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Unregulated Health Research Using Mobile Devices: Ethical Considerations and Policy Recommendations

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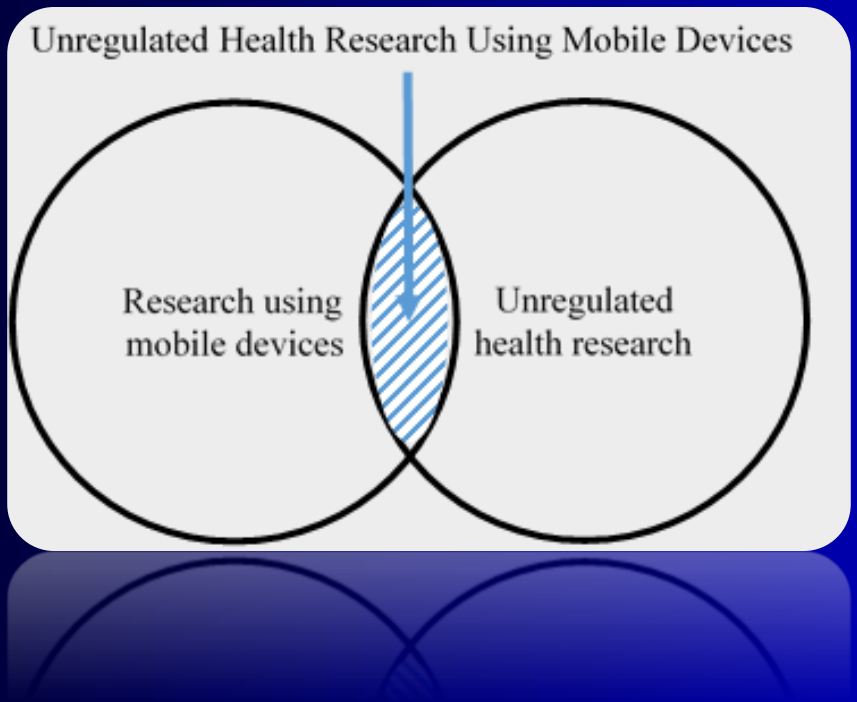
Handout materials and a pre-publication draft of Unregulated Health Research Using Mobile Devices: Ethical Considerations and Policy Recommendations have been posted on the following website:

https://louisville.edu/mobileelsi

A pre-publication version of the final report for another NIH grant, Legal and Ethical Challenges of International Direct-to-Participant Genomic Research: Conclusions and Recommendations, has been posted on the following website:

https://louisville.edu/research/dtp


Unregulated Health Research Using Mobile Devices
Research using mobile devices
Unregulated health research

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Research Methodology

1. Qualitative interviews with 41 thought leaders:
    - App and device developers
    - Researchers using mobile devices
    - Patient and research participant advocates
    - Regulatory and policy professionals

2. Working group meetings to hear from experts and discuss issues.

Working Group Meeting #1, La Jolla, CA, October 9-10, 2017
Surveying the Landscape: Technology, Researchers, and Participants

Working Group Meeting #2, Chicago, IL, April 24-25, 2018
Thought Leader Input and Regulatory Framework

Working Group Meeting #3, Atlanta, GA, October 25, 2018
Developing Ethical Guidelines and Policy Options

Working Group Meeting #4, Houston, TX, April 10, 2019
Formulating Policy Recommendations and Planning Publications

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3. App Developer Workshop

- September 12, 2019
- New York Genome Center
- Discuss research ethics and health apps

4. Policy Briefing

- November 12, 2019
- Georgetown University Law Center
- Presentation of recommendations

5. Publication of symposium issue of the *Journal of Law, Medicine and Ethics*

- 21 articles, including Recommendations
- Publication date: March 2020
- Open access

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1. Unregulated Health Research Using Mobile Devices: Introduction
2. Ethical Considerations in the Conduct of Unregulated mHealth Research: Expert Perspectives
3. Who Are the People in Your Neighborhood? Personas Populating Unregulated mHealth Research
4. mHealth Research Applied to Regulated and Unregulated Behavioral Health Sciences
5. There Oughta Be a Law: When Does(n't) the U.S. Common Rule Apply?
6. FDA Regulation of Mobile Health
7. Mobile Research Apps and State Research Laws

8. Mobile Research Apps and State Date Protection Statutes
9. Assessing the Thin Regulation of Consumer-Facing Health Technologies
10. The Federal Trade Commission and Consumer Protections for Mobile Health Apps
11. Diversity and Inclusion in mHealth Research: Enhancing Participation, Addressing Risks
12. Do Groups Have Moral Standing in mHealth Unregulated Research
13. Online Pediatric Research: Addressing Consent, Assent, and Parental Permission
14. Expert Perspectives on Oversight for Unregulated mHealth Research: Empirical Data and Commentary

