Webinar Follow-Up: Hot Topics in Online Survey Research

On March 12, 2015, PRIM&R hosted a webinar titled Hot Topics in Online Survey Research: Subject Identification, Consent, and Risk, which was presented by Elizabeth Buchanan, PhD, and B.R. Simon Rosser, PhD, MPH, LP.

Online research methods are increasingly common across scholarly disciplines. Particular scientific and ethical issues arise for online researchers in the areas of recruitment, consent, and risk/benefit analyses. This webinar addressed three "hot topics" in online survey research: subject identification, models of consent, and risk/benefit analyses. Following a vibrant discussion at the conclusion of the webinar, Dr. Buchanan and Dr. Rosser agreed to respond to some of the incoming questions in writing to share with the readers of Ampersand.

1. Is the review of the terms of service (TOS) the sole responsibility of the IRB, or an institutional or PI responsibility?

   Elizabeth Buchanan (EB): While reviewing TOS or end user license agreements is an extra-regulatory consideration, it is becoming more important to understand what is included and what might be significant for your research.

   A consent document may indicate that the research team will destroy all project data in a number of years, and the team stores project data in storage cloud (e.g., Amazon Cloud, Google Drive, or Dropbox). Typically, the TOS for each of those services does not specify how long data will be stored; thus, data may exist beyond the time frame outlined in the consent. Or, the consent document may say only the research team will have access to study data, when a cloud service will routinely access the data for maintenance: "We may use, access, and retain your files in order to provide the service to you and enforce the terms of the agreement, and you give us all permissions we need to do so. These permissions include, for example, the rights to copy your files for backup purposes, modify your files to enable access in different formats, use information about your files to organize them on your behalf, and access your files to provide technical support" (Amazon Cloud Drive, 2015).

   Also, we want to be sure we aren't conducting research that is in violation of the TOS. For example, many sites restrict automated mining, spidering, or scraping data. A site might disallow what might be considered exempt research from an IRB's perspective. Due to the complexity of these agreements, it is best to consider reviewing TOS a shared responsibility. They are...
legal documents, and even though most of us click through without reading them, we want to be aware of the potential implications for our research.

2. Do you have any concerns with minors participating in online research geared for an adult population?

Simon Rosser (SR): Yes and no.

Yes—because each study must be viewed on its own merits, the possibility of harm considered, identified, and where possible reduced and risks versus benefits analyzed. Researchers have to work within the law; in addition those of us who are mandated reporters are compelled—if we have the relevant information—to intervene. And where there is risk of serious harm (e.g., a study where the methods could expose a minor to inappropriate relationships with adults) then the onus is on the researcher (and IRB) to address the risk.

No—because in this webinar we were focused on minimal risk research which, by definition, is unlikely to harm children. It's rather difficult, if not impossible, in online research to expose anyone to serious harm (over and above that which is already found online) since anyone can click out of the study if they wish. A very important caveat, mentioned during the presentation, is that we are not talking about research involving deception or emotional manipulation.

Much of research geared for an adult population is low risk (e.g., participating in an online study on engine maintenance, advanced calculus, or appreciating Beethoven) where there simply isn't harm. Some potentially harmful topics (e.g., studying sexual abuse, suicide, and religious radicalization) may put a minor at no more risk than if they visit a website on the same topic.

As a parent and grandparent, I'd be more worried about my children being on an unregulated website promoting destructive or harmful behavior than in any research study. And there are probably some methods (e.g., using social media groups) where children interact with adults or adults have to access a child's information that introduce the possibility of harm. I also think we confuse what is distasteful from what is harmful (which seems to me to be a higher standard). There are a lot of things I choose not to watch or see online (e.g., graphic images in the news) but that doesn't mean I've been harmed. It means I leave the website. A different way to think about this is as follows: Because the online environment is not regulated, the bar to demonstrate that the research study has risk over and above that of just being online/everyday life seems, to me, to be a high bar.

3. Investigators often wish to use Facebook to recruit participants. We are very concerned that participants liking a page on Facebook then associates them with a study. What are your thoughts?

