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INSIDE

Billion-dollar lawsuit over unethical study puts past into the present

How can IRBs continue to learn from old wrongs?

From an IRB and research ethics perspective, when are historical wrongdoings truly in the past? Today's IRB and human research protection regulations are the result of public outrage over historic experiments that hurt and even killed people in Nazi Germany and the U.S. in the mid-20th century. But as the global research community has enacted safeguards against exploitation of research volunteers and generations of IRBs work hard to protect study volunteers and reassure the public that they won't condone unethical research, sometimes additional old wrongs are uncovered. New concerns arise as the past continues to haunt the present.

An example is the recent media barrage over a lawsuit to compensate victims of unethical medical experiments from 70 years ago. The new lawsuit that links unethical research to two leading institutions suggests the past is ever present.

Some 800 plaintiffs have filed a lawsuit for $1 billion against a foundation and major research institution over research conducted in Guatemala by U.S. public health scientists in the 1940s. The government deliberately infected hundreds of vulnerable Guatemalans with syphilis, gonorrhea, and other sexually transmitted diseases (STDs). The study was forgotten for decades until a historian uncovered the records in 2010.

> THE STUDY WAS FORGOTTEN FOR DECADES UNTIL A HISTORIAN UNCOVERED THE RECORDS IN 2010.

President Barack Obama immediately apologized to Guatemala for the experiments, and he asked his Presidential Commission for the Study

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of Bioethical Issues to investigate. *(See summary of commission's findings, page 64.)*

But ethical questions remain, several bioethicists say.

No one knows what possessed scientists and public health doctors to conduct the studies that included injecting women sex workers with STDs and then making them have sex with other subjects. The Guatemalan study was connected to the infamous Tuskegee syphilis study of black men by the common link of some of the same researchers and the use of minority or vulnerable research subjects, notes **Arthur Caplan**, PhD, director of the division of medical ethics at New York University School of Medicine in New York City.

"What happened in Guatemala was wrong," Caplan says. "At that time, you have to understand how the public was racist and prejudiced and biased against people with disabilities."

The culture of those times made such experiments possible, but even so, the researchers knew there was something wrong with what they were doing because they went to orphanages, prisons, asylums, and minority communities for research subjects, he adds.

"They felt those people were not morally equal to whites and able-bodied citizens," Caplan says.

In that context, modern bioethicists and IRBs are coping with the fallout of learning details of research atrocities committed by people from generations past.

"What's disconcerting for the public is that we're hearing about things from long ago and far away that we thought were ancient history and that predated the rules and regulations we put in place in the 1970s and 1980s," says **Eric M. Meslin**, PhD, director of the Indiana University Center for Bioethics in Indianapolis.

"There will be cases like the tragic Jesse Gelsinger case, where a young man died in a gene therapy clinical trial at the end of the last century," Meslin says. "That happens; it's understandable and tragic. But when we hear about the Guatemala syphilis study, we have to ask ourselves deep questions: How prevalent is this? Is it the tip of the iceberg, or was it only one instance?"

The Guatemalan study's victims and families sued the U.S. government in 2012, but a judge dismissed that lawsuit on grounds of immunity. They also asked for a victims' compensation fund, which has not been established. This latest lawsuit, filed April 1, 2015, names Johns Hopkins University and its hospitals and the Rockefeller Foundation; both institutions condemn the study and deny involvement. *(See public responses by JHU and the Rockefeller Foundation, page 64.)*

It's possible that past research wrongs will continue to haunt research institutions as new problems are discovered, experts say.

"I wouldn't be surprised to hear of another one," Meslin says. "Like a friend of mine says, there are no big boxes in warehouses, labeled 'Unethical research — don't open.'"

The Guatemalan study is an example that violates good sense and judgment, he adds.

"That's why the Guatemalan case is so worrying," Meslin says. "What's especially disturbing is to read some of the accounts of the researchers involved and their supervisors, who said, 'This is tricky business doing research on prostitutes, prisoners, and children.'"

Today, research is held to a higher standard than clinical care, notes

Ernest Prentice, PhD, associate vice chancellor for academic affairs at the University of Nebraska Medical Center in Omaha. Prentice formerly was the chair of the Secretary's Advisory Committee on Human Research Protections (SACHRP) for the U.S. Department of Health & Human Services.