15. Electronic Informed Consent in Mobile Applications Research
16. Privacy and Security Issues in Mobile Health App Research
17. Return of Results in Mobile Health Research
18. Data Sharing in the Context of Health-Related Citizen Science
19. International mHealth Research: Old Tools and New Challenges
20. To What Extent Does the EU General Data Protection Regulation (GDPR) Apply to Citizen-Scientist-led Health Research with Mobile Devices?
21. Unregulated Health Research Using Mobile Devices: Ethical Considerations and Policy Recommendations

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Growth of unregulated health research

Michelle L. McGowan

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Growth of Unregulated Health Research

- Enthusiasm for use of big data to understand and promote population health
- Extension of methods of citizen science into health research

Appeal of these approaches for health research

- Skepticism about “traditional” health research
  - Academic institutions
  - Commercial entities
- Disrupts traditional funding priorities and timelines for conducting health research
  - Discovery science
  - Small populations
  - Exclusions and pacing of research

Who is subject to federal research regulations?

- Researchers and institutional recipients of federal funding are subject to the Common Rule
- Researchers intending to submit drugs or devices for approval by the Food and Drug Administration

Which researchers may NOT be subject to these regulations?

- Independent researchers
- Citizen scientists
- Patient-directed or patient-driven researchers (e.g. N of 1 studies, rare disease groups)
- Self-experimenters

Unregulated mHealth research tools

- Use of health apps for mobile devices to collect biometric and passive user data
- Direct-to-consumer genomic testing
- Publicly available datasets
- Crowdsourcing platforms
- Social media to promote translocal engagement

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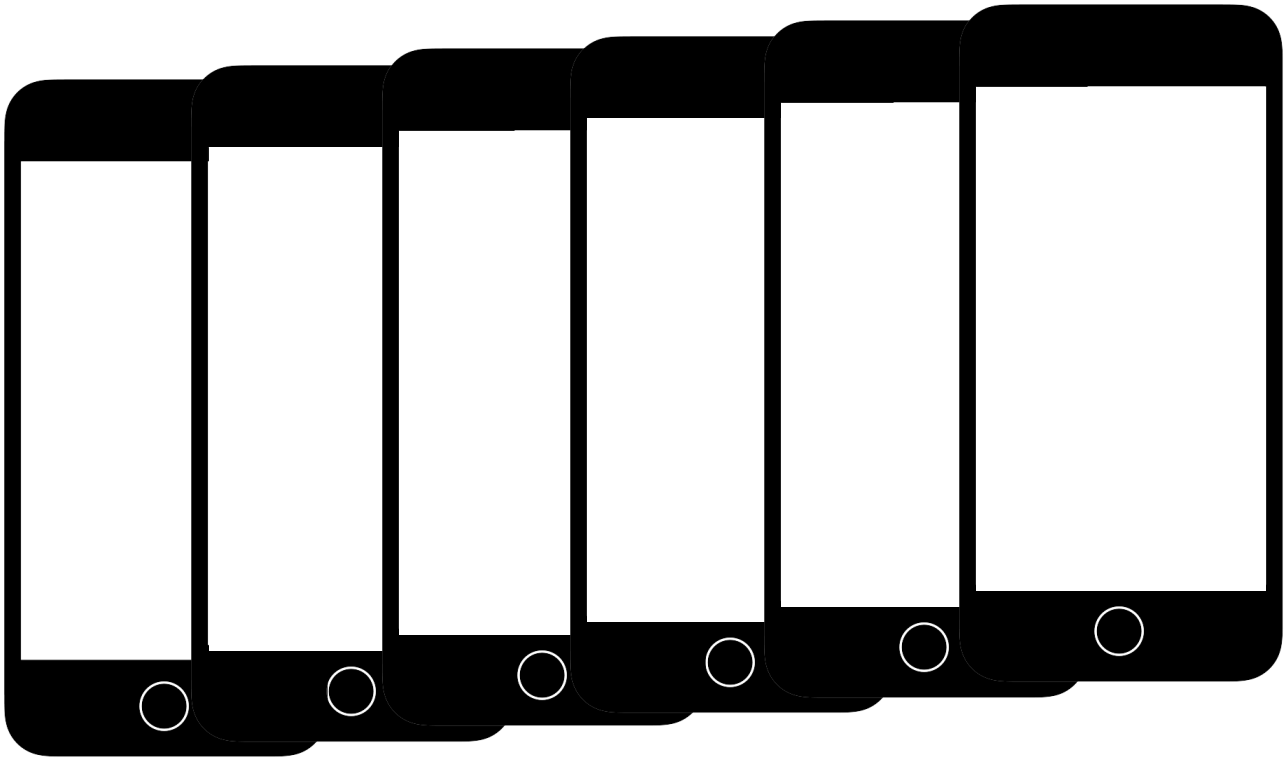
Role of mobile devices

