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INSIDE

Smartphone apps are a new frontier for minimal risk studies

Informed consent, security are big considerations

Over the last few years, the use of smartphone apps in minimal risk research has grown substantially. Researchers test the effectiveness of apps in tracking subjects' physical fitness, managing chronic conditions, tracking symptom progression, and use in areas such as smoking cessation. A search for "smartphone" in ClinicalTrials.gov shows 275 registered trials using the devices — up from 45 in late 2012. *(For more information, see "Ensuring clinical trial compliance? There's an app for that" in the December 2012 issue of* IRB Advisor.*)*

Now, entire research studies are being run through a handful of apps, released in mid-March, through the iTunes App Store. These apps consent study participants, determine eligibility of participants, and run study tasks — all without the need for participants to travel to study sites.

These studies are minimal risk and include the following:

• Asthma Health, an asthma symptom-tracking app study run by Icahn School of Medicine at Mount Sinai and Weill Cornell Medical College, both in New York. The app also uses GPS tracking to provide air quality updates in users' locations.

• mPower, developed by the University of Rochester in New York and Sage Bionetworks, a nonprofit research institution in Seattle. The app collects data on gait, voice changes, balance, dexterity, and memory in subjects with Parkinson's disease.

• Share the Journey measures long-term post-chemotherapy symptoms in

> "I KNEW RIGHT AWAY THAT THIS WOULD BE A NEW AND INTERESTING AREA WHERE PEOPLE HAVEN'T DONE ANYTHING YET."

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breast cancer patients. The study was developed by Dana-Farber Cancer Institute, University of California-Los Angeles Fielding School of Public Health, Penn Medicine, and Sage Bionetworks.

• GlucoSuccess, run by Massachusetts General Hospital, seeks to understand how diabetic patients' lifestyles affect glucose levels.

• MyHeart Counts, which uses participants' physical activity and lifestyle information as well as surveys to evaluate risks of cardiovascular disease. The study is run by Stanford University in CA, and University of Oxford in the United Kingdom.

Investigators can use apps to harness the features and data-gathering abilities of the smartphone, experts say.

"There is potential for great value with this type of data," says **David Forster**, JD, CIP, chief compliance officer of WIRB-Copernicus Group (WCG) in Princeton, NJ. WCG's subsidiary, Western IRB (WIRB) is the IRB of record for the mPower and Share the Journey studies. "A lot of researchers believe they have good methods to come up with data and remove the noise. There is potential for this type of information to grow."

The studies can also have a massive reach: By conducting a study through an app, subjects do not have to live near a study site to participate, which means researchers could have a much larger subject pool. "You can get a cross-section of the population; you can get people from every nook and cranny [of the country] and the only requirement is that they have an iPhone and you're not geographically limited to people who live near the research site," says **Jeremy Block**, PhD, MPP, assistant professor of Population Health Science and Policy, and an IRB chair/vice-chair at multiple hospitals within the Icahn School of Medicine at Mount Sinai in New York City.

Within two weeks of the app's March release, 5,000 subjects had enrolled in the study. "Sometimes it can take years to get 300 people for a study," Block says. "There are a lot of potential benefits for doing research this way."

Bringing these studies to smartphone apps was not without challenges: There is very little in the way of guidance for such studies, and issues such as data security and informed consent were at the top of the list.

"It's absolutely a new area, and it's been a part of our challenge," says **John Wilbanks**, chief commons officer at Sage Bionetworks.

The original idea for the studies was to use an open source Web platform that would allow patients to participate more directly in research, Wilbanks says. "In working with certain patient communities with Parkinson's disease and breast cancer, we can get into their phones to get them more into research and measure post-chemotherapy cognitive ability in cancer patients, and Parkinson's disease symptoms. We can get quantitative data from sensors in the phones and qualitative data from surveys without patients going to a clinical site. Since [the phones] can return results easily and track progress easily, mobile was where our charge would take us."

Back to basics

Ensuring that the studies fell within the regulations meant going back to basics, Block says. The interdisciplinary team of investigators who created the Asthma Health app approached Block about lending an

IRB perspective to the development process.