"It's been a long process to bring IRBs up to snuff, and it took the shutdown of research portfolios in the 1998 and 2000 era and tragic deaths like Jesse Gelsinger's to bring accreditation to IRBs," he adds. "But, I think the standard of human subject protection is so much improved over the pre-1990s era."

But when one views past research misdeeds, it seems that the medical Hippocratic Oath did not protect human subjects. The hallmark example is the Tuskegee experiments in which black men who had syphilis were studied for much of their lifetimes, but for more than three decades they were never told of penicillin or offered it as treatment, he says.

"When penicillin became available in the '40s, these subjects were denied any possible benefits — that's tragic," Prentice says.

"And to my amazement, there were at least 13 peer-reviewed publications about Tuskegee in prestigious journals over the years," he adds. "And many of these articles came out after penicillin was available, so how could a physician read a journal about Tuskegee and untreated syphilis and at the same time give their own patients penicillin treatment?"

Predictably, there will continue to be discoveries of rogue researchers taking unethical risks with research participants, Meslin says.

"But that is a different story from what we're going to do the next time we see a historical example uncovered by a medical historian or reporter," he adds. "Will it make us rethink what we're doing today?"

Research ethics evolve. U.S. researchers couldn't be involved in anything like the Guatemalan and Tuskegee experiments today because of IRBs and human subjects protection regulations, Prentice notes.

Still, it's possible that some research approved by IRBs and conducted in the glaring light of 21st century ethics will seem wrong to future generations, Caplan and Meslin say.

"Will our grandchildren look back on us today and say, 'You thought that was ethical?'" Meslin says.

"Some of the experiments we do today in poor countries with poor populations may seem in retrospect as somewhat exploitive," Caplan says. "And we still haven't taken the steps we should to use electronic and non-written consent with illiterate populations, so someone might ask, 'Why did they have people sign forms they clearly couldn't understand?'"

One area of research that needs more protection is the private research realm where volunteers are paid, Caplan says.

"These studies often are for household products, safety testing," he explains. "Are we building our safety just on the backs of the poor?"

Human research protections should be extended to privately-funded studies as well, Caplan adds.

IRBs and the human research protection field focuses considerable energy on informed consent and privacy issues, so it's possible that a different type of harm — one seen as benign today — is missed entirely, and some future generations will be shocked by it, Meslin says.

"I'm worried that our main focus on avoiding physical harm is covered so well that we'll miss out on some less obvious issues like harm to culture," he explains. "Our whole ethic has been about protecting individuals from harm, but I wonder if we're missing the bigger picture of communities and the public."

Examples might be Native American tribes that consented to research for a specific medical purpose, only to learn years later that their blood samples and DNA were used for purposes for which they had not provided informed consent, he says. In some cases, the tribes found these unapproved research studies to hit on cultural taboos, such as researchers looking for genetic markers for inbreeding or comparing DNA for migration studies.

"Those types of problems should never have to happen," Meslin says. "Researchers failed to tell research participants what they were doing, and it resulted in these communities feeling offended, insulted, and violated."

Researchers should be very sensitive to a community's concerns, he adds.

"At the end of the day, some of it is good common sense, and some of it is about understanding there are people in communities out there who are not just individuals who are pieces of data you want to analyze," Meslin says.

"That will be the future movement in research: We'll want to pay much more attention to research on communities," he adds.

And if another past research atrocity surfaces, then this ultimately is good for the research community because it keeps IRBs and ethicists focused on what could happen if they aren't paying attention, Caplan notes.

"I think they should remain controversial," he says. "It leaves people to understand them and revisit them; I don't want them to go away." ■

Presidential Commission found gross violations in Guatemalan studies

Commission reviewed 125,000 pages of records

After nine months and reviewing 125,000 pages of records, the Presidential Commission for the Study of Bioethical Issues found that the Guatemalan studies of sexually transmitted diseases (STDs) were "Ethically Impossible."

The commission's chief findings included the following:

• Dr. John C. Cutler led the study, which had 1,308 research subjects who were intentionally exposed to syphilis, gonorrhea, and/or cancroid.

• Subjects were prisoners, soldiers, and psychiatric patients.

• Commercial sex workers, who did not consent to the study, were infected with STDs and used to transmit disease.

