Modem Remote Support of Pulmonary-Function Testing and Quality Control Systems

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ABSTRACT: The data coordinating center (DCC) of the Asthma Clinical Research Network (ACRN) is responsible for the support of 11 pulmonary-function testing systems and two quality control systems. Pulmonary-function data from these systems are used as outcome indicators in studies conducted by the ACRN. Each of these systems is composed of a spirometer, a personal computer for data acquisition from the spirometer, a modem, and a printer. These systems are located at six clinical centers nationwide. An analysis conducted at the beginning of the first ACRN protocol identified the following requirements: (1) standard pulmonary-function testing, (2) standard methacholine-challenge testing, (3) the ability to handle simultaneous multiple protocols as well as have data from non-ACRN subjects, (4) the ability to separate data from different protocols as well as separate ACRN and non-ACRN data, (5) the ability to transmit data from the remote clinical centers to the DCC, (6) the ability to ensure quality data and to report on those results, and (7) the ability to provide remote support. Control Clin Trials 2001; 22:156S–167S © Elsevier Science Inc. 2001

KEY WORDS: Pulmonary-function testing systems, pulmonary-function quality control, modem remote support

INTRODUCTION

The Asthma Clinical Research Network (ACRN) is funded by the National Heart, Lung, and Blood Institute and consists of six clinical centers throughout the United States. The data coordinating center (DCC) is an integral part of this network. Many activities such as data management, research computing, project management, and statistical analysis occur at the DCC. One specific responsibility of the DCC was to develop a system for performing spirometry...
and then maintain this system throughout the life span of the ACRN. Although
the ACRN has continued into a second 5-year renewal period of funding, this
paper outlines the system created for the initial 5-year funding period.

When the network began in 1993, there was minimal electronic data collect-
ion from spirometry machines. The ACRN decided that it was necessary to
collect the data electronically that clinics normally get on printouts and to for-
mat the data into a file for quality control grading. Later, it was decided to
match the graded procedures with the data collected during the actual protocol
so incorrect or poor procedures could be identified.

The initial model for the ACRN spirometry solution was loosely based on
the Childhood Asthma Management Program (CAMP) study as some of the in-
vestigators were part of both clinical networks [1].

This paper discusses the requirements that led to the initial solution devel-
oped by the ACRN DCC. This information is provided to give readers an un-
derstanding of the goals of this project, the solution developed, and finally,
what worked well and what should be addressed for future clinical trials.

ACRN REQUIREMENTS

Prior to beginning the ACRN clinical trials, principal investigators iden-
tified seven key requirements, including the need to create one system to
perform pulmonary-function and methacholine-challenge testing that
would be standard across all of the clinical centers within the ACRN project
(see Table 1).

ACRN Spirometry and Overreading System

The ACRN spirometry and overreading system uses two software packages:
one for the clinics and one for quality control. Data is passed between the sys-
tems via batch files. Although this solution is not the most desirable due to the
number of separate programs and batch files required, it was determined to be
the best fit to the set of defined requirements.

Scientific and Medicine Instruments Software and Clinic Machines

Each clinical center in the ACRN has two complete spirometry and com-
puter systems, except for the New York site, which has only one system. The
type of spirometer used is the 10-L wet-seal Collins Spirometer Survey II
equipped with a Scientific and Medicine (S&M) Instruments analog-to-digital
(A-to-D) converter connected to a serial port on a personal computer (PC).
When a spirometer is operated, an analog signal is produced by a potentiome-
ter and is routed through the A-to-D converter where the digital signal is inter-
preted by the S&M spirometry software (marketed as the Pulmo-Screen IIE/
VRS System, S&M Instruments, Doylestown, Pennsylvania). The software gen-
erates various pulmonary statistics and reports based on the data from the
spirometer. Each clinical center also has a printer to print these reports and a
modem to transmit data electronically to the DCC.
Table 1  Key Requirements for Asthma Clinical Research Network Trials