"They approached my boss — the Senior Associate Dean for Research, Jeff Silverstein, MD, — and asked to have a conversation [about the app] because they wanted to talk about their idea and anticipate any issues," Block says. "I knew right away that this would be a new and interesting area where people haven't done anything yet. It was a purposeful choice on my part; I know the regulations and what needed to be considered during the design process of the study and the consent, and I wanted to be in it from the beginning."

Block went step by step through the protocol to make sure all regulatory questions were answered. "For the consent process, confidentiality, security, how the individual will interact with the app — for all aspects, I asked all of those questions and if the answers weren't enough, I said, 'Let's do more here and brainstorm how to accomplish it. If I was a reviewer, I would ask these 15 questions, so let's sit down right now and try to answer them.'"

Multi-tiered informed consent

Ensuring subjects fully understand the study objectives and informed consent was another challenge, Block says. Since there would be no face-to-face interaction with an investigator to explain IC, the team took advantage of the smartphone capabilities to offer multiple IC methods within the Asthma Health app. "After reviewing IRB literature and in conversations with others, we found it's preferable to have multiple modalities [of informed consent] to interact with a subject," he says. "There are three different modalities for consent and interacting with the subject and making sure they are fully informed — three different ways to try to do it is pretty good."

The three methods include:

• A brief video in which investigators explain the purpose of the asthma study.

• An interactive consent in which participants can swipe through brief explanations of the data-gathering process, time commitment, privacy, potential benefits, study tasks, and other information. Most of these screens include a Learn More button, which participants can tap to read more details about each item. There is a three-question quiz at the end of the interactive consent, consisting of true/false questions and information reinforcement.

> "WE THINK OF THE PROCESS WE DESIGNED AS A WAY [FOR PARTICIPANTS] TO FIND AS MUCH INFORMATION AS THEY WANT."

• A longer form "that is a normal consent document," Block says. After reviewing the consent document, participants can tap "Agree" or "Disagree" to continue. If "Disagree" is selected, the consent process is canceled.

"Something we also took into account when we discussed the consent process is that, since it's not a treatment study and there is no clinical care in any way, shape, or form, we could not have pulmonologists on call 24/7 for the unknown number of people who would sign up," Block says. "It's not a reasonable way to conduct it. We made it very distinctly clear that this [study] was not care or offering care. I think in order to provide clinical care through an app, the world would have to solve the telemedicine problem first."

The multi-pronged consent approach was also best suited for the mPower and Share the Journey apps, says Wilbanks. "If we were going to do this with a larger sample size of people, we knew we would have a consent process without a clinician talking to every patient," he says.

Consent includes a tiered hierarchy of information, he says. "There are different layers of information — it's not acceptable to just click 'Accept'."

The first level "is primarily pictorial information to communicate essential concepts for the clinical studies," Wilbanks says. The second level, Learn More, "has the text document in there so they can follow their nose from the high level of information to the details," he says. "The third tier is the actual informed consent. We think of the process we designed as a way [for participants] to find as much information as they want. We think it's appropriate because these studies are very low risk."

When approving the consent, the IRB took into account that the consent would be read from a distance without investigator interaction, Forster says.

"It's kind of a confusing regulatory area," Forster says. "The board has to determine whether there is sufficient electronic consent, or whether a waiver of consent is appropriate for a minimal risk study. Oftentimes what we do with e-consent is waive

documentation of consent. For these studies, subjects click through [the consent] and take the test at the end, and that's sufficient for documentation of consent."

There was an intensive six-month period to improve the informed consent after initially presenting the mPower study to WIRB, Wilbanks says. "As we built out the apps and worked with Apple, we made the consent process prettier with better graphics, better phrasing, and more accurate details," he says. "We worked with WIRB over six months with a series of revisions and amendments as we built out the governance and technology to make sure our protocol was consistent with the study we launched — something that brought together the cultures of independent review and software development."

The developers also took the time to educate the IRB on mobile apps, Wilbanks says. "It was a growth opportunity to teach IRBs about what mobile devices can and can't do," he says.

One of the main questions in the development process was the privacy risk, Wilbanks says. The Sage-designed apps are using cloud services on the back end, industry-standard encryption, and there is no data bleed to other apps. "The privacy risk was the top-tier risk," he says.