EB: If the project team creates a study page and potential subjects "like" the page, yes, their friends and followers will see that "like." As an alternative, study teams can use nondescript language, referencing a study on depression as a "mood disorder," or provide alternate forms of contact so that an individual can review the page but not "like"it. For more sensitive topics, Facebook pages might not be the best tool; Twitter and Mturk can be used with more confidentiality. But, ultimately, I agree with the University of Minnesota's IRB on the limitations of privacy inherent in using social media.

4. If it's necessary to collect the IP address, do you inform respondents that you will collect the IP address?

SR: Initially we would disclose this using a statement like: "Your information is confidential. We don't secretly collect any information (beyond IP address which is only used to validate the survey)." Typically now I don't even mention it for three reasons: (1) IP address is analogous to physical address. Many studies use physical addresses to locate a particular target demographic and maintain these addresses as process data. (2) I think of IP address as inherently observable. Whenever a
person completes any task online, any provider or external agent gains access to this information. (3) Since businesses and third parties use IP address all the time, requiring researchers to ask first holds us to a standard no one else is using.

5. Isn't using the IP address an inherently flawed mechanism for subject verification?
SR: Solely using IP address for verification is inherently flawed—and we don't recommend it. Instead, we talk about a "deduplication and cross-validation protocol" tailored to the study where IP address is one element of a larger protocol. In *The Story of Subject Naught: A Cautionary but Optimistic Tale of Internet Survey Research*, a paper by Konstan et al., where we found one person completing the study 66 times, using IP address and time information helped identify all the computers used as in a lab, and the timestamp showed the person finished the survey, which took researchers 25 minutes to complete, in 12 minutes. S/he would take three minutes off, then go through the survey on the next computer, etc. So, using IP address for verification is not perfect, but without it, our research results would have been fatally flawed.

6. Can you comment on the anonymity of Amazon MTurk? Although the researcher does not ask for any identifiable information and the online consent form may state the survey is anonymous, MTurk may collect IP address information.
EB: MTurk is not anonymous: Amazon has clearly said that the Turk platform is not meant to support participant anonymity. We are seeing this tension play out across social media research, where all kinds of identifiers are being tracked and maintained by the host or company. But—often, these data are not available to the researcher, as you may recall from our definition:

"Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects."

This is an important consideration and we need to be careful with promising anonymity at this point in time. We are truly moving away from the language of anonymity, toward confidentiality.

Also, the University of Texas put out good guidance for researchers wishing to use Turk.

7. How long should identifiers be maintained with data for verification? Should they be maintained as long as the data?
SR: Most studies I see maintain them sufficiently to conduct the verification, and then, I assume, they destroy or de-link the files. Some may keep identifiers as long as the data especially if there is some expectation that they may need to audit or independently repeat this step.

8. Could you provide links to or names of institutions that have come up with template protocols/consent forms for internet survey research?
EB: Sure, we have a compiled a list here. If you have guidelines for internet research that we've missed, be sure and let us know in the comments below Also, I like The University of Massachusetts-Amherst's online consent documents, here and here.

PRIM&R would like to thank Dr. Buchanan and Dr. Rosser for sharing their expertise on this important topic. Do you have an idea for a webinar? Share it with us at webinars@primr.org.

*If you were unable to attend this webinar and are interested in purchasing the archive, you may do so here.*
'Expensive' placebos work better than 'cheap' ones, study finds

How do you convert a simple saline solution into a useful treatment for people with Parkinson’s disease? Tell them it’s a drug that costs $100 per dose. And if you want to make it even more effective, tell them it costs $1,500 instead.

That’s what researchers from the University of Cincinnati discovered in an unusual clinical trial. Instead of testing a placebo against an actual drug, they pitted two placebos against each other. The only difference between the two sham treatments was their purported price.