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<th>Requirement</th>
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| Pulmonary-function testing              | • Respiratory symptoms arise as a result of alterations of the elastic or flow-resistive properties of the lungs.  
• Spirometry (calculations of FVC and FEV₁) is used as a surrogate for more sophisticated tests and is a major component of the evaluation of patients with pulmonary disease. The test identifies the presence and degree of flow obstruction and restriction.  
• Spirometry helps assess the degree of disturbance present, the progress of a pulmonary disorder, and the impact of therapy. |
| Methacholine-challenge testing          | • Methacholine inhalation challenge measures the degree of bronchial reactivity.  
• Increased airway reactivity is a basic characteristic of asthma and to a lesser extent of some patients with COPD.  
• The degree of reactivity is thought to correlate with the severity of inflammation of the airways and is determined from the provocative dose of methacholine that causes a fall in FEV₁ of 20%. |
| Multiple-study capabilities             | • The ACRN is structured to conduct multiple protocols running simultaneously. The systems developed accommodate an unlimited number of protocols.  
• Many of the clinics participating in ACRN clinical trials also participate in other research initiatives that require the use of a spirometer. Principal investigators at the clinics felt it was necessary to use the same system for both ACRN subjects and non-ACRN subjects. |
| Separation of data                     | • Since the clinical centers’ spirometry machines are used for multiple protocols and also for non-ACRN subjects, it was deemed absolutely necessary to separate data accordingly. First, the ACRN data is separated from the non-ACRN data and then separated by protocols. |
| Data transmission                      | • The clinical centers collect data on their spirometry machines. These data are then transmitted electronically to the DCC for the purpose of having a centralized location for all data as well as for quality control assessment. |
| Quality control reporting              | • A primary purpose of collecting the spirometry data is to ensure that the data can be interpreted and graded by an expert in the field. These grades ensure that technicians perform the procedures correctly and collect quality data. |
| Equipment support                      | • Having six clinical centers nationwide necessitates remote troubleshooting from the DCC. Multiple protocols with strict patient-visit windows require intensive scheduling. All centers must have functional spirometry systems at all times. The support solution developed minimizes downtime and shipment of replacement equipment. |

FVC = forced vital capacity, FEV₁ = forced expiratory volume in 1 second, COPD = chronic obstructive pulmonary disease.
The systems are configured to allow data to be gathered for multiple simultaneous trials. By placing multiple copies of the S&M software on the hard drive and configuring the software to store protocol data in the appropriate directories, it is now possible to conduct multiple protocol studies yet maintain the separation of data.

The clinical center principal investigators established the requirement that systems must allow testing of both study and nonstudy patients, because ACRN spirometry systems occupy valuable clinical space. To accommodate the investigators and maintain the integrity of ACRN-related data, the system was designed with strict separation of ACRN and non-ACRN data. To separate the data physically, ACRN data are directed to a discrete partition on the hard disk; other partitions are inaccessible and prevent ACRN data from inadvertently being stored with non-ACRN data. The non-ACRN partition of the hard drive also contains a copy of the same S&M spirometry and methacholine-challenge software for non-ACRN data.

A custom menu developed by S&M allows pulmonary-function technicians to select the study for which a subject is enrolled; this choice directs the operating system to the appropriate programs and storage directories. As another precaution against protocol data being stored in the incorrect directories, S&M Instruments customized a startup menu for the ACRN project. When testing a subject, the technician selects the appropriate protocol based on the subject’s identification number. The S&M software then requires the technician to enter the subject’s identification number and the unique identifier of the technician conducting the test. The first digit of the subject’s identification number determines to which protocol the subject belongs. The S&M software checks this first digit to determine if the subject’s identifier contains the proper digit for access to the protocol software. If the subject identification number does not contain the digit matching the study identifier, the testing process is disallowed. This customized screen choice directs the operating system to the appropriate programs and storage directories and is just a point of entry and is not used to collect data. The customized menu then brings the technician into the main S&M software menu. From here the technician selects the appropriate procedure and must again enter the subject number and the technician number, which are now captured for data analysis.

The S&M main software menu permits ACRN to add additional programs created by ACRN personnel that are useful for technicians. Such programs include a peak flow variability calculator and a body mass index calculator. These programs are called by batch files and are written in Turbo Pascal by DCC personnel.

