CLINICAL TRIALS
ADMINISTRATOR
An essential resource for managers of clinical trials

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IN THIS ISSUE

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New study suggests CT studies lead to better hospital patient care

All benefit when a few participate

Health care system administrators sometimes believe the investment in clinical trials may not be worth its benefits.

But a new study suggests otherwise. Investigators have found that hospitals that participate in clinical trial research do indeed demonstrate better patient outcomes for all of their patients, including those who are not in clinical trials.[1]

"A lot of administrators and nurses on the ground worry about trials slowing down the emergency department or not getting X-rays done quickly because a nurse is in there with the patient, getting an informed consent," says **Sumit Majumdar**, MD, MPH, an associate professor in general internal medicine at the University of Alberta in Edmonton, Alberta, Canada. Majumdar is the first author on the study.

"So there's often a perception from the hospital perspective that trials are a hassle," Majumdar says.

"We wanted to see if it was a good thing for patients and for a hospital to participate in a trial," he adds.

This particular study was designed a little differently than previous ones that have looked at this issue, he notes.

"There are a lot of studies that look at patients who get into a trial, and they compare them to patients who don't get into a trial," Majumdar says. "And those who get into a trial often do as well, if not better."

But the drawback is that patients who are enrolled in a clinical trial often have fewer comorbidities because of strict inclusion/exclusion criteria, he says.

The study's data came from 494 hospitals that treated 174,062 patients with a specific heart condition over a period from 2001 to 2006. All of the hospitals had collected comprehensive data as part of the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the American College of Cardiology/American Heart Association Guidelines). The patients each had non-ST-segment elevation acute coronary syndrome.[1]

"The hospitals were part of CRUSADE because they were interested in receiving information on how they cared for their patients," says

Matthew Roe, MD, an assistant professor of medicine at Duke University Medical Center in Durham, NC. Roe was a co-author of the study.

"These hospitals probably are the cream of the crop because they volunteered to do this," Roe says. "So if you were to look at every hospital in the United States and look at the data, the results probably would be even more dramatic."

An analysis of the CRUSADE data shows that patients at hospitals that participated in clinical trials to a greater degree received better quality of care, evidenced by better use of proven medications, and better procedures like heart catheterization and angioplasty, Roe says.

"One of our major conclusions is that the structure or infrastructure for care at these [research] hospitals may be different," Roe says. "Integrating research into everyday practice has tangible benefits."

The study specifically found that hospitals that participated in trials had significantly lower rates of early mortality when compared with hospitals that did not enroll patients in trials.

The findings could be markers of better protocols, better physician support tools, and better mechanisms of giving feedback to physicians among research hospitals, Roe suggests.

"We can't tell you the exact reasons why, but we think it's a lot of those things put together," Roe says.

The study shows what can be accomplished when hospitals participate in research and have a team of caregivers and an institution that's interested in doing the best they can do for patients, says **Stephen L. Kopecky**, MD, professor of medicine and cardiovascular diseases, Mayo Clinic, Rochester, MN. Kopecky also is physician reviewer and editorial advisory board member of *Clinical Trials Administrator*.

Kopecky saw the study as having both good and cautionary news.

One of the study's comparisons is the median composite adherence score related to evidence-based guideline recommendations at the 494 CRUSADE hospitals. Even among the group of hospitals that had the highest enrollment in clinical trials, the median adherence to guidelines was only 81%, Kopecky says.

"This is disconcerting that these hospitals that are the best of the best still are not adhering to guidelines," he says.

The most striking finding in the study was the difference in mortality between the patients treated at hospitals with high trial enrollment and those treated at hospitals with zero trial enrollment, Majumdar says.

"We found that there was an almost 3% absolute difference in mortality rates between the high trial enrollment and the zero trial enrollment hospitals," he says. "And that was adjusted for all sorts of clinical factors and characteristics of the hospitals."

While 3% doesn't sound dramatic, in relative

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terms it means that the mortality rate among patients treated at hospitals that were high enrollers in trials was about 20% lower than the mortality rate among patients treated at hospitals that did not enroll in trials, Majumdar explains.

Another finding that suggested better treatment for patients at trial-enrolling hospitals involved CRUSADE's nine quality measures.

"CRUSADE had quality measures that looked at every patient to see if they were eligible for those nine measures, and then it creates a score based on the care they received," Majumdar says.