"One of the things that was really interesting from an IRB perspective is that we were really careful to describe in a flowchart the kind of information that would be collected, where it would be collected, with whom it would be shared, and to what level of security," Block says. "If the people creating these apps have to go to the IRB, they have to be incredibly clear about what is going on in the app. This was a lot more detailed than any study I've seen."

Mobile apps such as these are better suited for low-risk observational studies, Wilbanks says. "It might not fulfill obligations on a more complicated scale such as genetic studies," he says. "We're going to see quite a bit of kicking of the tires. We're going to learn and ton and see what developers show up and what apps appear in the app store."

Block is planning to write a paper on the outcome of the app project and what the IRB community can learn from it. "This is an all new ballgame and I hope they're all successful and learn things from people — subjects and researchers — who didn't have access [to studies] before," Block says. ■

OHRP and FDA address electronic informed consent

FDA permits electronic signatures

Federal regulatory agencies acknowledged in recent draft guidance that research informed consent is moving in directions not quite imagined several decades ago.

The Food and Drug Administration (FDA) and the Office for Human Research Protections (OHRP) published draft guidance for industry, clinical investigators, and IRBs in the "Use of an Electronic Informed Consent in Clinical Investigations" in the March 9, 2015, *Federal Register*.

The agencies note that this is part of their efforts to harmonize their regulatory requirements and guidance for human subject research.[1]

The FDA's draft guidance applies to FDA-regulated clinical investigations, but OHRP might adopt the same positions and recommendations for non-clinical research.[1]

"FDA actively worked with OHRP in developing its draft guidance document on this topic," says **Irene Stith-Coleman**, PhD, director of the division of policy and assurances, OHRP.

Before deciding whether to issue a final joint guidance document on the topic, OHRP and FDA will review and consider all submitted comments, Stith-Coleman adds.

The FDA's Q&A states that electronic informed consent (eIC) must contain all elements of informed consent required by FDA regulation, and if it's interactive, it should be easy to navigate. Subjects should have the ability to move forward or backward within the system and to stop and continue at a later time. The eIC also should be presented in a manner that minimizes possible coercion or undue influence.[2]

FDA also says that when written IC is required, electronic signatures can be used and is equivalent to handwritten signatures. Clinical trial sites could use an encrypted digital signature, electronic signature pad, voice print, or digital fingerprint, for instance. The electronic system also must capture and record the date of the signature.[2]

In general, central IRBs are very supportive of electronic informed consent, says **John Isidor**, JD, chief executive officer of Human Subject Protection Consulting in Cincinnati. Isidor also is an editorial advisory board member for *IRB Advisor*.

The electronic consent process provides opportunities for helping research participants better understand a study, he notes.

"Hyperlinks to videos and things like that could assist subjects in their understanding," he says.

The only issue is the electronic signature, Isidor adds.

Technology that would provide a secure electronic signature could be very expensive for research institutions, potentially making eIC cost prohibitive, he says.

"I was at a recent meeting where electronic informed consent was discussed by a sponsor, and he said a template would cost between $100,000 and $300,000," Isidor says.

It also seems probable that eIC would require sites to present subjects with self-contained tablets, which are easier to control than using computers that are integrated into their computer systems, he adds.

Electronic informed consent already is widely used in social-behavioral research and studies conducted on the Internet, Isidor notes.

"I don't believe [the guidance] is anything novel or ahead of the curve," he says. "It's behind the curve, but those who are more risk averse might wait for a comment from a federal regulator before they engage in research with electronic informed consent."

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Clinical research training course provides interactive instruction

IRB staff feedback helps improve it

Human research protection program (HRPP) training at the institutional level often lacks uniformity and evidence-based strategies, some experts say. Some organizations and research programs require new investigators and IRB staff to have extensive online coursework or on-campus classes, and others provide only general guidelines and requirements.

A centralized, evidence-based approach could be an answer to making certain all parties affiliated with a large research organization are well educated on regulatory topics — this was why one HRPP's mission was to create an educational session that ensured all investigators were familiar with what they needed to navigate clinical research and ensure compliance.

"This class helps all students go back to their offices and operationalize, and that's why it's called 'navigating clinical research,'" says **Tina Chuck**, MPH, manager of research policy and training at North Shore-Long Island Jewish (LIJ) Health System in New Hyde Park, NY.

The interactive class includes classroom-style learning combined with technology, group discussions, and hands-on activities.

