sec) named a separate Department with Dr. Blessing as Department Chairman. The Statistical Office assumes responsibility from the Administrative Office for modality reviews. The SDC collaborates with the CHTN to initiate the GOG Tissue Bank (Protocol 136). The 25,000th patient is registered.

1992 The Group Chairman requests the Statistical Office to form a Quality of Life (QoL) Working Group which is the precursor of the GOG QoL Committee (formed in 1993). The GOG Quality Assurance Audit Committee is formalized. At the request of the Nursing Committee, the Statistical Office designs the first GOG study (Protocol 9102) in which the primary endpoint is based on the patient's self-evaluated adverse effects of chemotherapy. The Statistical Office hops onto the electronic superhighway.

1993 The GOG Tumor Biology and Applied Science Committee is formed which subsequently becomes the Committee on Experimental Medicine.

1994 A formal Data Monitoring Committee (DMC) is established which is charged with reviewing interim study results and monitoring the conduct of all GOG Phase III trials.

1995 The GOG Cancer Prevention and Control Committee is established.

1996 The designs for standard Phase II study queues are converted to multi-stage designs that permit early accrual termination when treatments are considered ineffective.

1997 The SDC collaborates with industry sponsors to provide data from Protocol 111 in order to obtain FDA approval for paclitaxel for the first-line treatment of women with advanced ovarian cancer.

1998 GOG data forms are redesigned to accommodate Common Toxicity Criteria (CTC) for reporting the adverse effects of treatment.

1999 The Statistical Office is restructured to create the GOG Statistical and Data Center (SDC) comprised of three Divisions: Biostatistics and Science, Data Management, and Information technology. The SDC collaborates with investigators from the US, Canada, Europe, Australia, and New Zealand to develop the first multinational and largest GOG sponsored trial (Protocol 182). This study ultimately evaluates five study regimens and enrolls more than 4,000 women from all over the world.

2000 The SDC successfully re-competes for increased funding to enable it to grow commensurate with the Group's broadened research interests. The SDC expands to include statisticians with specialized experience in health outcome research, epidemiology, and experimental medicine. The designs for Phase II study queues are converted to optimal and flexible two-stage designs, eliminating the need to pre-specify fixed accrual sizes for each study stage. Web-based patient registration is initiated. The GOG adopts RECIST criteria for reporting tumor response evaluations. The 50,000th patient is registered. A publications database is architected.

2001 Dr. Philip DiSaia is elected Group Chairman, effective July 2002. Translational Research Scientists join the SDC to support the GOG basic science effort. The Medical Informatics Committee is formed. The SDC created a user friendly, interactive website to foster electronic communication for the entire GOG. Annual accrual exceeds 3,000.

2002 The SDC collaborates with industry sponsors to develop the first GOG Phase III trial (Protocol 212) prospectively designed to seek FDA approval for a new agent.

2003 The SDC and the newly formed Biostatistics Department at UB form a symbiotic relationship. UB faculty members join the SDC staff and begin working on GOG studies, while SDC statisticians join the UB

faculty. The first data forms for GOG trials are submitted via the web through the SDC Electronic Data Entry System (SEDES). Based upon the ever-increasing responsibilities of fiscal management, efficiency and organization, quality assurance audits, and manuscript development, the SDC formally adds an Administration Division to its structure.

2004 The SDC begins development of a Bioinformatics and Specimen Tracking system (BAST) to combine clinical and research databases and manage specimen collection.

2005 The first studies are initiated in which all study data are submitted electronically using SEDES (Protocols 212 and 218). The GOG's first prospective study is initiated in which its primary objective is the use of a high-throughput technology to diagnose gynecologic cancers (Protocol 220).

2010 The first GOG Protocol (261) using the Open Patient Enrollment System (OPEN) is initiated. SEDES database for Protocol 218 utilized for regulatory review and potential drug approval.

2011 Members of the SDC begin interaction with NSABP and RTOG colleagues to initiate planning for the NRG Oncology Statistical and Data Management Center (SDMC). Simultaneously SDC Leaders participate in Working Groups to develop all NRG Oncology committees, procedures, functions, etc.

2012 The first GOG Protocol (229-N) utilizing Medidata RAVE for electronic data capture is initiated. The SDC collaborates on the first GOG Partners trial that is fully funded by industry (GOG-3003).

2013 The NRG Oncology SDMC grant application is submitted in January 2013. Incorporation of safety review system for trials utilizing Medidata RAVE EDC.

2014 The NRG Oncology Group and SDMC are funded as a National Clinical Trial Network Group and SDMC. Joe Costantino is officially named as Group Statistician. Automated on-line SOP framework developed and implemented by the Buffalo SDC for the NRG Oncology SDMC. SAE Portal developed for GOG Partners investigator-initiated trials.

2016 The first trials with remote monitoring initiated.

2017 CTDD SOPs and SOP system developed for industry funded trials. Initial training in CDISC standards was initiated. Pioneered the reverse auditing of regulatory and pharmacy components; this has become best practice within the NCTN and NCORP.