"So if you're eligible for a beta blocker after a heart attack and you receive one, then your score would be 100%," he explains. "We found that the high enrollment hospitals delivered better care on every single measure."

This study makes a business case for a medium-sized or small-sized hospital to consider selecting a common disease or condition and begin enrolling patients in a clinical trial, Majumdar says.

"It doesn't take much participation in research," he adds. "If you have enough infrastructure to enroll 1% of your patients in a trial, then you're actually doing better than if you never bothered to take part in research."

This particular study did not look at individual patients. "We looked at the average patient treatment at the hospital," Majumdar says.

Researchers used cardiology data because they needed a data set in which patients were asked whether they participated in a clinical trial.

"You'd think that would be commonly asked, but CRUSADE was the only dataset I could find that reliably asked the question across all sites," Majumdar says. "And that's why we were able to do this study, because of the simple question asked of every patient."

CRUSADE involved a voluntary registration of hospitals in the United States. All hospitals participating collected information on how they treated patients after a heart attack or with unstable angina.

Of the total number of patients with the condition, 4,590 or 2.6% were enrolled in clinical trials. There were 145 hospitals that enrolled no patients in clinical trials and others that had low to high enrollment in trials.

"If a hospital was in CRUSADE for five years and submits all patients' data for every year, and if over that time not one patient was participating in a trial, then the hospital was considered to be a [research] nonparticipator, Majumdar says.

"Thirty percent of hospitals never participated in a trial over the entire duration of follow-up care," Majumdar says. "We divided the rest into low and high enrollment, defining low enrollment as 1% of patients in a trial, and high enrollment was 5% of patients or greater were in a trial."

There was a median range of 2-4% of patients enrolled in trials, and there were some large hospitals that had 50% of their patients being enrolled in trials, Majumdar notes.

"That gives you an idea of what can be achieved," he says.

But the reality was that the vast majority of patients were never involved in a clinical trial.

"One of our major findings was that over five years in these hospitals across the United States, 97% of patients never got into a trial," he adds.

Since the hospitals in the CRUSADE study all were engaged in quality improvement efforts, the benefits a non-CRUSADE hospital might gain from clinical trial research could be even more dramatic, Majumdar suggests.

"From a hospital's perspective, it's encouraging news," he says.

While clinical trials require extra effort and staff training, the benefits include improved processes and quality, Kopecky says.

"The secret to clinical research is that when taking care of your patients you quickly take that leap from the research arena and apply [the better care, treatment, or technology] to your patient care," Kopecky says.

"On the other hand, you have institutions that don't do research and are still interested in doing the best they can to take care of patients," Kopecky says. "You don't have to be a hospital that's doing clinical research to give good care, but it certainly helps." ■

Reference

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Recruiting and retaining diverse CR subjects requires focused strategies

Building trust in community is crucial

Often clinical trial sites might have adequate success when recruiting minority patients

to a study, but then they are faced with high attrition among those same patients.

This suggests that when recruiting minority or diverse populations to participate in clinical research, investigators and clinical trial sites should follow a focused and strategic plan that will ensure success both in enrollment and retention, an expert says.

"If we take a more holistic approach to the whole clinical trials industry, we can start a cycle that helps us maintain numbers of certain groups in our trials," says **Daniel Bustillos**, JD, PhD, an assistant professor of health care ethics at St. Louis University in St. Louis, MO.

One project that has taken on this issue is the Eliminating Disparities In Clinical Trials (EDICT) research project. It was started in 2005 as a four-year program by the Chronic Disease Prevention and Control Research Center at Baylor College of Medicine and the Intercultural Cancer Council in Houston, TX, funded by Genentech Inc. of South San Francisco, CA.[1]

EDICT has identified the three 'Rs' of clinical trials, which are recruitment, retention, and return on investment, Bustillos says.

A fourth 'R' was added after EDICT began, and that stands for resources.

Keeping the 3Rs in mind, here are some of Bustillos' strategies for improving diversity in clinical research studies:

• **Recruitment of diverse populations.** "There is a plethora of information out there about what kinds of interventions work as far as recruiting people and which ones don't," Bustillos says. "A lot that work are short-term and have a high drop-out rate."

While this doesn't mean the recruitment strategies are fundamentally flawed, it does mean that they're not coupled with a continued commitment by clinical trial coordinators and researchers and others to do everything necessary to keep people in a trial," he adds.