"We transformed the lecture into more interactive adult learning, which makes it more effective," Chuck explains.

Chuck and co-authors studied the training course's effectiveness and found that the course was well received by researchers and research staff and that participants found the information to be simple and appealing.[1]

Three tests are given to course attendees: one before taking the course, one immediately after completion, and one three months afterward. The results showed that people retained the information they were taught, and — even more importantly — they returned to their offices and made changes based on what they had learned, says **Dorean J. Flores**, CIP, IRB manager at North Shore-LIJ.

"They told us the course helped them, and it did what it was intended to do to provide information about the overall process of clinical research," Flores says.

"We've had a lot of positive feedback, especially from investigators on research compliance," says **Richard Ramdeo**, CIP, IRB manager at the health system.

"The course gives them a good overview of everything they need to know," he adds. "Our staff and employees taking the course also gave positive feedback."

After taking the course, communication between the IRB and other departments improved, and IRB reviews were more efficient for investigators, Ramdeo says.

The training course was created as a one-day class, offered once a quarter, with 25 to 30 attendees. Based on early feedback, they converted into a two-day class. The health system does not require all research staff to attend the class, but some research programs make it mandatory for new hires, Chuck notes.

Also, the IRB will mandate the course for researchers and their staff on a case-by-case basis. For instance, if the IRB is aware of a regulatory compliance issue with an investigator or research team — such as deficiencies in obtaining informed consent — then the IRB will require them to take the Navigating Clinical Research course before continuing with the study, Flores says.

The first day shows attendees how to navigate the HRPP process, and the second day covers good clinical practice and clinical trials of devices and drugs, Chuck explains. *(See story on day-to-day coursework, page 55.)*

Part of the course's success is due to the way it relies on multiple types of learning strategies. There are lectures, but there also are group discussions and activities. The class is held in a room with dry erase tape on the walls and attendees are encouraged to write on the tape during group activities, Chuck says.

"The first thing we do is ask them what do they want to learn in taking this course, and we have them pair up as a group and write down the questions they have," Flores explains. "Then they can look at the walls and see all of the questions being asked."

Instructors also use humorous videos about research — found online — to keep it interesting. "Students pick up on that and laugh, and that provides an opening for us to feed them the right information," Flores says.

For example, one YouTube video is a cartoon with an investigator coming into an IRB office and stating in a robotic voice that he wants to conduct an investigational drug trial on children and neonates in an international setting. The investigator character says he doesn't understand the IRB process and wants his review expedited and approved by tomorrow because the drug is safe since it was tested on animals and a handful of adults, Flores says.

"The audience enjoys it," she adds. "We understand there are many different ways people learn, and we incorporate the many different types."

"As we start to find things that engage them more, we incorporate them into the course," she adds.

Another strategy was to employ technology in the form of remote control pads with clickers and numbers/letters students can press to answer multiple choice questions, Chuck says.

"When we start the PowerPoint, we open polling questions to the entire audience, playing 'Jeopardy!' [game show] music to make it fun," she explains. "Everyone picks up their clickers and votes, and when the polling closes, we can see a bar graph of votes, showing how many got it wrong and how many go it right."

This gives presenters an opportunity to engage with attendees, she adds.

The course was developed by senior IRB managers. Entry-level IRB staff helped them determine how to tweak and improve the material. IRB staff also take the entire course as students and can offer feedback from that experience as well, Flores says.

"After doing this job for a while, things become pretty routine, and you're under the perception that everyone gets it when that's not necessarily the case," she adds.

Initially, new research staff took the course. Now, some experienced researchers have taken it as a refresher course, Flores says.

"This class is more than a class," Chuck says. "It's a networking opportunity for all the students."

As they discuss obstacles and issues, attendees learn that others have experienced similar problems, and they can learn solutions from one another, she adds.

"We're trying to be proactive in educating our staff and researchers and entry level personnel," Flores says. "By having a lot of staff members contribute to it provides us with different perspectives consistently."

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IRB's HRPP training class covers multiple areas

Two days of presenters and topics

A research institution's centralized research training program began as a way to help new investigators and research teams learn more about the IRB process and human research protection. But the program, called Navigating Clinical Research, has expanded into a comprehensive training course that uses a variety of adult learning strategies.

