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Web Round Up: Clinical Trials on Trial

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By Moira Kyweluk

This month saw breaking news web-wide on one aspect of medicine that has drawn critiques and support from both social scientists and biomedical experts: clinical trials. Drug trials overseen by the United States Food and Drug Administration (FDA) (see clinicaltrials.gov) and often executed by research universities and hospitals rarely if ever include major segments of the United States population. Anyone who might be expected to fail to tolerate a new medication or intervention, or experience an adverse event during a trial, is likely to be excluded. Dr. Ken Covinsky of the University of California-San Francisco, a geriatric specialist, took to his Twitter account in outrage (@geri-doc) while perusing a recent article published in the Journal of the American Medical Association on a trial to assess sodium levels —an important health consideration when treating older adults. The trial only included otherwise healthy (not diagnosed with any medical conditions; taking no medications) adults ages 20-69 years. The population most in need of this research on sodium levels, older adults, had been excluded from the study. "Since when does the U.S. population stop at age 69?" asked Dr. Covinsky. His tweet about the JAMA article mirrored his outrage: "How is this possible? Unacceptable! I can think of no good rationale for this exclusion. This has got to stop." (@geri_doc)

The focus in clinical trials and other basic research on otherwise healthy, younger adults leaves major gaps in understanding of how drugs affect older people. This group tends to be sicker, taking more prescription medications, and dealing with multiple conditions simultaneously. Beginning January 2019 the National Institute of Health will require all grant applicants for clinical research funding to provide adequate justification for age groups left out of proposed studies. While a step in the right direction, for greater impact this change would also need to be applied to the FDA, which is tasked with assessing the safety and efficacy of new drugs, devices, and biologics. A volume of clinical research is privately funded, and thus would not be affected by age mandates. Notably, children are also frequently left out of both FDA trials and clinical research, and pediatric patients are often given adult medications at adapted doses that are the "best guess" of the prescribing clinician.

When clinical trials do include children, properly meeting enrollment criteria—including age, diagnosis, and previous medical history— and

parental informed consent are key. Renowned child psychiatrist Dr. Negamani "Mani" Pavuluri, a Distinguished Fellow of the American Academy of Child and Adolescent Psychiatry, was sanctioned and the University of Illinois Chicago (UIC) penalized for lax oversight in a research misconduct case. UIC previously considered Dr. Pavuluri a major asset; as founding director of the Pediatric Mood Disorders Program, her clinic for children drew patients, clinicians, and trainees. Dr. Pavuluri received grant funding from the National Institute of Mental Health for a project that ran from 2009-2013 (when it was shut down by UIC) on clinical care routines— including treatment with lithium—for adolescents diagnosed with bipolar disorder. Dr. Pavuluri violated study approvals specifying only children over 13 could be enrolled, and failed to discuss study risks or obtain assent from parents. She blurred the lines between her research project and her clinical practice; she was further charged with falsifying data to cover up experimentation with medications on children much younger than 13, some as young as 9, without parental consent.

In December 2017, UIC was tasked with paying back the $3.1 million dollars the institution had received from the National Institute of Mental Health to fund Dr. Pavuluri's study. The NIMH stated the university is responsible for oversight of research, and the UIC Institutional Review Board failed to protect human subjects, in this case vulnerable children. Dr. Pavuluri was found to engage in "serious and continuing noncompliance" with rules to protect human subjects that directly violated the terms of the grant she had been awarded. Due to these issues, her research record and publications based on the study in question have been deemed scientifically meaningless, which follows previous retractions of her work from top journals.

Outside academia, 23andMe, a company offering a direct-to-consumer DNA testing service made headlines earlier this year with the announcement it will be launching a massive study investigating the genetic basis of weight loss . The company is recruiting 100,000 people— beginning with contacting 1.3 millions previous customers— to participate in a trial assessing the efficacy of two different diets or an exercise plan on weight loss after three months. Participants will be tasked with reporting back on weight loss or gain, and that data will be analyzed in connection with genetic data on file with the company. 23andMe already holds DNA data from the saliva samples of more than three million people; the company is estimated to control one of the two or three largest biobanks in the world. This trial is intended to demonstrate that direct-to-consumer companies like 23andMe are capable of performing large-scale clinical trials, like those typically run by research hospitals and universities.

In related news, alleged "Golden State Killer" Joseph James DeAngelo was caught using DNA data from one of his unknowing relatives

had submitted to GEDMatch, a database for genomics researchers. The case has raised issues about privacy in the age of massive commercial biobanks, particularly those containing potentially incriminating genetic material. Most consumers are unaware of the myriad ways their data may be used by the company or sold to other parties; Slate Magazine has drawn parallels to the Facebook/Cambridge Analytica privacy controversy.

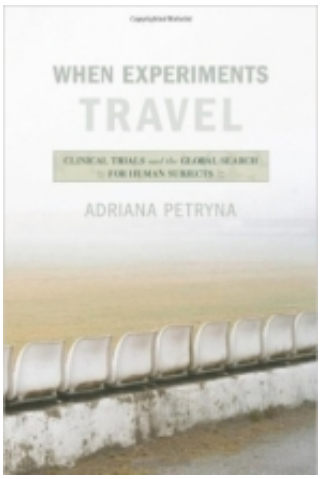
Clinical trials on three male birth control methods were also in the news this month. Investigations into male contraceptive options with minimal side effects have been reinvigorated over the past year. This upcoming summer, a multisite trial involving 420 heterosexual couples in the US, UK, Sweden, Kenya, Italy and Chile will examine the efficacy of Nestorone-Testosterone, a gel containing progestin a sex hormone that can suppress testicular production of sperm. The gel is applied to the arms and shoulders daily, and the couples will rely on this birth control method for 12 months once male sperm count has been adequately lowered to prevent pregnancy.

Data from trials of a male contraceptive pill, Dimethandrolone undecanoate (DMAU) were presented at the 2018 Endocrine Society meetings. DMAU appears to be safe when used every day for a month. Research examining side effects and the possibility of a longer acting injection—similar to Depo-Provera shots for women, is underway.

And finally, a nonsurgical vasectomy, termed “reversible inhibition of sperm under guidance” or RISUG, has long been under development and testing by researchers in India. Biomedical engineer Dr. Sujoy Guha, faculty member at the Indian Institute of Technology developed the technology using a polymer gel injected into a man’s vas deferens to block sperm in the 1970s. . An injection at a later date breaks down the gel polymer, making the procedure reversible, with no major side effects. To date 540 men in India have received the reversible injection, and it appears to be effective long term—up to 13 years! This technology is likely far off from clinical trials in the US or entering the US market commercially, but in anticipation California-based nonprofit the Parsemus Foundation has licensed the RISUG technology for investigations in the US.

More on clinical trials in anthropology and beyond:

Critical scholarly work from Adriana Petryna on clinical trials being offshored to low and middle-income countries.



A nice summary from Science on the history and current practices in protecting human research subjects

On why we don't have a viable male birth control option yet from Vice

From Somatosphere , a Web Round Up: A Not So Unified Theory of Birth Control Side Effects by Anika Jugovic-Spajic

On a lighter note, a cartoon from the April 22, 2018 Issue of the New Yorker

"How long before the clinical trials are over?"

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