• Hundreds of Guatemalan soldiers were infected with STDs through sexual exposure, superficial inoculation into the penis, deep inoculation into the penis, and superficial inoculation following sexual exposure. Their average age was 22 years old. There is no evidence that they gave consent or received compensation for the study. The researchers' own words suggest that they did not consider their subjects to be volunteers.

• Research staff for the experiments included leaders and senior medical personnel of the government of Guatemala, as well as U.S. researchers and officials.

• In 1947, *New York Times* science editor Waldemar Kaempffert described rabbit experiments with penicillin and intentional exposure to syphilis. Kaempffert said it would be "ethically impossible" to undertake such research with humans. But what he didn't know was that Cutler already had begun initiating that exact kind of experiment in Guatemalan prisoners and psychiatric patients.

• The National Research Council (NRC) reviewed the Guatemalan study in 1946, and on its subcommittee on venereal diseases were public health system doctors, as well as representatives from the U.S. Army, the U.S. Navy, the Veterans Administration, and several universities. The NRC approved funding for the study.

• Cutler's research team treated some of the subjects for STDs.

• They also conducted serology testing of 1,384 orphan children and subjected the children, who were used somewhat as control subjects, to physical exams, blood draws, and — sometimes — lumbar punctures.

• The study never accomplished its goal of testing the orvus-mapharsen prophylaxis wash as a prophylaxis for syphilis.

• Some prisoners objected to the study but were not withdrawn, and 83 people died during the experiments from causes that were not well documented.

The commission's report can be found at http://bioethics.gov/node/654. ■

Johns Hopkins and Rockefeller Foundation respond to lawsuits

Both institutions condemn the study, deny involvement

Both Johns Hopkins University and the Rockefeller Foundation recently issued statements saying that while they condemn the Guatemalan studies that harmed hundreds of people, their institutions were not involved or responsible for those studies.

According to Johns Hopkins University, the institution played no role in the Guatemalan study of the 1940s: "This was not a Johns Hopkins study. Johns Hopkins did not initiate, pay for, direct, or conduct the study in Guatemala. Participation in the review of government research was then and is today separate from being a Johns Hopkins employee, and no nonprofit university or hospital has ever been held liable for a study conducted by the U.S. government," wrote Ronald J. Daniels, president of The Johns Hopkins University; Paul B. Rothman, MD, dean of the medical faculty, and Michael J. Klag, MD, MPH, dean of Johns Hopkins Bloomberg School of Public Health. The letter was

published April 1, 2015, to the Johns Hopkins community. *(The letter can be found at http://www.hopkinsmedicine.org/guatemala_study/.)*

Also, the Rockefeller Foundation has no connection to the Guatemalan experiments, according to a public statement by the foundation (http://bit.ly/1F3Q5io).

"The lawsuit recently filed in Baltimore against the Rockefeller Foundation seeks improperly to assign 'guilt by association' in the absence of compensation from the United States federal government," according to the statement. "The complaint alleges that Dr. Thomas Parran approved the experiments as Surgeon General of the United States, at a time when he also sat on the Board of Trustees of the Rockefeller Foundation. There is absolutely no evidence that the Foundation or its Board — or Dr. Parran in his capacity as a member of the Board — had any connection whatsoever with the experiments."

The Johns Hopkins letter also stated that the plaintiffs' "essential claim in this case is that prominent Johns Hopkins faculty members' participation on a government committee that reviewed funding applications was tantamount to conducting the research itself, and therefore that Johns Hopkins should be held liable."

Historians previously have linked Johns Hopkins faculty members to other unethical government research studies in Tuskegee and Terre Haute, the authors wrote.

"Although separate from the Guatemala lawsuit, these studies were all deplorable and all demand reflection upon the broader legacy of unethical research. It is important to confront and learn from the past," they wrote. "At the same time, we cannot let unfounded allegations go unchallenged. We will defend the institution vigorously in court against legal responsibility for the government's Guatemala study." ■

Informed consent issues at the front lines of clinical trials

The IC form is a "roadmap"

IRBs spend considerable time poring over informed consent documents and learning all they can about a study's informed consent process. But how do these IRB discussions and changes translate into a living informed consent process after the study is approved?

One research nurse who has spoken at national conferences on the topic says that informed consent is complex, especially when the document is based on a sponsor's template language, which often is written in a way that's hard for the average person to understand.