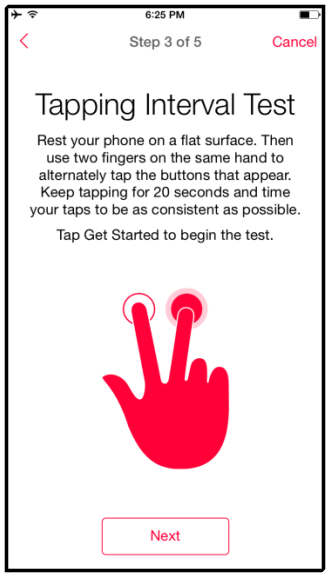
John T. Wilbanks

move beyond insular health tracking

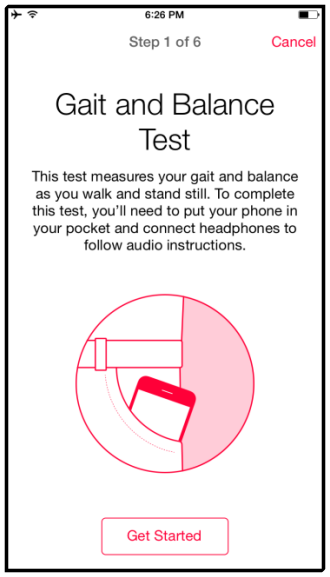


mPower activities

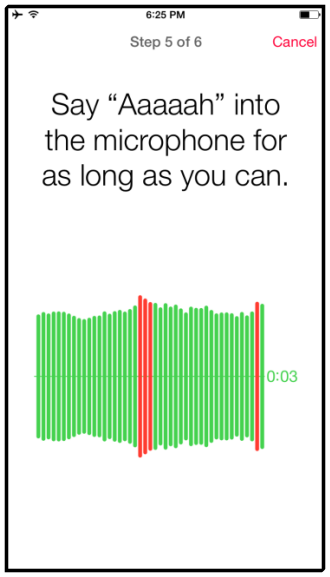
motor initiation



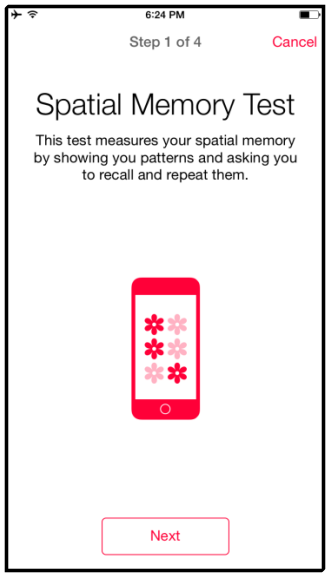
gait/balance



hypophonia



memory



data generation

mPower

first 6 months

16,585 participants consented

14,684 participants enrolled

9,520 agreed to ‘share broadly’

1,087 self reported PD diagnosis

mPower helps decipher Parkinson’s disease.

The variability in Parkinson’s disease symptoms has left many questions unanswered. So the University of Rochester and Sage Bionetworks created the mPower app to precisely measure data such as dexterity, balance, memory, and gait. This information could help researchers better understand how various symptoms are connected to Parkinson’s disease. In turn, participants could start to recognize their own signs and symptoms.

Sage BIONETWORKS

Robert Wood Johnson Foundation

ParkinsonNet

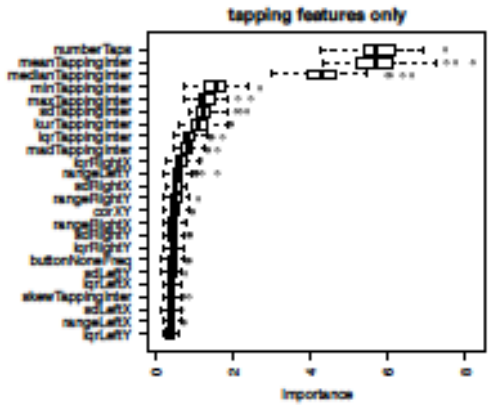
THE MICHAEL J. FOX FOUNDATION FOR PARKINSON’S RESEARCH

recruitment

dimensionality of lived experience

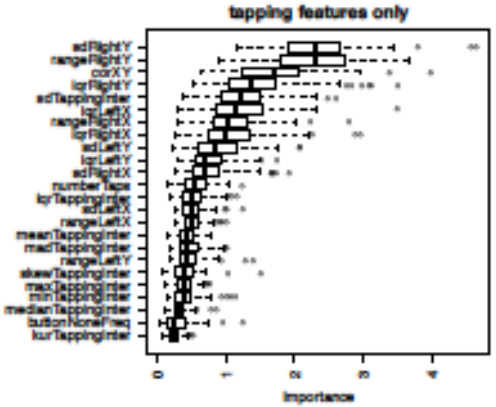
Traditional Measures	First-order Features
Number of Taps	Number of taps, Mean tapping interval, Median tapping interval, Minimum tapping interval, maximum tapping interval, Standard deviation of tapping interval, Kurtosis of tapping interval, Interquartile range of tapping interval, Interquartile range of right button X, Range right button X ,Standard deviation right button X, Interquartile range of left button X, Range left button X ,Standard deviation left button X, Interquartile range of right button Y, Range right button Y ,Standard deviatiion right button Y, Interquartile range of left button Y, Range left button Y ,Standard deviation left button Y, Correlation X and Y, Skew tapping interval, No-button tapping frequency