**Batch Files Data Transfer and Network Setup**

To transfer data files to the UNIX server at the DCC from each ACRN clinical center, the DCC staff provided several programs to S&M. S&M included these as part of the S&M main software menu as discussed above. These files included UUPC/extended V.1.12b (UNIX-to-UNIX copy), tar (a UNIX command for file archiving), and several batch files written by the DCC.

UUPC/extended V.1.12b is a public-domain PC-based version of UUCP written in C that implements peer-to-peer networking using the UNIX UUCP.
protocols. MS-DOS-based PCs can use these protocols to exchange files with a UNIX system over dial-up phone lines. The tar program compresses and extracts multiple files to and from a single file. Once compressed, the single file is transferred via modem to the DCC.

Several DOS batch files were written by DCC programming personnel to transmit files from the clinical centers to the DCC. The files were written to prepare files on the PC for transmission, transmit the files to the DCC UNIX server, and delete successfully transmitted files from the clinical center PC. Prior to transmission, all patient data not previously transmitted to the DCC are moved into a single directory. Next, the tar command is issued to archive the files in the transmission directory into a single file. The single file is then transferred via modem to the DCC UNIX server using UUPC. At the end of the transmission all the files that have been confirmed as successfully transmitted to the DCC are deleted. This prevents the hard-drive capacity of the PC from being exceeded. The data-transmission software is installed on the ACRN-associated hard-drive partition to ensure that only data associated with ACRN-related studies are transmitted to the DCC.

At the DCC, the UNIX server has an account for each spirometer at each center. The accounts are configured to have only download capability. For every corresponding account there is a set of directories on the UNIX server that contain scripts to extract the data. The directory structure is broken down by center, machine, protocols, etc., to keep all data separate. Scripts written in basic UNIX shell scripting are used to extract the data. When a machine finishes transmitting data, it issues a command that starts a script to extract the data into appropriate directories. At the end of the extraction, an e-mail is generated to the appropriate DCC personnel alerting them as to whether the transmission was successful. Centers transmit to the DCC once a week on staggered days, eliminating the possibility of all 11 machines transmitting at the same time. Clinical centers initiate the transmissions to the DCC so that the center’s computers are available for the centers to schedule patients at their convenience.

Remote Modem Software

The system was designed to transmit data via modem for the purposes of analysis, archiving, and quality control monitoring. The modem remote communications software, Close-Up 6.0 (Norton-Lambert, Santa Barbara, California, <www.norton-lambert.com>), was selected to provide hardware and software configuration support for spirometry PCs at both the ACRN clinical centers and the quality control supervisor’s PC.

Close-Up consists of two functionally discrete pieces of software: namely, the host and remote applications. The host program is installed at the clinical centers and runs in the background while another application, such as the pulmonary-function testing software, is running. The remote program is installed on a system at the DCC and allows personnel to view and cocontrol the host (clinical center or quality control supervisor) systems. The remote portion of Close-Up provides the ability to exchange files with the host system automatically via scripts. Security features, such as host screens, keyboard disabling, and password security are also a part of Close-Up. Administrative functions
include record-keeping features such as the recording and playback of sessions as well as transaction logging.

This software allows the DCC to troubleshoot clinic machines remotely, reducing the amount of shipping between the clinical centers and the DCC. This function was required by ACRN to minimize clinic downtime.

Overreading Software and PCs

Before sending data to the quality control supervisor, there are many steps that must occur to convert the data into a format that can be read by grading software. This “packaging” process occurs on a weekly basis and involves taking the proprietary S&M Instruments data format and converting it into a format that is usable by the methacholine-challenge and reversibility quality control software. This software was used by CAMP and was provided to the ACRN DCC by Robert A. Wise, MD, Johns Hopkins University, School of Hygiene and Public Health. A detailed description of the program is available from Dr. Wise. The source code for these programs was originally written in Turbo Pascal and later modified to include several subroutines of Object Professional V.1.1 (TurboPower Software, Colorado Springs, Colorado, <<www.turbopower.com>>).

The first step in this process is to select all data that have been transmitted to the DCC from the clinical centers that have not yet been overread. This step in the process is accomplished by using a batch file that utilizes date parameters to specify the period for which data should be selected. The second step in the process is to copy the selected data from the UNIX server to a PC called the DCC overread PC and is accomplished by using another batch file. The next step in the process is the actual repackaging of the data that were just copied to the overread PC. Following the repackaging, the data from the two individual systems are combined so that the quality control supervisor receives all data from the clinical center, also accomplished using a batch file. Finally, files are visually inspected to ascertain whether they contain data. Files that have no data are deleted. The data are now ready for transmission to the quality control supervisor.