Medical researchers are well aware that the dummy pills used in clinical trials often provide as much relief as the actual drugs being tested. This is what’s known as the placebo effect, and it’s quite common in people with Parkinson’s, a movement disorder that causes tremors, stiffness and balance problems. A 2008 meta-analysis found that placebos used in clinical trials of Parkinson’s treatments improved symptoms by an average of 16%.

http://touch.latimes.com/
So they recruited 12 patients with “moderately advanced” Parkinson’s and asked them to participate in a clinical trial of a medication described as "a new injectable dopamine agonist.” Patients with Parkinson’s lose the brain cells that produce dopamine, and a drug like this could pick up the slack.

The study volunteers were told that there were two versions of the experimental drug and that both were believed to work equally well. The main difference, the story went, was the way they were made. As a result, one version cost 15 times more than the other.

In reality, both placebos were composed of the exact same saline solution. And yet, the patients perceived the expensive version to be more effective than the cheaper one, according to results published Wednesday in the journal Neurology.

Both of the placebos improved motor function compared with a base line test. But when patients got the $1,500-per-dose placebo, their improvement was 9% greater than when they got the $100-per-dose placebo, the researchers reported.

In another test, 67% of the patients were judged “very good” or having “marked improvement” after they took the expensive placebo, compared with 58% of patients after they took the purportedly cheap placebo.

The researchers also used functional MRI scans to assess the patients’ brain activity and found that the "cheap" placebo prompted more action than the "expensive" one. To the researchers, this was a sign that the patients expected less from the placebo they believed cost less, so their brains responded by doing more work.

“Patients’ expectations have an important role in the efficacy of medical therapies,” the researchers wrote. Another manifestation of this is the preference many patients have for name-brand drugs instead of their generic counterparts, they added.

Placebos may be fake, but understanding the placebo effect – and finding ways to make the most of it – is a real priority for researchers. To the extent that doctors can use placebos to improve patients’ symptoms, they can use the real drugs less, which may be expensive or toxic.

“For medical news that's the real deal, follow me on Twitter @LATkarenkaplan and "like" Los Angeles Times Science & Health on Facebook.”

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Digital Multimedia
A New Approach for Informed Consent?

The ethical principle of respect for persons requires that individuals participating in research studies are provided with sufficient information to allow them to make autonomous and informed decisions. In general, the process of informed consent requires that investigators disclose pertinent information regarding procedures to be performed, risks, and benefits, etc. in a manner that participants can understand. In most cases, this information is reinforced by having the study participant or parent/guardian read a consent document, which is then signed to authorize participation.

Despite the ethical and legal imperatives of this process, concern exists that many study participants and parents do not fully understand the information provided and as such may not be truly informed. The reasons for this are multifactorial but often result from incomplete disclosure and/or poorly formatted and excessively long consent forms written above the recommended grade reading levels. However, rather than becoming simpler, the complexity and length of the traditional consent form appear to be increasing, particularly with consent forms designed for sponsored clinical trials.

In an attempt to address some of these concerns, the Office for Human Research Protections (OHRP) recently issued an advanced notice of proposed rulemaking that included limiting the length of consent documents, inclusion of prescribed content, prescribing how information should be presented, reducing institutional boilerplate consent forms, and standardizing the consent template. In light of this advanced notice, it may be time for investigators, institutional review boards, and regulatory agencies to reevaluate the mounting evidence that supports the use of innovative strategies to enhance participants’ understanding of research information.

Although the consent form represents only one aspect of the informed consent process, it continues to serve as a primary vehicle for disclosure of research information. However, in an attempt to meet regulatory and legal requirements, many boilerplate consent forms appear to do so at the expense of participants’ comprehension. As Waisel suggests, “focusing on the legal requirements suffocates the primary goal of the consent process to satisfy the decision makers’ needs.” Excessively long consent forms containing complex information in a one-size-fits-all format can be intimidating to many participants, particularly for those enrolled in randomized clinical trials or who have low education or poor literacy and numeracy abilities. Indeed, evidence suggests that approximately half of participants do not read the consent document carefully.

Given the concerns regarding the inability of many research participants to comprehend information using traditional consent forms, consideration of other modes of information delivery may be warranted. One approach that has shown promise in the delivery of health information is the use of digital multimedia. With the expanding societal use of computers and the universal trend toward medical informatics and electronic medical records, it may be that digital multimedia could offer unique opportunities for improving the approach to the informed consent process.