In some ways recruitment and a community's or individual's return on investment cannot be fully separated because the two work hand-in-hand, Bustillos suggests.

"Outreach shouldn't be an issue because we'll be approaching the community from the very beginning and asserting our commitment to the community," he says.

For example, academic research institutions often are located within urban areas in which the neighborhoods are diverse, Bustillos notes.

"But we often find that people are recruited not from the vicinity or the surrounding neighborhoods, but from the suburbs," he says. "What we've found is that our clinical trials primarily are composed of more affluent middle class whites."

It's a good strategy for researchers to get into their neighboring communities and build trust and interest in clinical trials through a long-term commitment to these neighborhoods, he says.

Physician investigators and other clinicians could offer free health screenings and make a true commitment to the health of these communities, Bustillos says.

"There are a million ways we could prove that commitment by going to a health fair, offering free breast cancer screening, help with the inner city asthma problem," he says.

Researchers and a research institution could make certain that they have a presence at every health fair, parade, and neighborhood celebration, Bustillos says.

"Why shouldn't an inner city research institution have a booth out there and have healthy food," he says. "They could talk about diabetes and give recipes for special diets and that sort of thing."

These kinds of efforts demonstrate that the research institution cares about the community and its problems, he adds.

And it's important that the people who work at the health fair booths or provide outreach into the community are ethnically diverse.

"Those sorts of community ties would go a long way to helping us with that initial problem of how to recruit," Bustillos says.

• **Retention of diverse populations.** "There are myriad reasons why people drop out of clinical trials," Bustillos says. "One is that continued involvement is often much more burdensome than patients first envisioned or that they're first led to believe."

From a trial site perspective, it's crucial to address retention issues because it's a waste of time and money when people drop out, he adds.

"Benefits do accrue to people who are on the trial even though we don't want to coerce people to stay for those benefits," Bustillos notes. "Also, when participants have a good experience on a clinical trial they're much more likely to spread the gospel of clinical trials in their communities and to their loved ones and friends, and they're more likely to participate in another clinical trial."

This, in turn, creates good public relations for the research institution within the targeted community.

The barriers to retention include daunting paperwork, transportation, and child care.

"One thing that comes up over and over in the literature as a barrier is the tangential and incidental costs to participants in a clinical trial," Bustillos says. "These are never fully addressed in a clinical trial protocol."

For example, a major barrier for some populations can be taking the time off of work to participate in the trial, Bustillos says.

"Let's say our population is maybe an inner city minority population, one of the things we'd like to see is for there to be some kind of awareness by research designers that it's a burden for this population to come and be part of the trial," he says.

"For a stay-at-home soccer mom, the burden to come in for a study is a low burden," he adds. "But for the inner city mom who is working two jobs and has no transportation, the burden to come into a research center is much higher."

Clinical trial sites can help ease this burden by providing transportation vouchers, child care during trial participation, and even meal vouchers for participants who might not have the time or money to buy lunch or dinner after participating in a trial.

"Maybe a research center has an on-site child care facility for its employees," Bustillos suggests. "They could make it available on a two-to-three hour basis for someone who needs to come in and do their clinical trial visit."

Another burden for trial participants involves the paperwork and navigation of a large research institution.

"Medical centers are daunting places to navigate from the paperwork to parking, and to some people they might seem like fortresses," Bustillos says.

"So a really good clinical trial coordinator should be good at helping people navigate the clinical trial enterprise," he adds. "And they also should be taught to be culturally competent and linguistically competent for certain populations."

One good suggestion would be for CR sites to have a designated participant navigator who is bilingual and trained in cultural competence, Bustillos says.

"The participant navigator can offer linguistically appropriate help to the population, and this is an expense we'd have to absorb somehow," he says.

• **Return to the community.** Interviews with members of diverse communities have shown that they often have really low opinions of researchers, Bustillos notes.

"From the community member's perspective, researchers often swoop in and tell people what the researcher needs and wants and places a high burden on them to get into a clinical trial," he explains. "Then as soon as the clinical trial is over, they're gone, and they don't give them results or anything."

This type of scenario guarantees that the community will be left hanging, and it leads to resentment and reluctance to participate in future clinical trials.

"We've found that communities that are approached for involvement in clinical trials often feel very disconnected from the enterprise, and there's a lot of paternalism in that realm," Bustillos says. "They don't feel any ownership."