Quality Control Reports

Quality control ("overreading") is an important aspect of spirometric data collection and ensures that results are comparable across several clinical centers over time.

File transfers between the DCC overread PC and the quality control supervisor’s PC are accomplished using the modem remote communications software, the same that is used at the clinical centers. DCC personnel activate the automated communications system (ACS) resident with the remote portion of Close-Up. Using scripts, files from the DCC overread PC are sent to the quality control supervisor’s PC.

Upon receipt of the overread data, the quality control supervisor grades each session using the methacholine-challenge and reversibility quality control software provided from the CAMP study. A numeric grading system is used
by the quality control supervisor to indicate the quality of a session and is based upon the numbers one (best) through four (worst). A grade of "X" is given if the quality control supervisor is unable to evaluate the session. For methacholine-challenge testing, numeric grades are assigned following evaluation of an overall performance.

For reversibility testing, numeric grades are assigned following evaluation of forced vital capacity (FVC), forced expiratory volume in 1 second (FEV\textsubscript{1}), and an overall performance.

After files have been graded, file transfer between the quality control supervisor’s PC and the DCC overread PC also is accomplished via the same script used to transmit data to the quality control supervisor PC. When data are sent for the current week, graded sessions are retrieved from the machine as well. When this occurs, all sessions are retrieved so they can be printed out later. A text file generated by the methacholine-challenge and reversibility quality control software that contains the grades for those sessions is also transferred and gets dumped into a grade database, described below. This text file must be inspected visually to ensure that the software pulled the correct fields to generate the grades.

On a monthly basis, grade reports are sent to each center. These monthly reports consist of listings of all spirometric maneuvers and methacholine-challenge tests conducted for the month by clinical center technicians and the associated quality control grades. A cumulative report lists all grades associated with clinical center technicians for the entire study to date. A bar graph is generated that graphically represents the average grades of all clinical centers to allow comparison of performance among the clinical centers. In addition to these reports, the downloaded graded images of each session are distributed to the clinical centers via paper reports.

The time that elapses from the performance of pulmonary-function testing at the clinical centers until the quality control supervisor evaluates the session is a minimum of 7 and a maximum of 14 calendar days. The variability in time is attributable to the staggered transmission schedule on which the clinical centers send their pulmonary-function data to the DCC. The quality control supervisor has the ability to detect a poorly performed pulmonary-function testing session and contact the appropriate pulmonary-function technician in as few as 7 days. A maximum of 14 days passage of time provides the quality control supervisor with ample opportunity to detect a degradation of performance of pulmonary-function testing.

The grades database mentioned earlier is a DOS relational database management system, Paradox (V.4.5, Borland International, Scotts Valley, California, <www.borland.com>) and was originally utilized in conjunction with the CAMP methacholine-challenge and reversibility quality control software. The relational database management system was retained for ACRN-related grade databases and was installed on the DCC overread system. All additional database reports related to the overreading process and monthly reports are created using Paradox spirometric maneuvers grades. Methacholine-challenge grades are maintained in a separate database.

At the request of the quality control supervisor, DCC programming personnel modified the methacholine-challenge and reversibility quality control software to include the following additional functions:

1. Accommodate ACRN usage of five-digit subject identifiers. The original quality control software utilized a four-digit subject identifier.
2. Include an option to allow the quality control supervisor to select both the next and previous spirometry sessions. The original quality control software allowed the selection of the next session only.

3. Provide the quality control supervisor the capability to both alter and insert grades while reviewing sessions.

4. Permit the quality control supervisor to display individual spirogram loops associated with a specific session.

5. Alter the “look and feel” of the interface to better suit the needs of the quality control supervisor. These changes ranged from cosmetic alterations of the interface to inclusion of information related to a session.

6. Allow the quality control supervisor to enter and edit comments associated with each test for the benefit of the pulmonary-function technician.