"What I've learned is it's very difficult for an IRB to change template language; it's very difficult for them to simplify that," says **Joy Jurnack**, RN, CCRC, CIP, a research nurse with North Shore–LIJ Health System in Great Neck, NY. Jurnack spoke about a research nurse's perspective on informed consent at the Association of Clinical Research Professionals (ACRP) 2015 Global Conference in Salt Lake City, April 25-28, 2015.

Jurnack views her role as a subject advocate, so she encourages IRBs and researchers to write IC documents at reading levels below high school level.

"I understand how a medical professional views informed consent, and I'm also looking at it through the eyes of the subject," Jurnack says. "I'm on the front lines, trying to explain the informed consent document to research participants for the IRB, pharmaceutical company or sponsor, and the research site."

Even college-educated research volunteers will have difficulty understanding an IC document when it is written with medical jargon and legalese, she notes.

"When people walk into a hospital, they're immediately walking into a stressful situation," Jurnack explains. "We call it 'white coat hypertension:' They see a white coat and their blood pressure goes up."

These same people will think something is wrong with them when they are enrolled in a clinical trial. They often are sick and have complicated medical issues. Then the research nurse sits with them and has 20 minutes to present the IC document and answer questions, she adds.

Often, the potential volunteer will ask to take the document home with them. This can be problematic when they share it with family members who don't understand it and were not available during the informed consent process to ask questions about it, Jurnack notes.

"So I try to simplify the document with my words and present it to potential subjects," she says. "I talk with subjects at length so they understand what's in the actual document."

When talking about study procedures, the key is to break it down into simple steps, Jurnack suggests.

For instance, a research nurse or

investigator might say, "On screening visit one, you'll be seen by the medical center staff, have blood drawn, and have blood pressure taken," Jurnack says. "During the acute phase of the study, you will be required to do this."

Separating information into one or two sentences makes it easier to explain and easier to follow, she adds.

"Informed consent is a process; it's not about the signature," she says. "It's about continuing to go back to the information to help people understand."

One area Jurnack refers to continuously is the IC form's part about how participants can withdraw from the study at any time. Another area she will refer to more than once involves adverse events and the study's safety profile.

At Jurnack's first meeting with someone who meets the study's inclusion criteria, she usually walks into the room with a copy of the informed consent document.

"I wear a lab coat — embossed with 'Research' — and a stethoscope," she says. "I talk about the protocol and why this person qualifies for this research."

Often, Jurnack will go into details about how the patient's disease or conditions make him or her eligible to be screened for the study. "Then I talk about how much time is expected of them in the study, and I'll say that I'm available on my cell phone 24/7 if they have any questions," she explains.

"If the person's spouse or significant other is there, I'll talk with them about their concerns," she adds.

Jurnack further explains what researchers have learned on the study's subject and discusses how many people already have been volunteers in the research.

"I say, 'This is a long document. We can go over it now, or, if not, here's my business card because I don't want you to get stuck on something and not be able to ask questions,'" she says.

Jurnack also might speak with the subject's physician, if that is what the person wants. "So I'm building relationships with both doctors and potential subjects," she says.

A research volunteer might sign the informed consent document at that first meeting, but that's not necessary, she adds. "Yesterday a man and his wife were interested in a study, but they're on their way to Florida, so I'm going to have them come back in a couple of weeks."

When volunteers take the time to read over the IC form and think about it, Jurnack will have them return for a second meeting to sign the document if they choose to do so.

At the second meeting, she'll repeat information about any study compensation for participation and the right to withdraw at any time.

"I suggest they bring in the informed consent document at every study visit," Jurnack says. "I tell them to write notes on the form if they have any questions because it's very important that they understand what's going on."

At a third visit, after the person has enrolled, Jurnack will provide whatever study procedures are necessary and continue to provide informed consent.

"The protocol is a scientific document, and I want the informed consent to be the roadmap that explains to subjects what's going on," she says. "The first thing I'll ask the person is, 'How have you been? Have you been to the doctor or changed any medication lately?'"

The goal is to encourage the study volunteer to give as much information as possible.

Even as technology is changing the way informed consent can be administered, the IC process needs to be thorough and a shared responsibility between researchers, sponsors, the IRB, and the research nurses who provide informed consent, Jurnack says. ■

Online cardiovascular study shows technological evolution of research

Social media use raises questions

A new research study involving social media highlights how challenging it is for IRBs when technology continually speeds up the evolution of human research protection.