Although the same concerns regarding the amount of information, readability, and formatting apply regardless of the mode of message delivery, digital multimedia offer several important advantages over traditional paper consent forms. First, computer-based multimedia can promote active participation in learning through interaction, whereas information acquisition using paper consent forms is typically passive. It has been estimated, for example, that individuals remember approximately 10% of what they read, 20% of what they hear, 30% if they visualize in addition to hearing, 50% if they observe someone doing something along with an explanation, and 90% if they perform the task themselves. Thus, whereas paper consent forms can only be read, digital multimedia have the potential to enhance understanding by utilizing all of these approaches (i.e., read, hear, watch, and do).

A second potential advantage of digital multimedia over paper media is to leverage the so-called pictorial superiority effect. This concept is best characterized by the phrase “a picture is worth a thousand words,” which, despite the cliché, is a concept firmly grounded in science. Pictorial superiority effect explains that individuals remember concrete items more readily when presented as pictures rather than words and that pictures drive conceptual processing, require less cognitive effort, and aid retention. The visual salience provided by the pictorial superiority effect is particularly effective when using graphical media to present risks and benefits and for participants with poor literacy/numeracy and for explaining complicated decisions in which shared decision making is important.

Third, digital media are able to incorporate interactive in-line exercises that can establish “real-time” understanding of information at the time decisions are made. This function can be enhanced by using corrective feedback that alerts the participant and investigator to an incorrect answer and provides the correct response. Results from these exercises could be downloaded via computer with the e-signed consent form directly into the patients’ electronic medical records. Several studies support corrective feedback;
Festinger et al\(^\text{18}\) showed that participants randomized to receive corrected feedback following disclosure of study information had greater long-term retention compared with those who received no feedback.

Fourth, digital multimedia have the potential to “tailor” information to the individual participants’ learning styles and information preferences. Computer tailoring has been shown to be effective in helping individuals understand and modify health behaviors by providing information that is personally relevant. For example, participants who require additional clarifying information can do so by simply clicking on a hyperlink. Options for risk-benefit presentations, eg, graph vs text based on personal preferences and understanding, can also be accommodated. Thus, both the amount of information and message delivery can be tailored to an individual participant’s information needs.

Evidence supporting the effectiveness and acceptance of digital multimedia for research and health care consent is increasing. Studies reveal that computer-based educational interventions for chronic conditions such as asthma, diabetes, and arthritis elicit a greater sense of control and empowerment, improve understanding of the conditions, and are preferred by patients.\(^\text{10}\) Video informed consent has also been shown to improve patient comprehension of various surgical procedures and increases the likelihood of clinical trial participation. Use of multimedia to help parents and children understand clinical trials has also been demonstrated. However, even though this technology has been shown to improve participant understanding, an investigator’s discussion with a participant remains the cornerstone of “informed” consent.

Despite the promise of digital multimedia, potential disadvantages exist, including cost, threats to confidentiality, and access. However, these issues are likely to diminish as technology and access advance. Creation of digital libraries from which investigators can download content and design their own study-specific documents is possible and would mitigate future costs.

Given the ongoing concerns regarding the inability of research participants to understand information using conventional consent forms and the recent OHRP-proposed rulemaking changes to the informed consent process, new and innovative approaches to the provision of research information are warranted. Continued reliance on traditional boilerplate consent forms that serve to meet regulatory requirements but inhibit comprehension is no longer acceptable. Regulatory agencies, institutional review boards, and investigators should consider and implement innovative evidence-based strategies to ensure that respect for persons through improved understanding remains central to the tenet of informed consent for both research and patient care.

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**REFERENCES**


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Downloaded From: http://jama.jamanetwork.com/ by a Northwestern University User on 02/19/2015
Recruiting patients for research? Simple explanations, queries from doctors are best

Patients want to be asked permission to participate in research that compares standard treatment options and that involves reviews of medical records, according to a new study.

