Opinion: Let's Bring the Informed Consent Process Out of the Shadows

The disclosures researchers use to obtain consent in clinical trials are rarely shared with the public. They should be.

Left: Patients are increasingly interested in experimental regimens that use drugs like LSD, psilocybin, and MDMA to treat post-traumatic stress disorder and other forms of trauma. For scientists interested in conducting such research, consent forms used in past studies are hard to obtain. Visual: Alice Adler via Getty Images (https://www.gettyimages.com/detail/illustration/woman-thinking-royalty-free-illustration/89797014)

BY MISHA ANGRIST (HTTPS://UNDARK.ORG/UNDARK-AUTHOR/MISHA-ANGRIST/) 09.22.2022

TAHLIA HARRISON HAS BEEN bombarded with questions about psychedelics. A practicing therapist, Harrison recently graduated from the bioethics and science policy program at Duke University (https://scienceandsociety.duke.edu/learn/ma/), where I teach and served as her master's thesis supervisor. Her patients are increasingly interested in experimental regimens that use drugs like LSD, psilocybin, and MDMA to treat post-traumatic stress disorder and other forms of trauma (https://www.nature.com/articles/d41586-021-00187-9).

Harrison's patients are hardly alone. Since 1970, psychedelics have been considered "Schedule I" drugs in the U.S., with the feds maintaining that they have no accepted medical use. But in recent years, the government has softened its stance and, accompanied by no small amount of hype (https://www.wired.com/story/psychedelic-hype-bubble/), psychedelic-assisted therapies are now being tested in dozens of clinical trials (https://psychedelicspotlight.com/5-psychedelic-clinical-trials-2022-maps-mdma-psilocybin-ketamine-lsd-dmt/). These studies can present substantial health and safety risks to the patient, and a number of trials have been attached to allegations of sexual abuse (https://blog.petrieflom.law.harvard.edu/2022/03/09/precautionary-approach-touch-in-psychedelic-assisted-therapy/). To better understand how these risks are communicated to prospective study participants, earlier this year Harrison set out to collect consent forms used in more than three dozen psychedelic-assisted therapy trials listed on the federally run website clinicaltrials.gov (https://clinicaltrials.gov/).

To her disappointment, she was able to download consent forms from just five of the trials that met her criteria. And despite directly contacting the organizations running the studies, only one responded to her queries.

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Since the long parade of ethics scandals (https://www.bioethics.nih.gov/sites/nihbioethics/files/bioethics-files/courses/pdf/2015/session1_lederer.pdf) that plagued biomedical research during the 20th century — from Nazi doctors' experiments, to the Tuskegee Syphilis Study, to a Brooklyn hospital study that injected patients with live cancer cells — informed consent has been a hallmark of research on human beings (https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/informed-consent/index.html). It enshrines the idea that we can't experiment on people without first informing them of the risks and benefits and, obviously, getting their permission. The consent forms used in clinical trials, as dense and lawyerly as they might be, are meant to answer questions like: What is involved in the study? How long will it take? Will I get paid? What happens if it goes sideways?

But in many cases, few people outside of the researchers, participants, and the institutional review boards charged with approving a study ever see the language used in a trial's consent form. Recently, there has been a push toward greater transparency (https://www.govinfo.gov/content/pkg/FR-2015-09-08/pdf/2015-21756.pdf), under the rationale that broadly publicizing the forms researchers use to communicate the risks and benefits of clinical trials will improve accountability, boost public trust in research, and inform the development of future consent forms. But what Harrison's experience, and

what my own look at clinicaltrials.gov seem to show, is that the science community isn't pushing nearly hard enough.

A **MAJOR WIN FOR** informed consent transparency came in 2018, when federal officials updated the so-called Common Rule (https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html) — a regulation that covers human subjects research funded by 20 U.S. agencies, including the Department of Health and Human Services, under which the National Institutes of Health falls. Effective January 21, 2019, the rule change requires federally funded clinical trials to publish an approved consent form on a public federal website (https://www.hhs.gov/ohrp/regulations-and-policy/informed-consent-posting/informed-consent-posting-guidance/index.html#:~:text=The%20revised%20Common%20Rule%20%28al the form is to be posted after the close of patient recruitment but no later than 60 days after participants' last required study visit. Researchers are given an option to upload the form either to clinicaltrials.gov (https://clinicaltrials.gov/) or to a designated folder (https://www.regulations.gov/docket/HHS-OPHS-2018-0021/comments) at the federal website regulations.gov.

Late last year researchers at Brigham and Women's Hospital and the National Library of Medicine found that while the number of posted consent

forms is indeed rising, it is hardly keeping pace (https://jamanetwork.com/journals/jamanetworkopen/article-abstract/2786296) with the Common Rule's requirements. The authors found, for example, that fewer than 18 percent of NIH-funded studies had posted forms.