"Our IRB is very interested in how technology is changing things in research," says **Madelaine Faulkner**, MPH, project director of Health eHeart, a cardiovascular study at the University of California, San Francisco (UCSF).

Health eHeart is unique in that the entire study is conducted online. Researchers check in with participants through e-visits, and the goal is to enroll one million participants worldwide over a 10-year period, Faulkner says. *(See article on study goals, page 68.)*

"We are trying to understand how your heart changes over time," she says. "You qualify to participate if you're over 18 years and have an email address; we want people who are healthy or not healthy."

The study collects data from participants on their family history, lifestyle, sleep, quality of life, and other information. It also has a mechanism for collecting electronic health record data for participants who provide the study with their patient portal login, she says.

"We're also working on pulling UCSF data," notes Faulkner, who discussed the topic of engaging the community using social media at a research community forum held by the Office for Human Research Protections (OHRP) on March 12, 2015, in Denver.

The study is partnering with the university's clinical data research network (CDRN), as well, she says.

Participants who have a patient portal will be able to see their own health results, and they can upload those into the Health eHeart study. "It's great the way it has been integrated," Faulkner says. "The IRB was very involved in its integration, and it was a lot of work."

Bluetooth technology also makes it possible for study participants who have defibrillator to send their activity data to the study, Faulkner says.

The IRB approved online informed consent for the study and online HIPAA consent to address privacy, she adds.

One of the chief issues that concern IRBs when studies involve social media is confidentiality, notes **Lisa Denney**, MPH, CIP, interim human research protection director at UCSF.

"What's happening with these new technologies is it's really not understood how individual data will be protected, where it will be stored, and how consent will be given for its future use," Denney says.

"And it's the technical aspects," she adds. "IRBs now are expected to understand IT security systems, which is very far from what IRBs have historically been worried about."

Here are some of the ways the study's use of technology might impact the IRB and human research protection:

• **Using social media.** "We use social media to touch base with our community members and to, hopefully, have visibility with people who are not part of the Internet study," Faulkner says.

> "THE REAL RISK IS THAT DATA IS BEING USED IN A WAY THAT A PERSON DIDN'T CONSENT TO OR WHICH PUTS THE INDIVIDUAL AT RISK."

"Our hope is that by using social media we can continue to engage participants," she adds. "We're not getting a conversion rate of participants from social media."

Also, the study's social media person engages with other heart- and health-related communities to support them. For example, the StopAFib group recently had a conference, and Health eHeart's social media contact posted information about their conference and gave them a shout-out, Faulkner explains. "We gave them a hashtag, which is a cool phenomenon that is like putting in a buzz word, and it is used to search Twitter."

• **Crowd-sourcing research ideas.** The study plans to incorporate participants' voices into the research, crowd-sourcing their research ideas: "We ask patients, 'What's the best way to disseminate the findings of this study?'" Faulkner adds. "We're turning clinical research on its head a little bit."

• **Maintaining community engagement.** On Facebook's newsfeed, the study's site presents engaging health news that can be entirely unrelated to the study and cardiovascular disease. "We try to put on something engaging so that it resonates with a wide group of people," Faulkner says.

Initially, the IRB was concerned about the study having a Facebook page because of concerns over it being a way people could see who was enrolled in the study, Faulkner says.

The solution was to limit the public's ability to post on the main page, she explains.

The website has attracted many followers who are not enrolled in the study, so someone visiting the page could not automatically assume that everyone who "likes" it is a participant in the study, she adds.

Also, the study has a Health eHeart study page. Some of the people who interact on the page are study participants, but many are not, she says.

"It's about heart content and fun things, and it's not an official arm of the study at all," she says. "We don't push this to participants actively, although there is a link in the newsletter."

When a viewer first sees the Health eHeart website, he or she can click to join the study or merely browse the site to learn more about the research. The site's registration

A big data cardiovascular study plans to learn a lot

One million volunteers is the goal

A big data cardiovascular study out of the University of California, San Francisco is enrolling volunteers from around the world in a quest to learn more about heart disease.

Conducted solely online, the study is expected to look at the heart health of a million people once enrollment is complete within the next decade, says **Madelaine Faulkner**, MPH, project director of Health eHeart at UCSF.