invisible impacts made visible



Number of Taps
Mean Tapping Interval
Median Tapping Interval

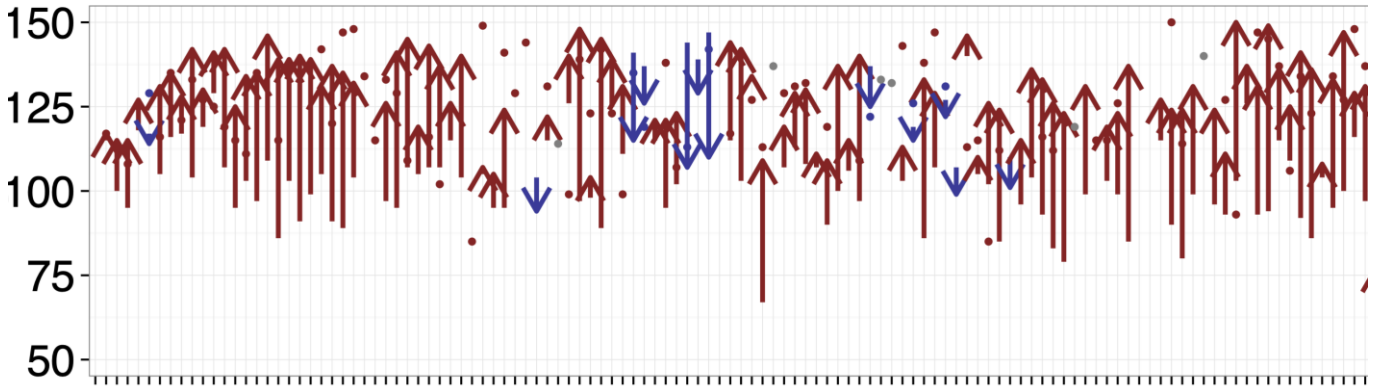
62 y old Man



Standard Deviation R Y
Range Right Y
Correlation X Y

67 y old Woman

the reality of personal health



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Benefits and risks of unregulated health research

Kyle B. Brothers

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Benefits of Unregulated Research

- Enables new funding streams, methods, and topics
- Democratizes research (including patient groups)
- Expands the base of researchers
- Crowdsourcing and Citizen Science Act of 2017

Risk of Harms

1. Physical and psychological harms
   - Inaccurate app provides erroneous health information
     (e.g., incorrect diagnosis, medication dosing)
   - Use of app makes condition worse
     (e.g., sleep trackers causing orthosomnia; diet apps causing orthorexia nervosa)

2. Dignitary harms

- Disclosure of private health information (e.g., transmission of sensitive data for marketing)
- “Authorized” access to cell phone data (e.g., study of 211 diabetes apps consent for download included: turning on camera and mic, collect tracking info, modifying info)

3. Economic harms

- Identity theft
- Access to text messages, phots and videos, credit cards, personal data