2019 CDISC Training initiated by statisticians and programmers.

2020 COVID-19 pandemic-initiated use of widespread remote auditing practices and collection of COVID related deviations.

2021 The Datacenter moved from UB Center for Computational Research to Roswell Park. Began development of efficient reconciliation processes for EDC and Vendor databases.

References

1. Bialy S, Blessing J, Stehman FB, Reardon A, Blaser K. Gynecologic Oncology Group strategies to improve timeliness of publication. *Clin Trials* (in press), 2013.

2. Bialy S, Reed J, Leventhal M, Blessing J. Efficient management of diversified funding within the Gynecologic Oncology Group (GOG) statistical and data center (SDC). *Proc Soc Clin Trials* 8(4) (Abst. #P11), 2011.

3. Sill M, Rubinstein L, Litwin S, Yothers G. A method for utilizing bivariate efficiencyoutcome measures to screen regimens for activity in 2-stage phase II clinical trials. *Clin Trials* (9) 4:385-95, 2012.

4. Sill MW, Sampson AR. Drop -the-losers design: binomial case. *Comput Stat Data An* 53:586-595, 2009.

5. Sill MW, Sampson AR. Extension of a two-stage conditionally unbiased estimator of the selected population to the bivariate normal case. *Commun Stat Theory and Methods* 36(4): 801-13, 2007.

6. Filiaci VL, Brady MF. A biomarker based adaptive two-stage randomized phase II study design. Proc Soc Clin Trials 8(4) (Abst. #A96): 492, 2011.

7. Hutson A, Markman M, Brady M. A permutation-based approach to phase II historical control trials in the GOG cooperative group setting. *J Appl Stat* 36(6): 589-99, 2009.

8. Filiaci VL, Carter R, Fleming G, Brady MF. Evaluation of clinical response as a surrogate for survival with application to a Gynecologic Oncology Group (GOG)

study of advanced endometrial carcinoma. *Clinical Trials* 2(Supp 1): s46 (SCT #57), 2005.

9. Brady MF, Priore RL. Accelerated hazard in cure model: a comparison of the weighted log rank procedure and a time dependent Cox model. Proc: *Soc Clin Trials* : (abst #P 07), 2001.

10. Blessing JA, Bialy SA, Whitney CE, Stonebraker BL, Stehman FB. Gynecologic Oncology Group quality assurance audits: Analysis and initiatives for improvement. *Clin Trials* 7(4): 390-99, 2010.

11. Leventhal M, Bialy S, Elgie B, Blessing J. Creating a digital library for Gynecologic Oncology Group (GOG) manuscripts utilizing the statistical and data center (SDC) information technology infrastructure. *Proc Soc Clin Trials* 8(4) (Abst. #P26): 507, 2011.

12. Kuras A, Stonebraker B, Jelonek J, Elgie W, Brady M, Bialy S, Blessing J Gynecologic Oncology Group (GOG): Quality control of electronically captured data. *Proc Soc Clin Trials* 5/17-19/10 Ann Mtg: 101, 2010.

13. Kuras A, Stonebraker B, Elgie W, Killion J, Kouis K, Blessing J. Gynecologic Oncology Group (GOG): remote paperless study chair reviews. *Proc Soc Clin Trials* 8(4) (Abst. #P64): 527, 2011.

14. Elgie WE, Darcy K, Miner Z, Qualman S. An online application for tracking and implementing specimen consent choices for clinical trials: a Gynecologic Oncology Group initiative. *Clin Trials* 4(46): 388, 2007.

15. Elgie WE, Killion J, Filiaci G. Web based submission of paper based clinical reports. Clin Trials: 76(P10), 2009.

16. Elgie WE, Killion J, Brehm P, Sill M, Brady WE, Fracasso P. Web-based management of phase I protocols in a cooperative group setting. *Proc Soc Clin Trials* 5/17-19/10 Ann Mtg: A34:52, 2010.

17. Elgie W, Le Q, Baskerville S, Brady M. Automated drug ordering in a cooperative group setting. *Proc Soc Clin Trials* 8(4) (Abst. #P62), 2011.

18. Gould S. Gynecologic Oncology Group Statistical & Data Center's (GOG SDC) approach to identifying the transmission of unsecured electronic protected health information (EPHI) using an open-source intrusion detection system (IDS). Clin Trials A06: 40, 2009.

19. Gould S. The challenges of facilitating and supporting the efficient and secure exchange of data in a multisite cooperative group that is funded by government and industry. Proc Soc Clin Trials 8(4) (Abst. #A72): 481, 2011.

20. Puehn K, Le Q, Klier S, Elgie W. Making a web-based-cardiff teleform generated pdf patient clinical reporting form dynamic with the use of adobe fdf files. Soc Clin Trials SCT Proc Program: 105 (Abs. #P14), 201.