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In September, I conducted my own search of clinicaltrials.gov and found that only 283 of the 1,112 federally funded interventional studies listed on the site as having started after January 21, 2019 and finished before January 21, 2022 had uploaded consent forms. Some of the studies had yet to upload any results at all, but even when I limited my search to those that had — an idea suggested to me by Geisinger (https://www.geisinger.edu/research/departments-and-centers/translational-bioethics-and-health-policy) research ethicist Michelle Meyer — little more than half had posted consent forms. (I also searched all of the more than 427,000 studies listed at clinicaltrials.gov — including past, ongoing, and upcoming studies in the U.S. and elsewhere that aren't subject to the Common Rule — and found

that consent forms had been shared by only 1.3 percent of them.) Meanwhile, the designated folder at regulations.gov, the alternative site where studies may deposit consent forms to satisfy the Common Rule, contained just 44 consent forms posted during the three-year window.

To be fair, some people have sounded alarms about publicly sharing consent forms. In practice, they note, researchers often use the forms less as a way to inform participants and more as a means to mitigate institutional liability (https://acsjournals.onlinelibrary.wiley.com/doi/abs/10.1002/1097-0142(19931101)72:9+%3C2811::AID-CNCR2820721507%3E3.0.CO;2-G). (*You can't sue us here at Big Academic Medical Center — it was all in the consent form!*) At least one group of health care attorneys argued (https://blog.petrieflom.law.harvard.edu/2016/01/19/the-common-rule-nprm-blog-series-part-3-posting-of-consent-forms/) that posting requirements could prompt researchers to write even more stilted, legalistic forms aimed at shielding themselves from lawsuits. The same group also fretted that a rule requiring the public posting of a consent form might confuse participants and the public (https://blog.petrieflom.law.harvard.edu/2016/01/19/the-common-rule-nprm-blog-series-part-3-posting-of-consent-forms/), because a clinical trial will sometimes use different versions of the form for different participants at different sites, and the consent form might get updated throughout the recruitment process. Who would decide which version to post, and how? Elsewhere, there were

concerns that a public posting requirement would stifle innovation (https://blog.primr.org/nprm-informed-consent/), for example, by keeping clinical investigators from exploring novel approaches to consent such as interactive video Q&As.

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I was and remain unmoved by these complaints. Publicizing consent forms will make them worse? Wait, what? And sharing them with everyone rather than with just the people you want to participate will necessarily increase liability risks? If so, that's a problem with American jurisprudence and not a justification for opacity. As for the potential confusion over multiple versions of a consent form, in an appropriate consent process (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5980471/) prospective participants should always be given the most updated version of the consent form, and an opportunity to ask questions. And one provision of the revised Common Rule mandates that multisite trials use a single institutional review board, which should help standardize consent forms across the

different sites. We now have some evidence that this is indeed happening (https://onlinelibrary.wiley.com/doi/full/10.1002/eahr.500092), although some local institutions have been reluctant to cede control.

With respect to video consent and other innovative approaches, the updated Common Rule says nothing about them other than references to "electronic format," and it's not clear why novel consent processes shouldn't be done transparently: Why not post a link to your consent video on clinicaltrials.gov for all the world to see?

As someone who has served on an institutional review board, read thousands of pages of mind-numbing consent forms, and participated in research as a human "subject" over the past 15 years, I think that the Common Rule more or less gets it right. Public posting of consent form language is a low-risk, low-burden act that could give motivated prospective participants a chance to see what they might be signing up for well ahead of time and gives all stakeholders an opportunity to flag problems. It could lead to more equitable, safer, better research. Or maybe not. But the only way we can know is by doing the experiment.

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For patients like Harrison's, who seek risky but potentially life-saving experimental therapies, the stakes couldn't be higher. Some contend — and, for what it's worth, I agree — that the fervor of the

current psychedelic hype cycle is driven more by a messianic push for legitimacy (https://psychedeliccandor.substack.com/p/to-the-field?s=r&utm_campaign=post&utm_medium=web) than by an unbiased search for truth. But what if MDMA really works? What if psychedelic-assisted therapy, delivered in a safe environment, can bring relief and healing to people suffering from PTSD and other traumas? Don't we want as many folks as possible considering all of the risks and benefits, the promises and disclaimers? Couldn't controversial psychedelic-assisted therapy studies have benefited from a few more eyes on their consent forms?

We can read millions of scientific papers, court documents, real estate listings, restaurant menus, drug prices, and movie reviews all with just a few keystrokes.

So why not consent forms?

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