1st. Annual Office of Human Research Ethics/IRB Retreat

Wednesday, February 17, 2016

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

Housekeeping Announcements

- Thank you for coming & Welcome
- Restrooms outside and to the right
- Lunch will be on the 1st. Floor in the Dining Room below this room
- Evaluation will be sent to you shortly
- Mark your calendars now for next year:
  - **Wednesday, February 15, 2017**

The Office of Human Research Ethics: An Update and Progress Report

February 17, 2016

Elizabeth Kipp Campbell, Ph.D., CIP
Director

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

Topics of Discussion

1. Staffing and Reorganization of the OHRE Staff
2. IRB Committees: Refinement and Expansion
3. Educational Opportunities
4. Metrics of IRB Activity
5. New Initiatives
6. Coming Opportunities and Challenges

Current OHRE Staff

There are currently 19 staff members

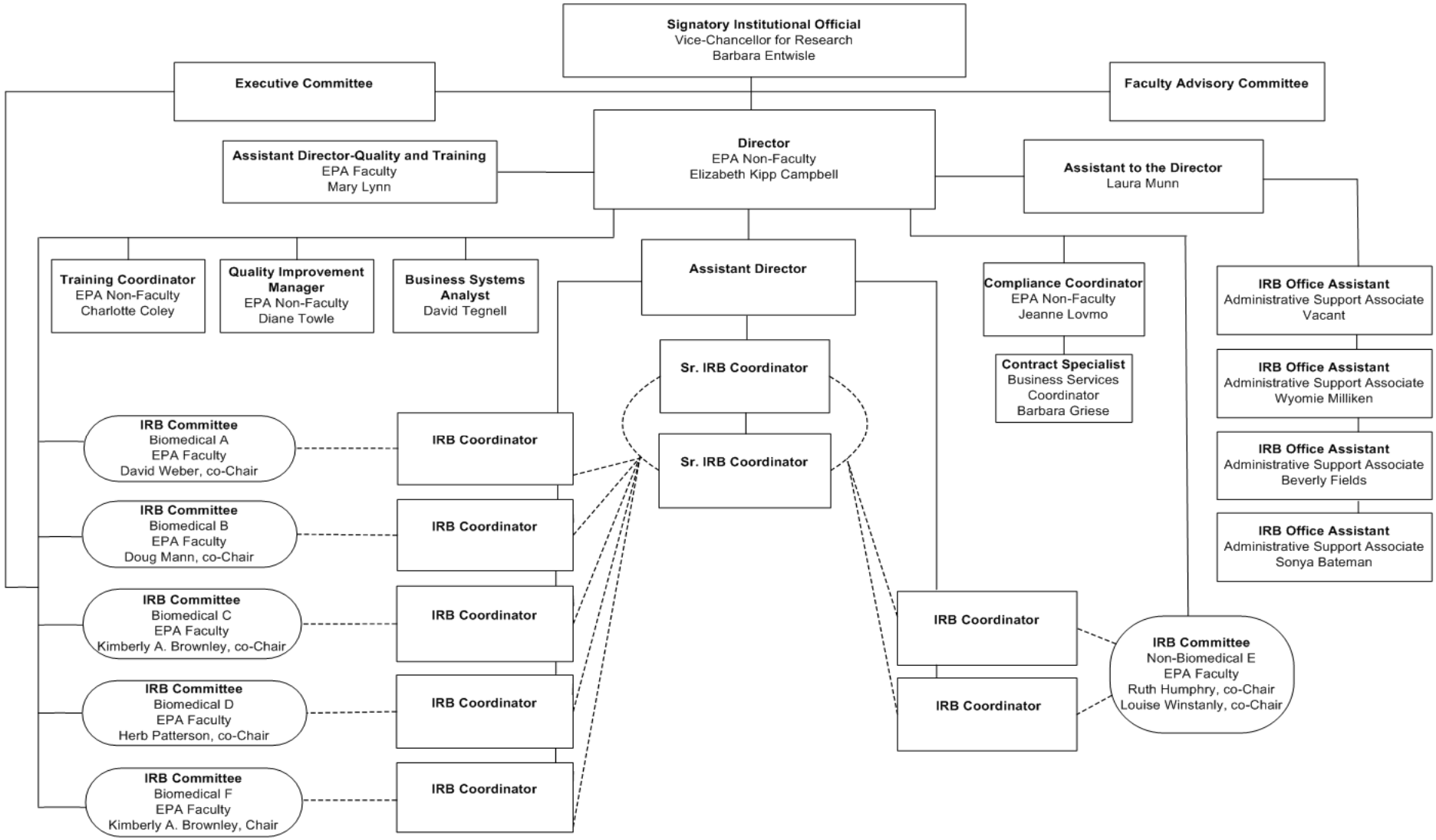
These include: Director, 6 Management level staff, 4 Administrative staff, 1 Business services coordinator, and 8 IRB Coordinators.