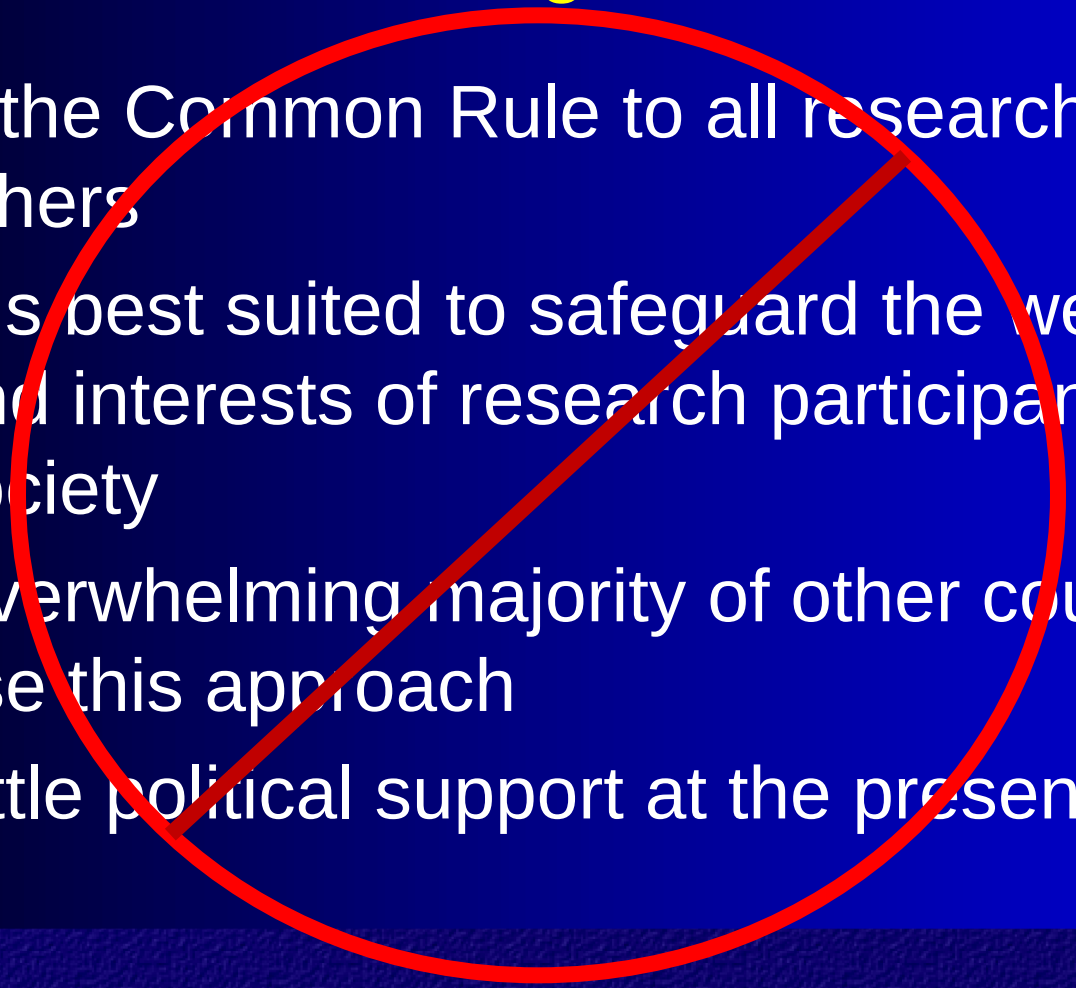
4. Societal harms

- Group harms based on questionable research leads to stigma
- Bad science leads to societal harms (note: unregulated research usually means no IRB review, funder review, peer review publication)
- Distribution over social networks

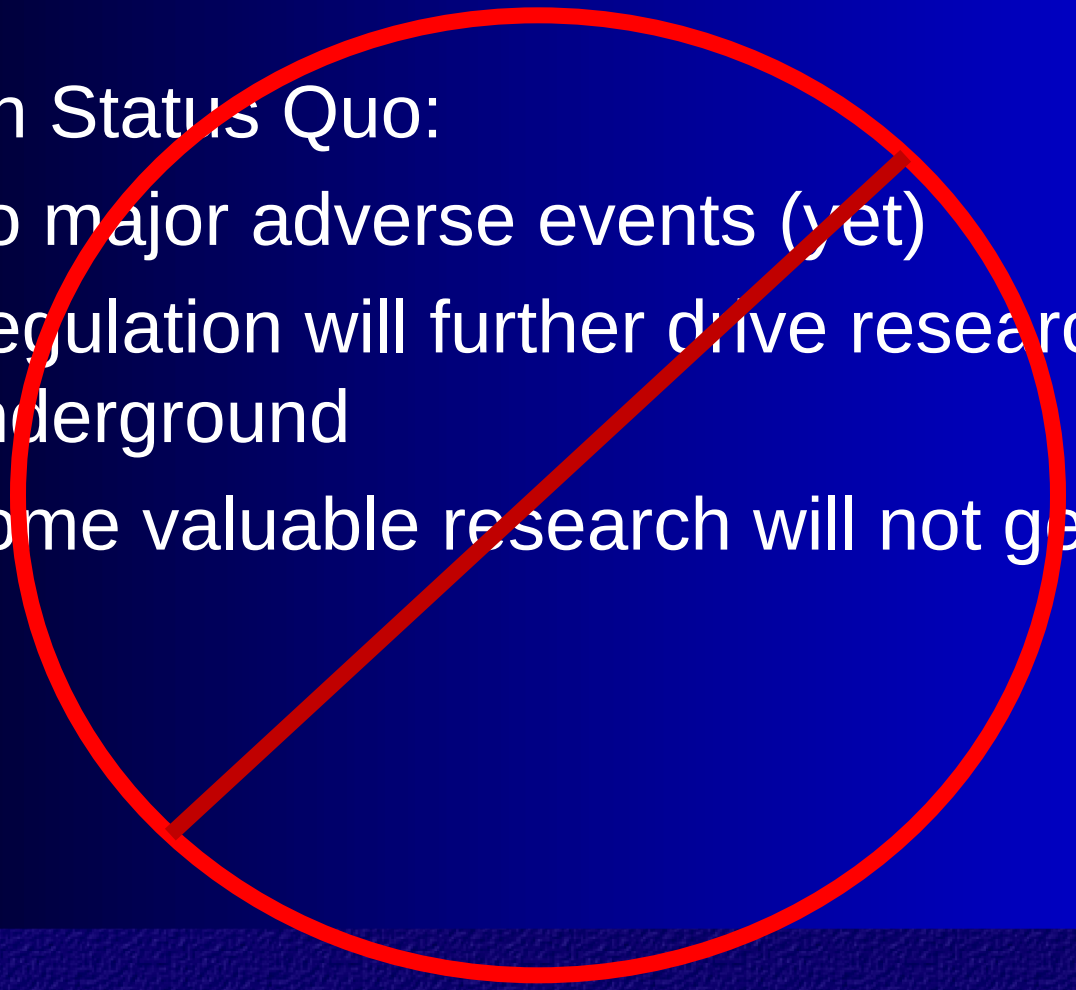
Recommendations

Options for Preventing Harms from Unregulated Health Research Using Mobile Devices