While a debate was raging between scientists and government regulators on how best to explain to patients the risks of participating in clinical research studies, a team of bioethicists boldly went where no experts had gone before — to the patients themselves.

What the patients said surprised them: Keep it simple, but always ask permission, even when the research only involves gathering data from anonymized medical records.

“We didn’t anticipate that patients would want to grant permission for medical record searches, a research method that involves much less risk than most randomized studies that compare standard treatment options,” said Mildred Cho, PhD, professor of pediatrics and of medicine at the Stanford University School of Medicine. “The good news was that most patients said they would forgo documented consent or accept simple approaches to granting permission, even verbal permissions, if requiring written agreements would hinder this type of comparative-effectiveness research.”

A paper describing the findings of the patient survey published April 14 in the Annals of Internal Medicine. Cho, who is also associate director of the Stanford Center for Biomedical Ethics, is the lead author of the paper. Benjamin Wilfond, MD, professor and chief of pediatric bioethics at the University of Washington School of Medicine, is the senior author.

The findings will be used to inform the U.S. Office of Human Research Protections and the Food and Drug Administration as they develop regulations on how to structure patient permissions for research conducted during mainstream clinical care and through mobile devices.

The patient perspective

The survey was the work of the Research on Medical Practices project, or ROMP, which was launched in the aftermath of a controversial research-consent form used in a study that compared two oxygen-delivery levels for extremely premature babies. While many researchers and bioethicists argued that the research was done in an appropriate fashion, others disagreed.

Even though these at-risk infants were randomly assigned to one of two standard treatment options, some people felt that the clinical risks of standard practices should be disclosed as research risks. Researchers, the public and the bioethics community were deeply divided about whether the consent form adequately warned parents about participation risks. The ROMP study was designed to gather evidence on patient attitudes toward risks and how to best ask for permission to conduct this type of research.

“Creating burdensome consent regulations for minimal-risk research may impede the collection of valuable medical evidence without actually increasing the protection of participants,” said David Magnus, PhD, a co-author of the study and the director of the Stanford Center for Biomedical Ethics.

Cho, Magnus and other researchers involved in the project began collecting data in August 2013 through a Web-based survey of 1,095 adults. The survey included questions about attitudes toward research, doctors and health systems, as well as questions to assess understanding of research concepts, such as variations in prescribing patterns among physicians, randomization and informed consent. The survey also asked questions about patients’ preferences for being notified about studies, and their perceptions of risk and willingness to participate in the context of three scenarios. The three scenarios were presented in videos, which are available on the ROMP website.

During the process of developing and testing the videos and survey, the bioethicists learned a great deal about the best way to educate patients on medical research, Magnus said. “One of our first challenges was to dispel the ‘doctors know best’ myth. Doctors don’t always know which treatments are best for individual patients,” he said. “In the absence of good evidence, these choices are often influenced by advertising, insurance coverage and local preferences. Busting this myth was essential in explaining why comparative-effectiveness research is so important.”

**Hearing it from their doctors**

One interesting survey finding was that patients preferred that their doctors, rather than medical researchers, ask them whether they’d like to participate in research. This runs counter to conventional wisdom in the research community, where the participation of doctors in the recruiting process can be viewed as a potential conflict of interest.

For supporters of comparative research in clinical settings, it was encouraging to learn that 97 percent of the respondents agreed that health systems should conduct this type of research. “I think that patients really want us to make it easier for them to participate in research,” said Magnus. “As medical research evolves, the ways that we engage and inform patients must evolve, too.”

Some ROMP team members were recently awarded a grant from the National Institutes of Health to continue researching the ethics of informed consent. Next, they will be translating their educational videos into Spanish and Mandarin, and developing strategies and tools for educating patients from diverse ethnic groups about research that makes use of electronic medical records and stored biological samples.

The project is supported by the NIH National Center for Advancing Translational Sciences’ Clinical and Translational Sciences Award to the Institute of Translational Health Sciences at the University of Washington (grant UL1TR000423) and to Spectrum, the Stanford Center for Clinical and Translational Research and Education (grant UL1TR001085).