On the other hand, if communities feel from the beginning that they are part of the clinical trial enterprise and process, then they're much more likely to stay in the trial and offer up their participation in subsequent trials, he adds.

One crucial strategy is to form a community advisory board (CAB), Bustillos says.

But it's important to make the CAB more than a board with lip service to the CR enterprise.

"In a lot of studies it seems to us that researchers were going in with preconceived notions of what the problem was and what the answers were," Bustillos explains. "Then they ask for the community's input, but in the process are imposing their needs and telling the community what they want."

Researchers often are unaware of the impact of the power differential and the reality that communities often will bend to the will of the person in the white coat, he adds.

"Often the communities have no input into the research question, and at the primordial stage of a research project they have no input usually," Bustillos says.

"So we involve the community through a CAB and a dialogue-rich and contact-full engagement with the community," he says.

"That's at the design stage," he adds. "Then after the clinical trial is over, we should maintain ties to the community."

This is seldom seen, but it's very important.

"Sometimes in international research, pharmaceutical companies will erect a clinic or have some other lasting presence in the community," Bustillos says. "We'd like to see more of that ongoing engagement with the community after

the clinical trial is over."

The lasting commitment to the community's health will go a long way to letting the community know that they're important and the researchers aren't just there to get their data and leave until the next time they need something, he adds.

"Even if it's just a once-a-year health fair, it would be nice to see the academic medical center be there to reassert that they're concerned about the community's health," Bustillos says. ■

Reference

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Creating role of data manager makes it easier for site to handle all EDC

What's good for sponsors is a headache for sites

One of the ironies of the electronic age is that while electronic data capture (EDC) makes collecting and analyzing research data a more efficient process for sponsors, it often is costly and challenging for clinical trial sites.

There probably are more than 20 different EDC systems that any single CT site might see, and CT staff have to learn each of these EDC programs, says **Debra Gabrielson**, BSN, RN, research administrator of Regional Clinical Research Inc. of Endwell, NY.

"We have to learn the program the sponsor is using to collect the information," Gabrielson says. "So research coordinators who are working on five or six studies might have five or six software programs to use."

This adds considerably to the front-end costs of conducting a clinical trial.

"The hardest part for us was how much time it took a coordinator, who might be a nurse, to be trained on a software program," Gabrielson says. "The coordinator might spend hours training, receive a certificate, and wait months to start putting in data."

Then there will be the headaches of passwords that don't work and other EDC glitches.

"It took us way too much time doing data entry," Gabrielson says. "It was taking us hours more per visit to do this."

So Gabrielson came up with a solution: She designated a coordinator to the role of data entry.

"We had a coordinator who was very good at computers, and she puts in all data for all of our studies," she says. "She makes herself available when we have monitoring visits, and she has a certificate showing that she's trained."

Researchers and research staff give her their source documents and notes, which she reads and then types into the EDC program.

"Since she's a coordinator she knows the kind of information that's needed and the correlation needed with adverse events, concomitant medication, and medical history," Gabrielson notes. "So it's a nice double-check, and if something's not complete, she can go back to the coordinator and have it clarified."

This provides the added benefit of another quality assurance check.

While this change has solved some problems, there remain other issues.

For instance, investigators have to review the electronic data pages to make sure everything is accurate before signing off on them with cumbersome electronic signatures that are more time-consuming than a handwritten name, Gabrielson says.

And for investigators, the EDC training is yet another time commitment and training program they have to add to their protocol training, good clinical practice (GCP) training, and, sometimes, special questionnaire training, she adds.

Also, the site needed more computer stations, which is expensive both in the initial purchase and also in the maintenance of the computers.

"We have to have virus protection and Internet access and pay for that," Gabrielson says. "That's something that shouldn't be minimized — every little bit adds up for a site."

The site designated a separate room for monitors to use when they're accessing the computer files, and the room needed to have Internet access.

All of these expenses can result in thousands of dollars per year.

"EDC takes us longer, and it's not that we don't agree that it's an efficient method," Gabrielson says. "But some sponsors are recognizing how much it costs sites and are increasing what they pay." So Gabrielson tries to get sponsors to cover a one-time fee for EDC training.

The data coordinator has to be trained to use the specific software, and at least one additional person has to be trained as a back-up.

"The problem is that you have a password, so we have to have a few people trained with the password so that we can have access to the information when needed," Gabrielson says.