"One of the improvements we've made to the course is to explain the whole IRB process, as opposed to assuming our audience knows what an IRB is," says **Dorean J. Flores**, CIP, IRB manager at North Shore-Long Island Jewish Health System in New Hyde Park, NY.

The training initially was for one day, but was expanded to cover good clinical practice (GCP) in greater detail. Now, attendees must complete the first day of training before enrolling in the second day.

"Day two is heavy on GCP training, geared toward an advanced audience," Flores says. "So newbies can take day one and that's fine, but senior researchers can refresh their memories with day one, and on day two they will really test themselves and bring home additional information."

Here's how the two-training works:

• **Prior to first day of training:** "Before the class actually starts, we send out a reminder to people who are registered, suggesting pre-work activities," says **Tina Chuck**, MPH, manager of research policy and training at the health system.

"They also must take a CITI program course and a conflict of interest course," she adds.

The CITI training is required before they are eligible to work on a study, so the IRB asks that the CITI coursework be completed as a prerequisite to taking the Navigating Clinical Research course, says **Richard Ramdeo**, CIP, IRB manager at the health system.

Attendees also are expected to do some pre-course preparation, including a human subjects research handbook and learning management system.

"Pre-work is determined by the presenter and the topic they speak on," Flores says.

• **First day, morning:** A research administrator presents information about clinical research. And the chief operating officer of the Feinstein Institute for Medical Research might provide an overview of the institute's research in the health system, Chuck says.

"They oversee research for the health system," she says.

The morning session also includes a presentation from the grants management office. This segment includes a review of definitions related to clinical research funding, resources of information on funding opportunities, pre-award and post-award services, and a discussion of grant and contract proposal application procedures.

"The grants office and vice president for administrative funding goes over databases for researchers to look for funding opportunities and tells them how to work with the grants office to apply for those grants," Chuck says.

Next up is a presentation by the IRB: "We start off with background information about why IRB committees are required and how they came about in the world," Ramdeo says.

"Then we discuss the IRB's principles and regulations," he adds.

The IRB session also goes over the different types of research studies, and explains how research sites can submit each study.

"We navigate the class through different forms, protocol templates where people can write their protocols and information," Chuck says.

"We incorporate videos into it to elaborate on the discussions we're having," Ramdeo says. "Also, we'll have training point questions, an interactive polling question that we provide as they see PowerPoint slides."

Presentations, including the IRB 101 segment, involve discussions with attendees. People are encouraged to talk about their own research, Flores notes.

Lunch follows the IRB 101 segment of the course.

• **First day, afternoon:** The first afternoon topic is about consenting research participants.

An IRB manager will discuss these issues:

- define research informed consent;
- how to create an informed consent document and how to use templates;
- explain waivers of informed consent;
- discuss who can obtain consent and how to obtain it through both the consent process and documentation;
- provide information on consenting populations with special

considerations, including limited English proficiency, minors, and limited capacity.

Research compliance is next. A presenter from the office of research compliance explains the office's mission, services, and education. Other topics covered include how to navigate the regulatory environment, conflicts of interest, research misconduct, and protecting research subject privacy and security.

The last segment of the day is about research billing. A clinical research service/finance core representative describes research billing policy and procedures and covers Medicare coverage analysis and billing grid development, as well as ensuring compliance and research billing reviews.

"Research billing people explain how to fill out forms for outpatient and inpatient to let billers know that the person is a research subject and shouldn't be billed to insurance," Chuck explains.

• **Day two, morning:** The second day's curriculum begins with the topic of good clinical practice (GCP). A presenter from the office of research compliance defines GCP, discusses its history, lists the basic principles, and utilizes strategies for compliance with GCP. Medical care of trial subjects and good documentation practices also are covered.

"This part gets into the nitty-gritty of good clinical practice and randomization," Flores says. "This provides all the information the researcher or coordinator needs to know as they manage the trial and take on more intricate studies like multicenter research."

The same presenter next will discuss how to conduct quality research, including these items:

- research team readiness,
- protocol and regulatory compliance,
- how to ensure protection of subject safety, welfare, and rights,
- how to ensure device procurement, accountability, safety, and management,
- how to ensure study data accuracy, integrity, and quality through good documentation practices,
- quality assurance, and
- external monitoring, auditing, and inspection.