The videos and information about the study are available at [http://spectrum.stanford.edu/romp-videos](http://spectrum.stanford.edu/romp-videos).

The Office of Human Research Protections guidance on patient disclosure can be reviewed at [http://www.hhs.gov/ohrp/newsroom/rfc/draftstandarreseach.html](http://www.hhs.gov/ohrp/newsroom/rfc/draftstandarreseach.html).
THE ETHICS SQUAD

Bioethicists are setting up consultancies for research — but some scientists question whether they are needed.

BY ELIE DOLGIN

Stacy Hodgkinson and Amy Lewin had the best of intentions when they enrolled the pregnant 15-year-old in their study. The psychologists were evaluating an educational programme for young parents-to-be, and the teenager met all the inclusion criteria: she was 15–32 weeks pregnant with her first child, under 19 years of age, and her partner — who did not live with her — was willing to participate in the study. There was just one problem. Dad was 24 years old, and according to local laws he was guilty of child sexual abuse for sleeping with a minor.

The couple had apparently lied to each other about their ages, but not to Hodgkinson and Lewin, both then at the Children’s National Health System in Washington DC. This presented a dilemma. The scientists had promised the participants that their information would be kept confidential. But did that trump their legal duty to report the crime to the police? And how would that affect the family?

“Here was a young father telling us he’d like to be involved in his child’s life in a positive way,” says Lewin, who is now at the University of Maryland in College Park. Telling the authorities, she says, “could potentially do more harm than good”.

In search of moral and legal guidance, Hodgkinson and Lewin contacted Tomas Silber, a paediatrician who also runs a research ethics consultation service, a ‘one-stop shop’ for advice on thorny research issues.

To Silber, the course of action was clear. “There’s only one thing you can do,” he says. “You have to report it.” After explaining their legal obligations to the couple, Lewin and Hodgkinson told the police, who launched an investigation. The teen and her partner broke off contact with the researchers, and Hodgkinson does not know whether the father maintained a positive presence in the child’s or the mother’s life — which was ultimately the goal of their programme. “Sometimes you do the right thing, but the consequences aren’t good,” says Silber.

Ethical dilemmas in research are nothing new; what is new is that scientists can go to formal ethics consultancies such as Silber’s to get advice. Unlike the standard way that scientists receive ethical guidance, through institutional review boards (IRBs), these services offer non-binding counsel. And because they do not form part of the regulatory process, they can weigh in on a wider range of issues — from mundane matters of informed consent and study protocol to controversial topics such as the use of experimental Ebola treatments — and offer more creative solutions.

The consulting services are “a really new area”, says Joshua Crites, a research ethicist at the Pennsylvania State College of Medicine in Hershey. “Even some of the most basic questions get complicated really quickly, and it’s better to have a group of ethicists working together to sort this out.”

But many scientists either do not know that they exist or fear using them because they could add red tape to an already heavy administrative burden. And this year, the US National Institutes of Health (NIH) scrapped funding for a working group to support ethics-consultation services and to develop best practices for the profession.

Although financial support could return in some form, ethicists are not waiting around for it. Benjamin Wilfond, director of the Treuman Katz Center for Pediatric Bioethics at Seattle Children’s Hospital in Washington, has set up the Clinical Research Ethics Consultation Collaborative, a group of around 35 bioethicists who hope to keep improving the consultation service model, even without NIH support. “There’s energy behind continuing what we started,” says Holly Taylor, a research ethicist at the Johns Hopkins Berman Institute of Bioethics in Baltimore, Maryland, and a member of the group.

HERE TO HELP

IRB approval is required for almost all human-subject research in the United States. The foundations for current IRB practices emerged 40 years ago in the wake of numerous ethical lapses in research, including the infamous Tuskegee experiments performed in Alabama between 1932 and 1972, in which doctors allowed syphilis to progress untreated in hundreds of African American men. Today, IRBs are the main channels for policing ethics in academic medical studies. But their primary function is to ensure adherence to regulatory and legal requirements. They do not always include members with bioethics expertise, and
discussion of ethics sometimes takes the form of box-ticking rather than careful deliberation.