The study's investigation goals include:

• Predicting heart disease based on measurements; behavior patterns including sleep, diet, activity; and family and medical history,

• determining what causes episodes of atrial fibrillation and studying how behaviors, diet, genes, and other diseases interact to cause it,

• using technology to develop ways to improve cardiovascular health and to rigorously test them to determine their effects on health,

• using mobile technology and sensors to keep people with heart failure out of the hospital;

• assessing whether it improves heart health to be connected with people and whether there are physical benefits to engaging in online social networks,

• predicting when heart disease will get worse before someone needs hospitalization and even before the patient knows something is wrong, and

• answering questions about whether people with different kinds of genes are more vulnerable to particular heart disease risks, such as alcohol. ■

process is secure and unique to that site, Faulkner says.

• Creative marketing to potential volunteers. Since the study's enrollment goals are high — about 26,500 people from more than 85 countries have enrolled so far — researchers have to be creative in how they market to potential participants. They market the study electronically through partners, including healthcare Internet groups and device companies. For instance, one device company, which has 250,000 users of its product, will send its users a message about Health eHeart, Faulkner says.

In reviewing studies that involve new technologies and social media, IRBs might need to have an information technology expert on the board or at least consult with one, Denney says.

"When we're talking about Facebook, you have to understand Facebook's securities and what it can do with that information," she explains. "Those issues are ones the IRB is grappling."

Without a better understanding of how security and data collection work on social media sites, an IRB might not make the best decision, Denney adds.

It's a struggle for IRBs to protect research participants' confidentiality and privacy in the world of social media studies, she says.

"When researchers do social media studies, that's not our data anymore," Denney says.

Another new area where technology and human research protection clash is when researchers use body cameras to observe people's daily habits. "These cameras could be taking a picture every five seconds, so how do you consent the individuals who are suddenly bystanders in the project?" Denney asks. "How do you inform these people about the researcher taking pictures for research purposes?"

Even subtler problems can arise. If a study is using smartphones to collect data, then participants might find that the apps they upload on the phones could be automatically collaborating with GPS and recording information about the person's location, Denney says.

"The real risk is that data is being used in a way that a person didn't consent to or which puts the individual at risk," she adds. "Health eHeart has done a good job of making individuals aware of their participation in this study, and we are managing the data." ■

Recent measles outbreaks show dangers of bad research

One discredited vaccine study's ripple effects

IRBs need to be reminded how even the smallest of studies based on bad science or being performed by an unethical researcher can have long-lasting dangers and impact on society, a regulatory coordinator says.

The best example is the now-discredited study that linked autism to childhood vaccination. Although the study later was found to be poorly done and inaccurate, celebrities and others who grasped it as the truth have corralled a movement that has convinced a higher percentage of parents to avoid or postpone their children's vaccinations.

"It's fascinating to me that one small study comes out, and the media puts out headlines, and celebrities talk about it," says **Tonya Edvalson**, CCRP, regulatory coordinator for Intermountain Healthcare in Salt Lake City. Edvalson recently spoke about autism and vaccines at the global conference of the Association of Clinical Research Professionals (ACRP), held April 25-28, 2015, in Salt Lake City.

"Yet, even when the study is found to be fraudulent research, and so much is wrong with it, we still fight this battle," she adds.

Edvalson refers to the example of the 1998 study by a British physician that reported to find a direct link between autism and the common vaccine for measles, mumps, and rubella (MMR).

Many parents panicked soon after the study was published and vaccination rates fell to dangerously low levels, leading — in the past 15 years — to multiple outbreaks of once-controllable childhood diseases.

For example, the United States went from having nearly eradicated the three diseases to having disastrous outbreaks, including the recent one in California in which measles cases were linked to an amusement park, according to an April 2015 report by the Centers for Disease Control and Prevention in Atlanta.[1]

Last year, the U.S. had a record number of measles cases with 668 reported cases from 27 states. That was the most cases since measles elimination was documented in the U.S. in 2000.[1]

The original study reported on 12 patients' medical histories and was published in *BMJ*. After other scientists raised questions about the study, mistakes and misrepresentations were discovered, and *BMJ* retracted it. Britain took away the researcher's medical license in 2010. In the many years since then, scientifically credible studies have disproven the connection, showing that rates of autism among non-vaccinated children are not lower than those among vaccinated children, according to various news reports.