• **Day two, afternoon:** After lunch, the session begins with a biostatistics unit presenter discussing the randomization process.

The presenter explains what is a randomized clinical trial and goes over randomization-related data integrity.

Delving into the nuances, there is an explanation of the mechanics of randomization, stratification, open-label, single and double blinded, and "double dummy" randomized clinical trials. Attendees also learn of the step-by-step documentation of the randomization procedure, implementation of randomization procedure, record keeping, and special considerations.

The second day's session ends early, following an hour-long presentation of the management of investigational drugs in compliance with GCP standards. Presented by the clinical research service's investigational pharmacy core, this segment goes over these items:

- GCP standards for the management of investigational drugs,
- the investigational pharmacy core,
- the process for managing investigational drugs,
- considerations for study feasibility,
- procurement, accountability, storage, dispensation, preparation, and disposal of investigational drugs, and
- utilization of a health system pharmacy. ■

Case study: IRB deals with social network analysis issues

Consider recruitment, consent issues

The IRB at the University of Illinois at Urbana-Champaign had a number of issues to consider when researchers submitted a study involving a social network analysis on sensitive issues. In this case, the sensitive issue was sexual assault on a college campus.

Social network analysis is new and growing in popularity, says **Anita Balgopal**, PhD, director of the university's Office for Protection of Research Subjects (OPRS).

"Our board was mindful of keeping every aspect of this research in check," Balgopal says. "It also was dealing with a highly sensitive topic."

The research findings also have potential to inform the university's administration about sexual assault on the campus, she adds.

"Everything about the study was treated with the utmost respect to participants, confidentiality of identifiable data and privacy of participation," Balgopal adds.

"Sexual assault on college campuses is a hot topic right now," says **Emily Dworkin**, MA, a doctoral candidate and co-investigator of the study, which is being led by associate professor Nicole Allen, PhD. Dworkin is a research assistant at the University of Illinois in Urbana-Champaign.

Dworkin's and Allen's study addresses gaps in research through the exploration of social networks with university sororities as contexts for help-seeking after sexual assault. Investigators examined the structure of friend networks within these sororities, the knowledge they contain about available resources, and the presence of social normal like rape myths as they recover from rape.[1]

"People experience the aftermath of sexual assault fundamentally in a social context," Dworkin says. "They may disclose it to friends and family members, or they may choose to not disclose but just get information."

Whether they disclose and the kind of responses they get could affect their later decisions and choices, so researchers wanted to find out more about characteristics of the social context and what influenced victims, Dworkin explains.

The two issues they are trying to understand are whether a victim seeks help and her ultimate sense of well-being. "Did the social contexts impact mental health?" Dworkin says. "We assessed the structure of the social contexts and the information they contained to understand these issues."

The IRB had several ethical points to consider, Balgopal notes.

They included the following:

1. How would they enroll participants? Researchers planned to approach sororities and speak with their members, but the IRB questioned the feasibility of this. "We were not aware of how they were able to obtain a list of sorority members," Balgopal says.

Typically, sorority membership lists are not pubic information, and a gatekeeper — such as a sorority president — is in charge of access to this information, she says.

2. Would the recruitment incentive create ethical concerns? Researchers proposed giving each sorority house a $500 recruitment incentive that they could donate to charity or keep for the sorority's use. To receive the financial incentive, they would have to meet an 85% participation rate in study enrollment, Balgopal notes.

"The IRB was concerned about how a sorority might get to 85% — it could be coercive," she says.

For instance, a sorority president might pressure members to take part in the study so her house would receive the extra funds, she says.

3. How would recruitment take place? "How were these sorority members going to be notified about the research study?" Balgopal adds. "It was difficult because sometimes the sorority chapter president was the gatekeeper, and the IRB wanted to make the distinction that recruitment should be from members of the research team and not members of the sorority house."

Plus, sorority leaders were not researchers involved in the study and they wouldn't be able to answer potential participants' questions, she adds.

4. How would consent work with potential secondary subjects? The study's goal was to understand links between victims and their friends and social support circle. If a woman, who agreed to participate in the study and acknowledged that she was a victim of sexual assault, were to name several women as people with whom she shared this information, it was entirely possible that one or more of the friends had not consented to participate in the study, Balgopal says.