"What do you do when if the only person who knows the password isn't in the office and the monitor needs some information?" she asks.

Still, it's asking a lot of sites to have them absorb the costs of EDC training, which typically can last four hours.

"Sometimes we have sponsors who pay the training fees," Gabrielson says. The site also tries to have sponsors pay an increased coordinator fee for each visit to cover the time spent on data input.

"Some sponsors do have data capture fees, which I appreciate because they recognize the time it takes to put it in," Gabrielson says. "There is a learning curve — once you learn it you can get better at it."

This is why it saves the site some time to have one person take the lead on data capture.

"I recommend using a medical person," Gabrielson says. "Our data coordinator has worked as a study coordinator before, and she's an LPN."

In this particular case, the role worked out well for both the CT site and the coordinator, who wanted a part-time and more flexible schedule after having a child, she explains.

"She can do work at home at night if needed," Gabrielson says.

Typically, the data coordinator will come into the office, boot up the computer, start taking charts and putting in data from all of the visits, she adds.

"She works in the same office as the coordinator and can get answers from coordinators," she says. "You have to find the right person, just like finding the right coordinator."

A good match for a data coordinator role might be someone with a medical background who is detail-oriented, Gabrielson suggests.

"It worked out for us that we had someone who liked EDC and understood what it meant and who liked working on her own time," she adds.

Study coordinators initially were resistant to the change because they feared that it meant giving up some of their control over the data they collect, Gabrielson notes.

"But after they did it this way for a while, they loved it," she adds. "It gives the coordinator more time to see another patient rather than to have to sit down and put in data after each visit." ■

Compliance Corner

Set up 'research insurer' to keep CT billings accurate and compliant

Financial analyst reviews all charges

Research billing might continue to pose challenges for hospital research centers, but there are specific steps they can take to ensure accuracy and compliance with all regulations.

They key is to make certain there is correct interpretation of the rules, solid policies and procedures, thorough budget analysis, and continual checks and balances. Then, professionals representing all of these perspectives need to meet and discuss how to improve or establish a billing process that is as airtight as possible.

"Get all of the correct people in the room, including the process people who are in charge," says **Patricia Bass**, JD, MPH, an associate general counsel at the Boston Medical Center in Boston, MA.

"You need the frontline people because they know exactly what happens when someone comes in the door," Bass says. "You need people from legal and compliance to say, 'These are the official rules,' and you need research staff, faculty investigators, and the billing office."

Often, great solutions come out of this process of putting so many different people together.

For example, at Boston Medical Center, the billing staff suggested that they set up an insurance company model that could be used to hold all patient care charges that would be paid through the clinical trial agreement, Bass says.

Bass describes additional ways a clinical trial site can improve its billing process and ensure compliance:

• **Provide a financial analysis of proposed study.** Financial analysts can work from the moment when clinical trial protocol negotiation begins to see which charges would be related to the research intervention and which would be

allocated to Medicare or insurance.

"What is and isn't paid for by the sponsor has implications for budget negotiation," Bass says.

The analysis relies on what the protocols say is routine care and what is not. Also, the analysis provides information about what expenses are associated with the trial, such as training for the research coordinator staff, Bass says.

The end result is a list of what cannot be billed to Medicare.

"Then we are able to say to sponsors, 'It's our best estimate that insurers won't pay for these things so if you want us to do the study this is how much money we need," Bass says.

• **Form spreadsheet listing all costs.** At BMC, the grants department sets up a spreadsheet, listing each procedure and where it will be billed, Bass says.

"This is before the insurance company is set up," Bass says.

"They rely on the financial analysis about what is covered under the cover decision," she says.

The spreadsheet should include costs that sometimes aren't directly reimbursed, include the IRB submission and review, a clinical trial office fee, records storage, and other indirect costs, Bass says.

Then the grants office uses the new information when completing negotiation with sponsors, Bass says.

• **Set up billing entity for research costs.** When a research insurance company is created, it's given a number and a starting and ending date, Bass says.

"They set it up as though it is an insurance company, and this makes it easy when the charges come through the system," Bass explains.

The fictional research insurance company then is the entity that receives all of the charges that cannot be billed to Medicare or an actual payer.

"When the research subject comes in to have a procedure done, he reports to the study coordinator and is registered using the fictional insurance company," Bass says. "Instead of listing Medicare or Blue Cross as the insurer, it lists the research insurance as a billing source."