The latest study, published in the *Journal of the American Medical Association* (*JAMA*), found that autism rates for more than 95,000 children who were vaccinated with the MMR vaccine were no higher than rates for children who were not vaccinated — even when they had older siblings with autism. About 1% of the children enrolled in the study were diagnosed with autism.[2]

But these later studies arrived after the major damage was done, Edvalson says.

Edvalson is in a unique position to discuss the issue, as she worked for an IRB for seven years before moving to the clinical side to work with investigators. Her current role includes reviewing all studies submitted to the IRB. And she has a son with autism.

Autism scares parents, and this fear may have fueled the irrational belief that vaccines were causing the disorder, she suggests.

IRBs should keep in mind that once bad science is out in public, it's very hard to control what's said, Edvalson says.

"Make sure studies are designed appropriately from the beginning, and make sure there are protections in place and it's done according to the plan," she adds.

The discredited vaccine researcher did not follow the rules, Edvalson notes.

"He used a specific procedure that wasn't in any IRB submissions, a lumbar puncture," she adds. "And when the general medical council reviewed it, they said they thought it wasn't germane to the study at all."

Knowing what she does about how to conduct ethical and regulatory compliant research, Edvalson says she takes it personally to see how one bad study can cause so much damage to public health.

"I have a child with autism, and it really bothered me to see all of these articles come out with misinformation about vaccines," she says. "If our kids with autism are not protected by immunizations, then they are even more at risk."

IRBs, researchers, and others in the human research protection community have a role to play in keeping bad science from being conducted, Edvalson says.

"Most of the people I speak to are research coordinators and study monitors, and I tell them that when they suspect something doesn't look right, they should point it out and bring it up to whoever they think can do something about it," she says.

"This is more than having a culture of compliance," Edvalson notes. "It's doing the right thing for the right reason."

The vaccine-autism research was continuing despite not having proper ethical approval, and someone involved with it had to know this was happening, she says.

"We need to create a culture of, 'This is how it's done,'" she says.

IRBs can help prevent this type of lone-wolf researcher fraud by getting to know investigators and research staff. "Having a collegial relationship between an investigator and IRB goes a long way to preventing problems," Edvalson says. "You need to have a safe place for research staff to go and to say, 'This is not in the consent form, but he's asking me to do this.'"

Also, IRBs should make sure there are processes in place for reporting fraud and bad research behavior.

Some IRBs conduct not-for-cause audits of studies to make sure there are no problems or disturbing trends. The idea is to be accountable and make sure the good research is what's put out there in the public, Edvalson says.

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Handling sensitive topics with teenagers raises issues

It also highlights an evolution in research

The use of digital storytelling and social media to engage a vulnerable population is part of the research frontier that is possible because of technology. It might change the way IRBs view human research, and it might make investigators of community members, one socio-behavioral scientist says.

"This issue gets to the core of the areas where IRB committees need to be retooled," says **Marty Otañez**, PhD, assistant professor of the anthropology department at the University of Colorado Denver.

"Historically, some of this type of research would have been looked at as oral histories," he explains.

But it's more than that when researchers add a more robust set of research practices from collecting stories, including pre- and post-test surveys, semi-structured interviews, a survey of 200 young people, videographies, discussions with storytellers in public settings, and produce data systematically to analyze, Otañez says.

The study Otañez describes involved reproductive rights access for young pregnant or parenting teenagers.

Researchers worked with 26 young women in digital storytelling workshops in a high school with a classroom-based art therapist. Each woman made a short video about reproductive rights and access and healthcare issues. The idea was to use the videos to generate discussions with the women's peers and with policy makers, Otañez says.

The study's stated goal was to stimulate youth development through an innovative use of digital technology promoting positive sexual and reproductive health outcomes for Latina teens in Colorado.

"We want to increase the discussion around these difficult issues that young women face who are pregnant and from marginalized communities and to also understand women of strength and counter the stereotypes that work against these women in their daily lives," Otañez says.

While some people in human research protection might argue that this type of work is more community-based projects than research, Otañez disagrees.

Everything involving the project is research in the sense that it is approved by the human subjects committee and is designed to promote generalizable knowledge and further the notion of digital storytelling as a method for community engagement, he says.

"The specific process I subscribe to and use is creating a space where individuals from the community create and share their own stories, as opposed to scholars making stories about them," Otañez explains.