After completing the monthly report, DCC personnel query the two grade databases to determine certification status of clinical technicians. Clinical center technicians must conduct spirometry maneuvers and methacholine-challenge procedures under supervision of certified pulmonary-function technicians. Certified status is achieved when a technician performs ten or more passing procedures for both pulmonary-function testing and methacholine-challenge testing. All new technicians are required to obtain certified status. Previously certified technicians can become uncertified by the quality control supervisor and need to reobtain certified status.

LOOKING BACK ON THE SOLUTION (PROS AND CONS)

Looking back on the solution that DCC personnel created to answer the needs of the ACRN, there are some positive outcomes as well as some challenges that remain to be addressed. The pros and cons for each of the ACRN requirements that were defined at the beginning of the project are explained below.

Pulmonary-Function and Methacholine-Challenge Testing

Pros

The S&M software provides a display of the flow rate during the FVC maneuver before and after inhaled bronchodilator, so that alterations can be made. S&M’s software also provides a display of the change in FEV₁ and the FVC maneuver following increasing concentrations of inhaled methacholine, so the degree of reactivity can be assessed.

The S&M software is easy to configure for standard pulmonary-function and methacholine-challenge testing. Printouts done at each clinical center are configurable and easy to understand. For use in a multicenter, multiprotocol environment, it is easy to configure titles and headings so as not to misidentify data received at the DCC. Customized programming done by S&M allows DCC personnel to add ACRN programs that help the technicians in their daily routine, but yet do not require the technician to actually start the S&M software. These programs are used to determine eligibility and peak-flow variability.
Cons

The software itself is relatively expensive, and the spirometry hardware fails on occasion. The ACRN has had to replace many potentiometers, a large expense for the network. The S&M software is written in BASIC and consists of numerous DOS files tied together by menus. While this allows for customization, it does not provide an integrated solution. There is no on-line help or on-line documentation with the system. The ACRN approach is to collect data on separate forms and send them to the DCC. S&M does have software that allows its system to dump data into a database directly. This approach does not allow for data integrity or validation and therefore was not chosen as an option for this study.

Multiple-Studies Capabilities

Pros

Multiple copies of the software allow for data separation between ACRN and non-ACRN subjects as well as separation among multiple protocols. This approach also allows customization of the software to print titles and headings to avoid confusion.

Cons

While ease of customization and configuration is desirable, multiple copies of the same software require numerous changes if the ACRN decides to have data collected differently (e.g., when standards of care are revised, leading to a change in data collection). This means that DCC personnel must reconfigure multiple copies of the same software on multiple machines at multiple centers. It is very easy to misconfigure a system at one center, leading to inconsistency of data. Adding a new protocol or center is easy to do just by making or deleting a copy of the software using simple DOS commands. However, when this occurs, numerous batch files must be edited before being placed on clinical machines, the DCC overread PC, the UNIX network, and the quality control supervisor’s PC. This is time-consuming and susceptible to mistakes if changes are not made at the appropriate places.

Separation of Data

Pros

The system works well if clinical center personnel are careful. This permits possible future analysis with protocol data already being separated. The separation of data also allows easy data retrieval on a case by case basis. The separation of data allows the DCC to pinpoint where to find the data using only subject identifier, date of procedure, and clinical center. This approach allows the DCC to transmit only ACRN-related data while allowing centers to conduct ACRN and non-ACRN visits.

Cons

The separation of ACRN and non-ACRN data can be achieved only if clinical center personnel are careful to begin sessions in the correct partition. It is
the technicians’ responsibility to back out of a partition when they are finished using the software so that the next technician begins the procedure in the correct area of storage. On numerous occasions ACRN spirometry data received at the DCC are mixed with non-ACRN spirometry data. Also, protocol data can be collected in the wrong protocol partition. This occurs when technicians do not back out of the software all the way to the first screen. The only menu that asks for a protocol subject identifier is the initial screen. From that point on, it is possible to enter any demographic data as well as any subject identifier, visit number, technician identifier, clinical center, and so on. Technicians must exercise caution. Also, it also is possible to overwrite patient data if technicians do not back out of the software properly. The separation of data also requires additional batch files to combine protocol data for ease of grading by the quality control supervisor; this requires edits when adding a new protocol to the ACRN study.