"The IRB was concerned about whether it was appropriate to out one of those three members. Perhaps the participant went to this individual as a friend, for support or consult, or perhaps this was someone who was vocal about being a victim of assault, or not — we wouldn't know," she says.

Also, the IRB was concerned about the kind of questions the participants would be asked.

The IRB worked with researchers to develop procedures that would address the IRB's concerns and reduce risk to participants.

Ultimately, all ethical questions and concerns were addressed to the IRB's satisfaction, Balgopal notes.

For example, researchers handled recruitment by notifying all sorority presidents and inviting them and their members to participate, while specifying that presidents must not be involved directly in recruitment, Dworkin says.

"We set up protocols to have middle men let sorority presidents know we would be contacting them about the study," she says. "We gave them full transparency about the study."

In network surveys, standard practice is to list the names of people who have not directly consented to be part of the list but who are listed as members of an organization. Requiring consent before a name is listed would be the same as publishing the names of people who were participants in the study, eliminating all confidentiality,

according to a presentation on the subject by Balgopal, Dworkin, and colleagues.[1]

Secondary subjects are considered to be the people about whom survey questions are asked about their behavior. The sexual assault study asked questions only about participants' own behavior and their relationships to the people listed in the network.[1]

Researchers are keeping the sorority incentive from being coercive by not communicating participation rates to the sororities and by discouraging sorority leaders from conducting their own recruitment. So if a sorority reaches 80% participation, the sorority's leadership will not know that with one or two more women participating they could receive the incentive money, Dworkin says.

Data were de-identified. All sorority member names were replaced with ID numbers, and researchers do not access data until it is replaced with the numbers, she adds.

"So we couldn't know who was assaulted and who wasn't," Dworkin says. "What we found with the social network research is that someone doesn't become a secondary subject until someone reports on their behavior, so we felt that our methods didn't raise secondary subject concerns."

Dworkin attended dinner announcements for the sororities. These were venues where outsiders were asked to be speakers. She told sorority members about the project and how it was up to them whether they wanted to participate.

"We sent a link about the study to their email addresses, and they could opt out," she says.

The women who chose to participate would have to read a two-page, electronic informed consent document and check the box showing they were adults and volunteering to participate, she adds.

Participants were directed to a survey on a secure platform. They were asked whether they had an unwanted sexual experience and about their relationship with other women in their sorority. Specific names were given, but only first names and last initials. Participants would indicate whether a particular person was a good friend or acquaintance, Dworkin explains.

As the sensitive nature of the study required researchers to work closely with the IRB, the two groups decided to publish a case study on the process of social network analysis on sensitive issues. The collaboration was highly informative, Dworkin says.

"We've been thrilled with the process — given the care and concern and collaboration and having the IRB meet with us and discuss issues in a thoughtful way," she says.

REFERENCE

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Network of bioethicists gives guidance to investigators faced with complex ethics issues

Group complements the work of IRBs

IRBs typically give guidance to researchers only during the pre-study regulatory review process, but investigators also struggle with ethical questions that arise during research. "For years, this has been done informally," says **Benjamin Wilfond**, MD, director of the Treuman Katz Center for Pediatric Bioethics at Seattle Children's Research Institute.

When facing an unexpected ethical issue, researchers sometimes seek advice from ethics consultants at their institutions; the final recommendation is often to discuss any proposed change in protocol with the IRB. "IRBs have varying degrees of expertise and comfort with more complex ethical issues," notes Wilfond. "Some of these are hard cases."

Increasingly, investigators are anticipating ethical issues in advance of conducting their projects and seeking advice, says **Mildred Cho**, PhD, associate director at the Stanford (CA) Center for Biomedical Ethics. "In addition, investigators also have been working with ethicists to publish co-authored articles about ethical issues they identified, and strategies they developed to address the issues," she notes.

Wilfond founded the Clinical Research Ethics Consultation Collaborative, a group of 40 bioethicists at 30 institutions, as a resource to help investigators resolve

ethical issues that arise during research.[1]

"In building this collaborative, we want to be very clear that we need to supplement, not replace, the IRB," he says. Wilfond co-authored a 2009 paper that examined how a research ethics consultation service may differ from and complement the role of an IRB.[2]

"Ethics consult services have varying degrees of success," adds Wilfond. "Often, it's a combination of the overall institutional enthusiasm and the people running the program."