"The story circle is a process: people in the community, with a few

facilitators, share their stories, and these are not usually public," Otañez says. "They're a way to collect data."

In Otañez' digital storytelling research, the young women share their stories publicly online through their videos. The University of Colorado has a Web page titled, "Teen Moms Talk Back." Links to some of the young women's videos are on the page. The page can be found at http://teenmomstalkback.ucdenver.edu.

Since the research uses social media platforms, especially YouTube, a key issue from an IRB perspective is how social media is used for communication between the study participants and for communication to the public, Otañez says.

"The videos are used to communicate to the general public about the women's stories and to create safe places to talk about these issues and to counter stereotypes of pregnant and parenting young women," he adds.

The idea that these women are considered part of a vulnerable population because of their age is an outdated legacy that IRBs need to change, Otañez suggests.

"These young women are parenting at age 14," he says. "They grow up faster and are using social media in ways that are new and uncertain, and they shouldn't be treated in a patronizing or paternalistic way."

From an IRB's perspective, this type of research is tricky, he notes.

"There needs to be some retooling because of the fast pace of social media and how it's changed society and is being used by younger people," Otañez adds.

The end result of this type of research is not just publication and evidence-based research, but the process of developing relationships with community members so these young mothers can one day do their own research, Otañez says.

He envisions a time when research isn't conducted only by academic or medical professionals and when community members can be trained to design their own studies.

"When I go into a community project we come in with a proposal," he explains. "Once these are done, they're intended to give [the participants] a set of skills, contacts, and confidence so they can design their own projects."

Someday, the teenage mothers and other communities like theirs might become researchers who share stories, findings, and knowledge with academics and professionals, so scholars and researchers will better understand the community's needs and desires, he adds.

"This is an innovation in research," Otañez says. "We're fine-tuning things so the members of the IRB have the knowledge and skills to not create obstacles for researchers who do community-driven work, where people are working in partnership to conduct research."

Before members of a community could become researchers, they would need to follow all training and other requirements. For instance, when researchers set up the young Latina mothers' study, they had an art therapist, who was enlisted to work with the teens on their videos, go through appropriate training to be a co-researcher on the project, he notes.

"She is a staff member of the Florence Crittenton Services and a certified teacher," he says. "In the future, one of the tangibles could be that these young women, who could do their own research project, would have to go through all the human research protection program training."

The benefits of research involving members of a stereotyped community and using social media are clear, Otañez says.

"The design and intent of the research are to promote health equities and also the scholarship, knowledge production, and increased space for non-academics to participate directly," Otañez explains. "This research increases the capacity of community members to take control of processes they've typically been subjects of, and it helps us promote innovative knowledge, evidence-based research, and also serve the communities where we're located." ■

COMING IN FUTURE MONTHS

- Evaluating risk-benefit ratio ethically
- Strategies for preventing research noncompliance
- How to make HRP training community responsive
- Training new IRB administrators

IRB ADVISOR

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CNE/CME QUESTIONS

1. According to Arthur Caplan and Eric M. Meslin, future generations may not find ethical issues in studies currently being approved by 21st century IRBs.

A. True
B. False

2. While IRBs often focus on wording and details in informed consent documents, Joy Jurnack says the human research protection community should focus on the entire IC process. She suggests the IC document be used as what?

A. An ancillary tool to the IC process
B. A roadmap for the IC process
C. A primarily legal instrument
D. None of the above

3. Which of the following is not a problem that could arise when conducting studies using new technologies and social media, according to Lisa Denney and Madelaine Faulkner?

A. Researchers capturing pictures of unconsented bystanders
B. The possibility of seeing who is enrolled in a study via the study's Facebook news page
C. The potential for a participant to leave his or her laptop or smartphone with study information visible
D. Participants' smartphones inadvertently collecting and sharing location information with researchers

4. Why does the now-discredited study that reported a link between autism and the measles, mumps, and rubella (MMR) vaccine serve as a good example of the dangers to public health when a rogue investigator shortcuts regulatory rules and IRB supervision is lax?

A. Because the study led to a widespread anti-vaccine movement in the United States and other nations, resulting in recent measles and other outbreaks
B. Because the study resulted in school systems no longer requiring vaccination of children
C. Because the investigator's fraud highlights how ethical lapses in research continue to plague 21st century science
D. None of the above