• **Checking for compliance and accuracy.** "All of the research insurance charges are reviewed by a clinical trial financial analyst and the grant staff for anything that has been released for billing to a third party," Bass says. "The charges are reconciled to make sure that they were done correctly the first time."

One issue that makes it more complex is that since research participants often have already been seen as patients in the hospital, they will have an existing patient registration.

To avoid confusion, these patients, when they become research participants, have to be registered again, Bass says.

So all research participants are given a new registration number, and this is what's used for their billing during the research trial.

The clinical trial financial analyst then reviews all charges for research participants to make certain they're billed under the correct registration number and to the correct payers.

Sometimes a research participant will come into the hospital for a regular, non-research associated procedure, and this charge will accidentally be categorized as a research insurance charge, Bass notes.

When this happens, the financial analyst will undo the charge and make certain it's sent to the correct payer under the correct patient registration number, she adds.

The legal team provides oversight of the rules and regulations, to make certain everyone on the research team knows when changes take place, Bass says.

"My job is to look at the various Medicare rules and national coverage decision," she adds. ■

Today's CR challenges bring past trends to critical juncture

Tighter budgets, more oversight among issues

Clinical research in the 21st century is no less important than it was in the last century, but changes in how studies are conducted and regulated have made the business much more difficult, an expert says.

"I think there are a number of challenges now, and it's to the point where it's unclear to me if the reward exceeds the challenges," says **Colleen M. Schmitt**, MD, MHS, FACG, FASGE, chief of the gastroenterology section of Galen Medical Group in Chattanooga, TN.

Schmitt has published a paper about how tighter budgets, increasing competition and litigation costs, more oversight, and financial headaches have led to a challenging environment for clinical trial sites.[1]

"I don't mean to be a pessimist, but the reality is that clinical research has changed in the last 15 years," Schmitt says.

For one thing there are more litigation risks with a growing entrepreneurial niche for trial lawyers, she says.

"What that translates into for sites is there are many more risks that are unknown," Schmitt says. "It's like Whack-a-Mole, you fix one problem and another problem comes up that you didn't know was a problem."

The second major change in the past 15 years is an increase in regulatory burden for clinical trial sites, Schmitt says.

"That was sparked on the national level by disasters that occurred at academic sites," Schmitt explains.

The instances of bad publicity for clinical research have led to a public view that some private medical research sites are mercenary and coerce patients to participate in clinical trials for the sake of generating profits, Schmitt says.

"Nothing could be further from the truth," she says. "Sites operate on increasingly tight budgets."

The budgets are constructed with a fee schedule that's based on the protocol's physical requirements, she adds.

While there's a push among the National Institutes of Health and FDA to increase diversity in clinical trials, there also are greater enrollment pressures and competition among trials.

"And they want you to increase enrollment among populations that have traditionally been fearful of the clinical trial process because of disasters like the Tuskegee syphilis study," Schmitt says.

"There are big pressures related to the way protocols are implemented," she adds.

"A site that has been trained carefully in good clinical practices and is meticulous in informed consent and enrollment criteria can operate in this field successfully," Schmitt says. "But the less well-trained sites may not be as savvy about how careful they need to be when working in this kind of environment."

Today's protocols require more procedures and more face-to-face time with participants, and sponsors have taken the attitude that this is the site's cost of doing business and it's non-negotiable, Schmitt says.

Given these current financial pressures, it would be naïve for any new investigators to believe that research is a cash cow, she adds.

"It was possible in the early 1990s as the shift moved trials from academic medical centers, which were very expensive, to sites in the community that they could operate on a profit," Schmitt says. "But that was then and this is now."

Clinical trial sites will survive in today's environment only by understanding the costs of doing business and by being cautious about hidden costs. **(See story about strategies to survive in CR, p. 70.)**

"Most of the uncompensated costs are uncompensated salary for hours devoted to study start-up, screening patients, attending meetings, and screen failures," Schmitt says.

The single most important investment investigators can make when starting clinical research is to hire a qualified clinical trial coordinator, Schmitt suggests.

"The FDA doesn't require certain education or training," she adds. "What's key is that the individual you hire is highly self-motivated and an independent worker."

The ideal clinical trial coordinator will be someone who doesn't require continuous oversight and coaching, but is a person of unquestionable integrity and is very detail-oriented, Schmitt says.