That is where consultants come in. Unlike IRBs, consultants can provide guidance throughout a study — not just at the point of regulatory review — and do so in a non-confrontational advice-giving capacity. They offer “an open space for talking about research ethics in a way that is not driven by the regulatory environment,” says Marion Danis, chief of the bioethics consultation service at the NIH Clinical Center, a research hospital in Bethesda, Maryland.

The Clinical Center was the first organization to launch a research ethics consultancy, in 1996, and a handful of academic medical centers followed suit over the next decade. Then, in 2006, the NIH launched the Clinical and Translational Science Award programme to enhance drug development and testing in academic settings, and it led to a rapid expansion of the concept in the United States. According to a survey published last year, by 2010 more than 30 academic institutions had set up research-ethics consultation services. That said, fewer than half of them had fielded calls by researchers seeking advice in the previous year, and just six got more than ten calls1. “In most places, these have not ended up being high-volume activities,” says Steven Joffe, a medical ethicist who led a fairly idle service at Harvard Medical School in Boston, Massachusetts, until moving to the University of Pennsylvania Perelman School of Medicine in Philadelphia in 2013.

“You need some independent person to say, ‘Well, let’s step back and think about this.’”

Amy Hagopian, a global-health researcher at the University of Washington in Seattle, found herself turning to an ethics consultant for help with a study in Iraq to find out how many people had died as a result of the US-led conflict that began there in 2003. Her team needed to consult research ethics from participating countries, but the researchers on the ground in Iraq were concerned that including the University of Washington’s name on the consent forms — a requirement for IRB approval — would make it difficult to get the data they needed. “They feared that being associated with American institutions would get them killed”, says Hagopian. “They dug in their heels and refused” to carry the form.

Hagopian wanted to strip the university’s name from the consent document, but the IRB insisted that it was an important part of informed consent, which is meant to protect participants, not the investigators. The impasse brought Hagopian and her team to Wilford. He concluded that it would be ethical to remove mention of the institution, for three main reasons: first, research subjects would also be placed at risk by signing a document linking them to the University of Washington; second, apart from the link to the United States, the research involved minimal risk to the participants; and third, the study would not happen unless the name of the institution was removed.

The IRB eventually agreed with Wilford. The researchers went ahead with the study and found that nearly half a million people had died from causes attributable to the Iraq war between 2003 and 2011 — a figure much greater than most previous estimates2. “We couldn’t have done this without him,” Hagopian says of Wilford.

WORLDLY ADVICE

Of course, bioethicists have been providing advice about research for years, long before the NIH created a formal service. Outside the United States, ethics consultations mostly happen through the regional equivalent of an IRB or take place in casual conversations or “kerbside consults.” “All in all, it’s pretty ad hoc,” says Mark Sheehan, who studies ethics at the Ethox Centre of the University of Oxford, UK.

At some institutions in Canada, ethics advice about research studies can also be sought through the services that help patients and doctors to settle end-of-life decisions and other moral issues in health care. Unlike in the United States, where training programmes in research ethics and clinical ethics are usually separate, in Canada “we all tend to have both kinds of expertise pretty much”, says Ann Heesters, a bioethicist at the Toronto Rehabilitation Institute in Ontario, one of the only Canadian hospitals that publicizes the availability of ethics consultations for researchers. According
to Heesters, around one in every seven of her consultations pertains to research.

In Australia, "it's very difficult for researchers to be able to seek advice before they submit the full application" for official ethics review, says Nikola Stepanov, who studies research ethics and law at the University of Queensland in Brisbane. And if a human-research-ethics committee — the Australian equivalent of an IRB — finds ethical problems in a study's protocol, researchers may have trouble finding a formal channel for further guidance.

"We're obviously in the stage that the United States was at before it brought in these ethics consultations," says Stepanov. "Something more formalized would be very appropriate."