1. Extend the Common Rule to all research and researchers
    - It is best suited to safeguard the welfare and interests of research participants and society
    - Overwhelming majority of other countries use this approach
    - Little political support at the present time



2. Maintain Status Quo:
    - No major adverse events (yet)
    - Regulation will further drive research underground
    - Some valuable research will not get done



3. Middle ground approach based on pragmatism

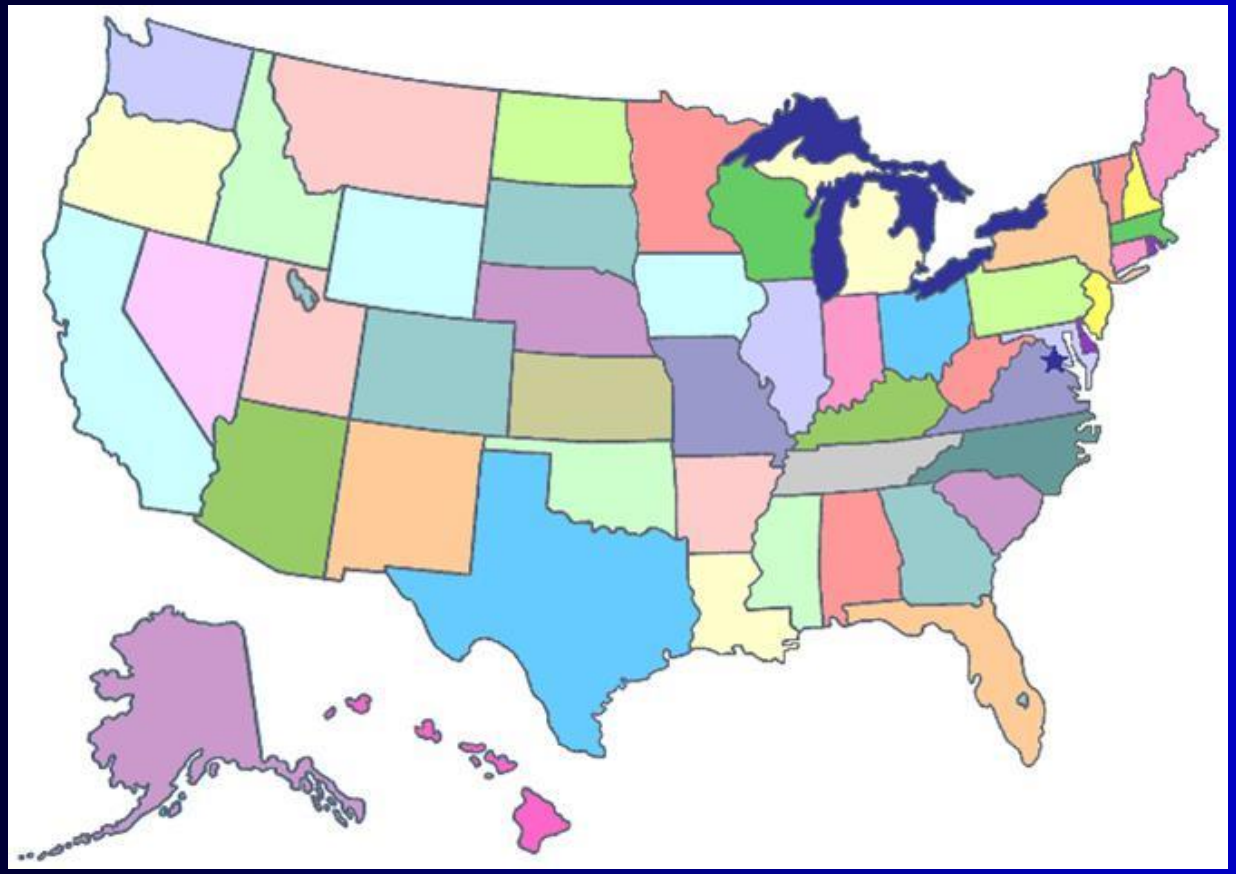
Question: How do you persuade independent-minded individuals and entities to do what you think is right when they have no legal obligation to do so and they think it's unnecessary?

Answer:

1. Establish outer boundaries
2. Provide education and assistance
3. Appeal to their self-interest and sense of decency
4. Make it easy to do

Federal Research Regulations

State Research and Data Protection Laws



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Background

Maryland	Applies the Common Rule to all research conducted in the state.
Virginia	Provides coverage for all research, with its own set of rules.
New York	Only applies to “physical or psychological interventions.”
California	Only applies to “medical experiments.”
Illinois	Only applies to “physician-researchers.”
Wisconsin	Only applies to “patients.”

Recommendations

1-1. States that do not currently regulate all non-federally funded research should consider enacting a comprehensive law (or amending existing laws) to regulate all research conducted in the state.

1-2. States considering such legislation should review the Maryland research law, which contains a broad definition of “person” performing research and expressly applies the most recent version of the Common Rule.