Many ethical issues confronted by researchers involve communication of findings to study participants. "There may not necessarily be a plan to return the findings of laboratory or clinical evaluations to individual participants. But suddenly, the information seems important to convey," says Wilfond.

This issue arose during a study in which participants were given the option of knowing results of genetic testing. Two siblings participated; one was sick and one was healthy. The healthy sibling said he didn't want to know the results.

"The researchers ended up having findings that suggested he had the same condition as the siblings, but decided not to tell him because those were his wishes," says Wilfond. However, the investigators then learned that the man was scheduled to be a bone marrow donor for his sibling. "This raised the question of whether the researchers should tell him against his stated wishes," says Wilfond. The group considered that he was also committed to the health of his sister, and the information was disclosed.

The Clinical Research Ethics Consultation Collaborative is currently developing a website to allow investigators to learn about the members and the service. "Some are willing to do consults for people who are from other institutions," notes Wilfond. "Not everybody has access to groups like this."

Recently, a dozen ethicists participated on a conference call with an investigator faced with a difficult ethical issue. "This consult focused on research studies that provide more frequent standard clinical data for which the clinical meaning is not clear, and could result in unnecessary subsequent clinical interventions," says Wilfond.

This allowed the investigator to hear a wide range of views. Some thought disclosure was necessary, while others thought it was problematic. "There were a number of people throwing out ideas that I hadn't thought of," says Wilfond. "We've only done this twice now, but I think it's a new, interesting way of trying to help investigators."

Since 2012, the group has recorded the cases from ten institutions in a database. "Our fantasy at the time was for people to use the database to get immediate advice. It turns out that people would rather have a listserv," says Wilfond. Researchers prefer to consult with someone who can tell them right away what they think about the particular issue the researcher is dealing with.

"We are in the process of creating opportunities, when we do a complicated consult, to get input from other people," says Wilfond. Another possibility is for a group of ethicists to be invited to call in at a certain time, if available, to address a particular question.

"People often try to resolve this on their own. Most things never get to an outside consultant for advice — it's only when people are really, really stuck," says Wilfond. "We can provide greater clarity of thinking."

REFERENCES

1. Cho MK, Tobin SL, Greely HT, ET AL. Research ethics consultation: the Stanford experience. *IRB: Ethics & Human Research* 2008; 30:1-6.
2. Beskow LM, Grady C, Iltis AS, et al. The research ethics consultation service and the IRB. *IRB: Ethics & Human Research* 2009; 31(6):1-9. ■

COMING IN FUTURE MONTHS

- New strategy for ER research community consultation
- Ethical issues of patient-centered outcomes research
- Technology and changes in personally identifiable information protection
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IRB ADVISOR

CNE/CME INSTRUCTIONS

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CNE/CME QUESTIONS

1. Which of the following is not an advantage of using smartphone apps for research mentioned by Jeremy Block and John Wilbanks?

A. Investigators can reach a large cross-section of the population and are not geographically limited
B. Smartphones are easily accessible to the public at large
C. Smartphones can easily track progress and return results
D. Both B and C

2. In a Q&A related to the FDA/OHRP new draft guidance on electronic informed consent, the FDA states that electronic IC must contain all elements of IC required by FDA regulations, and if it's interactive, it should also be which of the following?

A. Easily accessible by smartphones
B. Easy to navigate
C. Accessible only through fingerprint security
D. All of the above

3. When creating a human research protection or clinical research training program for new researchers and IRB members, which of the following aspects of informed consent should be addressed, according to the program's creators?

A. How to create an informed consent document and how to use templates
B. Explanation of waivers of informed consent
C. Discussion of who can obtain consent and how to obtain it through both the consent process and documentation
D. All of the above

4. According to Anita Balgopal, which of the following is a good example of research that involves social network analysis?

A. A study looks at victims of sexual assault and how often they sought mental health counseling
B. A study assesses the incidence of sexual assault on a college campus
C. A study analyzes the characteristics of the social context of sexual assault victims disclosing their assault to friends, and the study looks at what influenced victims
D. None of the above