Data Transmission

**Pros**

Data transmissions are very easy for technicians to perform because they are all batch-file driven. Transmissions are made weekly to reduce transmission time, keep data files small, and lower phone costs. The staggered weekly transmission schedule that clinical centers use also allows them to transmit with minimal chance of not connecting due to busy signals.

**Cons**

These data transmission files are not part of the S&M software. Each time a new protocol is added or removed, these files must be altered. Technicians must initiate the process and run the different batch files on the machine. Since this is not an automated process, technicians must remember on what day to transmit and make arrangements to transmit to the DCC if the clinic machines are not available. Also numerous configuration files are required to ensure that only center machines can access center accounts on the UNIX server. A strong knowledge of UUPC and UUCP is needed to use a UNIX-to-PC connection using modems.

Quality Control Reporting

**Pros**

Quality control of the spirometric data is necessary to ensure the collection of high-quality spirometric data. By performing quality control assessments of these spirometry and methacholine-challenge tests, it can be assured that these procedures are performed correctly. This quality control process creates high confidence in the data used in analysis as key outcome responses.

**Cons**

The main challenge of the overreading process is that all of the software and batch files have to be developed to work with the S&M software. The CAMP software used is not part of the S&M software and numerous batch files are re-
quired to integrate the programs. These batch files must be initiated manually on a weekly basis and must be executed in a prescribed order. The elapsed time between the initial clinic transmission, overread, and monthly quality reporting is roughly 1 month. Despite the fact that the quality control supervisor can detect procedure problems, the DCC personnel may not be aware of system usage problems until it is too late. Certification for technicians is only checked at the end of each month, which often creates scheduling conflicts at clinics. Due to the nonintegrated nature of all the software used to create this solution, data conversions between software may often not occur, and some incidental data such as dates and comments may be lost. Technicians must avoid using certain characters when entering comments to avoid losing their data in the conversion process.

Other problems with the quality control software include the five digits for subject identifiers. This allows for a limited number of protocols. Using a six- or seven-digit identifier would allow for a greater number of protocols and/or clinical centers.

Equipment Support

Pros

Remote support for the multiple clinical centers occurs almost at the point a problem arises. Technicians can start the Close-Up program, which allows DCC personnel to log on to the machine and begin investigations. With this support system, clinical centers do not lose the use of their spirometry machine until all other avenues have been exhausted. This provides clinics with a sense of reliability that their spirometry machines will be working for all subject visits. Also, technicians at the clinical centers can view the screen and, working together, the DCC personnel and the technician can troubleshoot while talking on the phone.

Cons

For the DCC to log on to the spirometry machines, technicians must actually begin the software and connect their machines to phone lines. This creates some scheduling problems for routine updates for the DCC. Since Close-Up does not handle graphic-intensive programs, software running at the same time as the S&M software often crashes. The ACRN’s distributed system environment creates problems in general that are not unique to the software or equipment.

CONCLUSION

The electronic transfer of data has resulted in a very rapid quality control process. Feedback happens usually within 1 to 2 weeks and ensures that problems are quickly identified and the ACRN is collecting only the highest-quality data.

The ACRN DCC continues to support 11 pulmonary-function testing systems and two quality control systems. Pulmonary-function data from these systems are used as an outcome indicator in studies conducted by the ACRN.
The use of the spirometry systems at pulmonary clinics is a common practice. Perhaps the greater significance is the introduction of remote support and quality control. The system allows DCC personnel to handle technical issues related to the spirometry and spirometry PC without leaving the DCC. All but the most severe hardware problems are resolved remotely at the time of occurrence. This quick turnaround in problem diagnosis has ensured a high level of system performance.

The system as deployed satisfied a significant portion of the established objectives. Data continue to move reliably from the clinical centers through the DCC to the quality control supervisor. Numerous protocols have been implemented with the system without any adverse impact to the network.

While the goal was to create a system that would integrate all requirements, the biggest remaining challenge is data separation. As ACRN moves forward into future protocols the separation of data will continue to require attention. For now, ACRN protocols will continue to collect trial data on paper and rely on printouts with the established quality control process. Clinical center personnel will still be required to exercise caution when entering data into the system.

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