1-3. States also should consider extending the application of data breach, data security, and data privacy statutes to all mobile device-mediated research.

National Institutes of Health

Contra Arguments

Why NIH should not take the lead:

1. NIH epitomizes the “research establishment”
2. NIH has a compliance role (with current grants) that scares unregulated researchers
3. NIH is not a source that app developers would likely consult

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Pro Arguments

Why NIH should take the lead in unregulated health research using mobile devices:

1. NIH has numerous programs promoting novel research strategies (e.g., Common Fund)
2. NIH has various programs of scientific education and workforce development
3. NIH already has an interest in mHealth and citizen sci. (e.g., Cit. Sci. Working Group)

Recommendations

2-1. NIH should expand its support for unregulated health researchers and centralize responsibility for providing assistance. NIH may accomplish this by establishing a new Office of Unregulated Health Research, designating an existing Institute or Center to oversee initiatives on unregulated health research, funding grantees to provide assistance to unregulated researchers, or through other means.

2-2. NIH should appoint an advisory board of diverse stakeholders to assist the NIH official or entity in charge of unregulated health research.

Recommendations

2-3. Unregulated health researchers need accessible, consolidated, updated, and curated information about research laws and ethical considerations from a trusted source. NIH should provide technical and understandable information about mobile and wireless technologies for app developers, researchers, and research participants. Therefore, NIH should develop and maintain a website containing the following.

a. Information and FAQs identifying the laws applicable or inapplicable to health research, including the Common Rule, FDA, FTC, state research laws, and the HIPAA Privacy Rule;

b. Information about externally developed best practices and ethical principles for unregulated health research;

c. Directory of open source tools for health research apps, including sample consent documents, privacy protection measures, and security information; and

d. Directory of resources for technical assistance.

2-4. NIH should fund studies on unregulated mobile health research to determine the most effective ways of encouraging compliance with best practices, attaining and maintaining quality, and developing open-source tools.

2-5. NIH should, in consultation with the OHRP, work with citizen science groups and other organizations of unregulated researchers to support educational programs for mobile health app developers, unregulated researchers, and participants, as well as to provide technical support.

2-6. NIH, in consultation with OHRP, should consider the feasibility of establishing or supporting cost-free, independent, research review organizations to advise unregulated researchers on identifying and resolving ethical challenges raised by their research.

Food and Drug Administration

Background

After the 21st Century Cures Act, the FDA has said its coverage of mobile medical apps will apply to "only those mobile apps that are medical devices and whose functionality could pose a risk to patient safety if the mobile app were to not function as intended."

FDA has indicated that it will not bring enforcement actions against mobile health apps that pose no apparent risk to patient safety.

Along with ONC, FTC, and OCR, FDA has published an online, joint decision aid to help app developers identify which federal laws apply to their apps.

Recommendations

3-1. The FDA should continue its interagency collaborative efforts to reduce regulatory duplication and identify and assess areas unaddressed by current regulations. One area for immediate interagency consideration is how best to ensure transparency in validation of mobile health app algorithms.

3-2. The FDA should increase its engagement with the health app developer community to raise awareness of its guidance documents issued in September 2019.

3-3. The FDA should require developers of mobile health apps to make transparent disclosures regarding the intended use (including research) and technical capacities of their apps, especially mobile medical apps.

3-4. The FDA's guidance documents have failed to address how its regulations apply to citizen-led research using data from mobile health apps. In particular, the FDA needs to clarify the following: (1) when such research may require an IDE; (2) what forms of research using data from mobile health apps constitutes "significant risk" research under the IDE regulations; (3) how the concept of a "sponsor-investigator study" applies to nontraditional and citizen-led research; (4) what forms of communication about citizen science projects could subject organizers to charges of unlawful promotion of unapproved uses of a device; and (5) what constitutional constraints limit the FDA's power to regulate nontraditional, citizen-led research efforts.

Federal Consumer Protections through the FTC and CPSC

Background

Because FDA's jurisdiction does not extend to some mobile health apps' software functions and uses, such as fitness trackers and medical calculators, regulatory responsibility could fall to consumer protection agencies.

FTC has initiated enforcement actions involving health since 2011, especially focusing on entities that have claimed to identify or cure health conditions, such as acne, skin cancer, and vision problems.

Background

CPSC is authorized to protect consumers through surveillance functions and enforcement.

CPSC issued a report to guide consumer safety and protection in relation to digitally connected devices called “A Framework for Safety for the Internet of Things,” which focused on devices that could result in physical harms, illness, or death of consumers.

Recommendations

4-1. The FTC should increase its efforts to encourage self-regulation of unregulated mobile health researchers by providing guidance and educational resources to app developers, unregulated researchers, and participants in unregulated mobile health research through, among other things, best practice guidelines and web-based, interactive educational tools.