Investigators might find such individuals among nurses or phlebotomists, she adds.

When physicians first begin to conduct clinical trial research they could create a good research site by making certain their research staffs are well trained and highly motivated.

"But it all hinges on the training, and they must have adequate time to perform the task required," Schmitt says. "Clinical research is not an area that can be rushed."

For many nurses, clinical research affords them time with patients that they haven't had in years.

"They can spend as much time as they need with each patient to discuss the procedure and provide informed consent," Schmitt says. "It's an ongoing and time-consuming process, and if they feel rushed or distracted by other clinical responsibilities then it's a recipe for failure."

So with the increasing number of challenges to conducting clinical trial research, why do physician investigators continue to work in the industry?

"That's a question I review continuously, but I've thought about it more in the last few years," Schmitt says. "You have to weigh financial and legal risks against benefits."

For example, in Schmitt's role as a gastroenterologist, one of her key benefits is having access

to key therapeutic agents that may not be available to physicians who are not researchers.

Since many Crohn's disease patients have failed existing treatments, it would be difficult for physicians to treat them without having access to clinical trials, Schmitt says.

Another reason to conduct clinical trials is an altruistic one: "There is so much that is unknown and could potentially benefit others," she says.

Building trust and esteem among patients are also good reasons to do research. "Patients enjoy seeing a physician who is on the cutting edge of health care," Schmitt says. "Communities take pride in having an academic research health care center, and most physicians doing it are interested in advancing health care." ■

Reference

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Expert offers strategies for survival in today's CR environment

Formal SOPs, training necessary

Clinical trial investigators and professionals who hope to survive the regulatory and other burdens inherent in today's clinical research (CR) industry might take some tips from successful sites.

For instance, it's important to make certain all staff receive a thorough on-site orientation and training, says **Colleen M. Schmitt**, MD, MHS, FACG, FASGE, a long-time investigator and the chief of the gastroenterology section of Galen Medical Group in Chattanooga, TN.

Budget negotiation, the finances of clinical research, and compliance issues also are challenges for CR staff and sites.

Schmitt offers these suggestions on how to handle the challenges and improve your site's performance:

1. Invest in a comprehensive staff training program. "Our orientation and instruction process lasts two weeks and it's formalized and written," Schmitt says. "We have standard operating procedures [SOPs] that are updated regularly, and they're required to become very familiar with those."

Research staff must review and thoroughly understand the SOPs, and they must take an online training course through the National Institutes of Health, she adds.

"Also, we require attendance at a good clinical practice conference that we started in Chattanooga six years ago," Schmitt says. "It's a two-day conference for investigators and clinical research coordinators."

The conference reviews these elements: contracts, budget negotiation, litigation risks, national updates, changes in rules and regulations at the FDA, and clinical trial reviews, she says.

"Also, we participate in a forum in Chattanooga that was started by our wonderful compliance officer," Schmitt says. "It's for clinical research coordinators, and it's a monthly brown bag lunch that they review and openly discuss."

Among the topics discussed are inclusion/exclusion criteria and protocol violations.

"Even in small areas like Chattanooga, which is not a big city like Los Angeles or Chicago where there are hundreds of research coordinators and millions of subjects, you can develop good resources and training for people," Schmitt says. "You have to be determined to do it."

2. Treat every budget as negotiable. "If I thought a budget was non-negotiable, the discussion is over," Schmitt says. "Nothing should be non-negotiable because sites are not cookie cutters, and everything varies."

The first step is to do a very careful review of the protocol, she says.

This means looking at more than the timeline and trial procedures.

"Review how much time each activity will require, and look for the hidden costs," Schmitt advises.

"We use a simple spreadsheet, and we know how much it costs to do an EKG exam and a physical exam or a screening visit and informed consent," Schmitt says.

If the costs exceed what the sponsor proposes in the budget, then it's time to show the sponsor your data and negotiate a more sensible budget. Or sometimes the solution might be to change the protocol to reduce enrollment costs.

"Sponsors respond better to data than emotion," she says. "You need to say, 'If you keep this exclusion in the protocol then in our experience your screen failure ratio is going to be 5:1 instead of 4:1, and here's why I'm telling you this.'"

When given data, sponsors are much more likely to respond and make changes, she adds.

"There occasionally are reasons to participate in a protocol when you know you're going to lose money," Schmitt says. "And we'll do that if there's a particular therapeutic area we want to break into, or if there's a novel therapeutic that we think has potential."