But not all ethicists agree that a separate service is needed, even within the United States. "If the IRB has the responsibility for ethics review, why are we pulling in someone else?" asks Susan Kornetsky, director of clinical research compliance at Boston Children's Hospital in Massachusetts. Norman Post, who studies ethical and legal issues in research at the University of Wisconsin—Madison, would rather see bioethics panels folded into the standard IRB structure. Because IRBs are "a toll gate that everybody has to go through," Post says, these panels, which would ideally include qualified ethicists, should "look at every single protocol and identify problems that nobody else has yet identified." Relying on a separate, optional service means that some problems could be missed. "It's the cases they're not getting called about that worry me," he says.

**COMPLEMENTARY SERVICES**

Advocates say that the aim of consultancy services is to complement IRBs and other oversight bodies, not to become entwined with them. "For innovative research designs, you need some independent person to say, 'Well, let's step back and think about this not just from the standpoint of do the regulations permit it, but does it fulfill the spirit of what people want done with the public research enterprise?,'" says bioethicist Steven Miles at the University of Minnesota.

Wilfond has been working to increase the visibility and the rigour of ethics consultancies. Last year, for example, he and Taylor launched a biannual series in the *American Journal of Bioethics* entitled 'Challenging Cases in Research Ethics.' The latest case, from Silber and his colleagues describing the obligation to report statutory rape, was published in September. Wilfond is also collecting descriptive data about consultations and has expanded the reach of his service at the University of Washington by welcoming external requests — including from pharmaceutical companies, which typically employ armies of lawyers but rarely bioethicists. In such cases, the University of Washington consults on a fee-for-service basis: US$200 an hour for drug companies, less for non-profit organizations.

The Stanford Center for Biomedical Ethics in California also works with drug firms. There, panellists provide their time and advice at no cost, on the condition that they can publish case studies. In 2011, for example, a start-up company approached the centre for guidance on the sale and promotion of a prenatal genetic test that involves analysing fetal DNA circulating in maternal blood (see *Nature* 478, 440; 2011). The consultation led to an academic paper that called for amendments to informed-consent procedures and restrictions on the sale of direct-to-consumer tests.

"Many of our consults end up that way," says Mildred Cho, associate director of the Stanford centre. "We do treat these things as scholarly activity as well as a service." Cho estimates that around one-quarter of her service's cases come from the drug industry.

Wilfond is currently working to expand the panels to draw in a wider range of views and to broaden the experience of panellists, a move that he considers one of his most innovative for ethics consultancies. In June, he was called into a meeting at Seattle Children’s Hospital with Ron Gibson, director of the hospital's cystic fibrosis centre. Gibson had been gathering data from several studies that were using laboratory tests that can be performed only in a research setting or fall outside of recommended guidelines, but he was unsure whether he should incorporate the results into patients' routine clinical care. Seven bioethicists from Wilfond’s collaborative telephoned into the meeting, ready to offer their take.

As the consultation began, Wilfond explained that the point of bringing the ethicists into the discussion was twofold. First, it would offer Gibson a wider range of opinions, and second, it would expose the advisers on the phone to a case they might not otherwise have been involved in. "There's a lot of learning that goes on bidirectionally," Wilfond says. The hour-long meeting was "educational," says Gibson, who has since implemented a new policy for his research programme, although he declined to discuss specifics. "The spectrum of opinions on various levels of data sharing was reassuring that there is likely not one best way to address the issue."

Wilfond and his colleagues hope that more scientists and clinicians will start to see the benefits of their services. "There just hasn't been an awareness of how important this is," says Charles MacKay, a consultant in clinical and research bioethics in Bethesda, Maryland. But getting scientists to actually buy into such services may require a shift in attitudes. "Researchers generally have become members of a culture of research compliance," says Christian Simon, a bioethicist at the University of Iowa Carver College of Medicine in Iowa City. They are responsive to what IRBs require, he says, but that sometimes means that they are unwilling to step back and consider the finer ethical details.

"We're not the ethics police," says Reid Cushman, co-director of the ethics consultation service at the University of Miami in Florida. "We're just another resource to help you stay out of trouble."

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