4-2. The FTC should promote privacy, transparency, and fairness in unregulated mobile health research using preventative and remedial approaches, such as the following.

a. The FTC should increase targeted enforcement actions against developers of unregulated mobile health research platforms who engage in deceptive or unfair trade practices (e.g., making false or misleading statements, failing to provide adequate privacy or security for mobile Internet-connected devices) and seek monetary redress and other appropriate relief on behalf of injured consumers.

b. The FTC should develop and provide multi-media educational materials for consumers about the kinds of harms and complaints being monitored, and publicize bad actors in the unregulated mobile health research sector through consumer advisories.

4-3. The CPSC should increase surveillance and monitoring of research software, applications, and systems enabled through mobile, Internet-connected devices by establishing a consumer hotline or website for reporting safety concerns, such as breaches of privacy and confidentiality; and it should assess monetary penalties against researchers and developers who violate consumer product safety regulations pertaining to Internet-connected mobile devices.

Centers for Disease Control and Prevention

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Background

There is a serious deficiency in the availability of information concerning unregulated health research using mobile devices, such as how much is taking place, of what kind, by what types of researches, and with numbers and types of adverse events.

Surveillance can help define the scope, scale, and impact of perceived health threats, and point the way to prevention efforts.

Recommendations

5-1. CDC should work with NIH and private entities (e.g., philanthropic foundations) to establish the prevalence and nature of unregulated health research using mobile devices and then establish a system to monitor trends of activities in this area over time.

5-2. CDC, in consultation with NIH, OHRP, and private entities (e.g., philanthropic foundations), should develop a system for compiling and reporting data on adverse events caused by health research using mobile devices, perhaps as part of a general effort to monitor the health effects of mobile devices, such as transportation accidents caused by the use of mobile devices and the health benefits and harms conferred by wellness apps and fitness wearables.

5-3. CDC, along with collaborators in the academic and non-profit communities, should study the data on adverse events caused by regulated and unregulated health research using mobile devices and issue reports and recommendations to promote actions to prevent or lessen such events.

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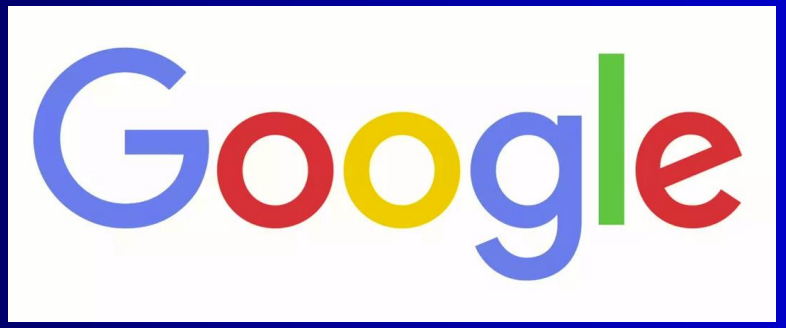
Consumer Technology Companies and App Developers



ResearchKit

It's open source.
So the world can
make the most of it.

ResearchStack

An SDK for building research study apps on Android

Source Code (GitHub) | Documentation | Announcements & Forum | Contact Us

What is ResearchStack?

ResearchStack is an SDK and UX framework for building research study apps on Android.

It is designed from the ground up to meet the requirements of most scientific research, including capturing participant consent, extensible input tasks, and the security and privacy needs necessary for IRB approval.

Recommendations

6-1. Google should join Apple in requiring a signed informed consent document for any mobile health research applications emerging from the use of ResearchStack.

6-2. Apple and Google should require developers to upload IRB approval letters as PDFs, and make those documents available in-line to consumers contemplating installing a mobile research app. This disclosure requirement is compatible with both traditional institutional review and with unregulated research where there is more than minimal risk.

6-3. Apple and Google should implement and enforce a “floor” for privacy policies and terms of use. For example, such a floor could include provisions that no data may be transferred to third parties without specific consent for each use.

6-4. Developers of research apps should leverage the existing, community-standard toolkits, such as ResearchKit and ResearchStack, each of which contains informed consent workflows and developer tools. These apps should (1) accommodate independent review when required by the app store platforms; (2) allow for isolation of malicious code elements; (3) publish a "software bill of materials" for any code integrated from a repository such as GitHub; and (4) publish a privacy disclosure notice."

6-5. Makers of wearable devices should implement encryption both for data at rest and in transit. We further encourage federal and state investment in fundamental encryption research and development to support encryption on wearables that is easier to include for developers without overly damaging battery performance.

6-6. Security also must be implemented once the data have left the wearable and moved to the consumer's phone (or directly to the servers of the wearable company), and therefore we recommend that manufacturers of wearables adhere to basic cybersecurity practices.

Organizations of Unregulated Researchers

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Recommendations

7-1. Organizations of researchers conducting studies in unregulated environments, such as community organizations, member associations, and patient research networks, should adopt guidance and/or standards for their members, including on the following issues:

a. Guidance on how best to transparently communicate the goals, risks, benefits, and data handling procedures of their research prior to enrolling a participant.

b. Guidance on privacy policies and terms of service for mobile device-based research.

c. Guidance on the privacy policies and terms of service of third party developed devices or apps.

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Discussion

Megan Doerr