Or there might be an opportunity for several studies from that sponsor or there might be a principal investigator who has access to a large number of poor patients who need an opportunity for therapy and have no other choices, Schmitt says.

"There are many sites that are quite altruistic," she says.

3. Know what you're signing in the contract. "One of the big concerns I have, and I see it all the time although it still surprises me, is how novice investigators sign the contract without reading it or understanding it," Schmitt says.

One area of the contract that is accepted without challenge is the cross indemnification, Schmitt says.

"My personal opinion is that physicians have no business indemnifying big pharma," she says. "It's the transfer of risk regarding informed consent to the investigator."

But PIs have no long-term gain invested in the product, and the pharmaceutical company has everything to gain, Schmitt notes.

"Pharmaceutical companies should be indemnifying the investigator because otherwise the investigator is standing alone there," she adds.

Yet, sponsors expect PIs to sign contracts with the indemnification clause, and Schmitt refuses to sign it.

"I really urge sites to review their policy on that subject," Schmitt says. "The majority of time the pharmaceutical company will send us an indemnification letter, and they will indemnify us as they should do."

4. Be wary of disadvantageous fee schedules. "For reasons that escape me except that it's tradition, this is the only business where the payers don't pay their bills on time," Schmitt says. "On average, there is a half-year delay in payment."

This means that clinical trial sites essentially are floating a loan to pharmaceutical companies, she says.

"When you have a discussion with them about this, the rare company will say they'll agree to monthly payments," Schmitt says. "Most of them have never had to do this before, and no one has ever held their feet to the fire."

Nonetheless, this is a practice that should stop, Schmitt says.

"Even more ridiculous is the concept of block payments or payments that are tied to performance at other sites," she adds. "Those are terrible — but a novice investigator would not recognize the language in the contract."

While individual investigators can improve their own sites' financial and overall performance by focusing on these areas, it ultimately will be up to the CR industry to make changes that will encourage rather than discourage new investigators and sites, Schmitt notes.

"It'll never change unless we do it," she says. "This is not an easy field to break into, and I would encourage people who are interested in

CNE/CME Objectives / Instructions

The CNE/CME objectives for *Clinical Trials Administrator* are to help physicians and nurses be able to:

- **review** pertinent regulatory mandates;
- **develop** practical clinical trial oversight strategies;
- **review** best practices shared by facilities that successfully conduct clinical trials.

Physicians and nurses participate in this medical education program by reading the issue, using the provided references for further research, and studying the questions at the end of the issue.

Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity at the end of each semester, you must complete the evaluation form provided and return it in the reply envelope provided to receive a letter of credit. When your evaluation is received, a letter of credit will be mailed to you. ■

COMING IN FUTURE MONTHS

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■ Watch for these new CR technologies

this business to attend national meetings where they can gain a lot of insight from their colleagues." ■

CE/CME *questions*

21. A new study that compares patient outcomes among research hospitals versus hospitals that have no patients in clinical trials reports which of the following finding?
    A. There is no difference between outcomes for patients at research versus non-research hospitals.
    B. Patients at hospitals that have clinical trials typically reported more optimism and confidence in their medical care.
    C. Patients at hospitals that have clinical trials have better mortality rates and other outcomes than do patients at hospitals that have no clinical trials.
    D. None of the above

22. When clinical trial sites focus on improving diversity among their participant pool, it's important to focus on which areas?
    A The 3 Rs: Recruitment, retention, and return on investment to the community
    B. Offering the right incentives
    C. Marketing the study's benefits to individuals and the community
    D. All of the above

23. Clinical trial sites could solve some of their problems with electronic data capture (EDC) by hiring a data coordinator to handle all EDC. What are the potential benefits of having a data coordinator?
    A. One person will learn the various software programs and eventually need less front-end training to a sponsor's EDC system.
    B. The data coordinator reviews the information collected and could serve as a checks and balance.
    C. Having one person handling data input will free study coordinators from some of the paperwork and give them more time with study participants and other tasks.
    D. All of the above

24. When sites analyze a protocol to determine how much it will cost, which of the following items should be included in any budget spreadsheet?
    A. The cost of an EKG and other procedures
    B. The cost of a screening visit
    C. The cost of providing informed consent
    D. All of the above

Answers: 21. (c), 22. (a), 23. (d), 24. (d).