There are currently 6 staff members who are certified as IRB Professionals (CIP). Four more staff are taking the CIP exam next month.

Reorganization of the OHRE Staff

Due to increased volume, desire for better customer service and turnaround, and to attract and retain high quality staff and remain competitive with peers, a new staffing configuration was proposed and approved by the Vice Chancellor for Research in early fall of 2015.

OHRE Proposed Reorganization Chart



I certify that this organizational chart accurately depicts the Office of Human Research Ethics, UNC-Chapel Hill

_____ _____

Elizabeth Kipp Campbell Date

Rev. 10/29/2015

Refinement and Expansion: IRB Committees

1. Adding Vice-Chairs to all committees: succession planning
2. Developing training program for new Chairs and Vice-chairs
3. Adding expertise across all committees, including discussions with School of Medicine and Lineberger
4. Refining on-boarding process for new IRB members
5. Developing annual evaluation process for IRB Chairs and members

Educational Opportunities

Held 2-day PRIM&R special educational seminar in October 2015

Sent 9 staff members/chairs to the national Advancing Ethical Research (AER) Conference

Participated in numerous Webinars from OHRP, PRIM&R, and AAHRPP

Implemented first annual IRB Retreat

OHRE IRB Metrics

- Total volume continues to increase, averaging about 6% per year over the past 4 years
- Reviewed over 5000 studies last year, and took over 10,000 actions this past year
- The largest portion of reviews is Expedited, followed by NHRS, Exempt, and then Full Board
- Anecdotally there appears to be an increase in complexity of Full Board studies

New Initiatives

1. Process Improvement Project
2. Faculty Advisory Committee
3. QA/QI full program implementation

Process Improvement Project

1. Undertaken in conjunction with ORIS and facilitated by Jeremy Dott
2. Review our ENTIRE process from the moment we receive a study until the final letter is sent
3. Map current process, revise/improve the process, and determine how IRBIS can support this process and our business needs
4. Done through group and individual interviews, group meetings, and RPI techniques
5. Began early February 2016 and plan to complete by end of May 2016

Faculty Advisory Committee (FAC)

- Composed of faculty from key colleges/schools across the university
- Goal to increase input from and satisfaction of researchers
- Provide advice and new ideas for customer service, education, collegiality and problem resolution
- Currently in the planning stages
- Proposed implementation by May 2016

OHRE Quality Improvement and Quality Assurance Program

- Led by Diane Towle on the OHRE side and Val Buchholz on the Office of Clinical Trials side
- For-cause audits of researchers as directed by the IRB
- Routine auditing of a percentage of approved studies based on risk profile
- Education and auditing assistance as requested by researchers
- Auditing of our internal IRB reviews and processes

Coming Opportunities and Challenges

- New Vice Chancellor for Research and Institutional Official
- New direct reporting relationship to Associate Vice Chancellor for Research Compliance, Robin Cyr
- Notice of Proposed Rule Making – Final Rule and implementation dates????

Elizabeth Buchanan, PhD

Elizabeth Buchanan, Ph.D. is Endowed Chair in Ethics and Director of the Center for Applied Ethics at the University of Wisconsin-Stout. During 2015-2017, she is serving as Director of Research Administration, where she is responsible for overseeing IRB, IACUC, research misconduct, and grants and contracts.

Elizabeth's research focuses on the intersection of research regulations and Internet research. She has written and presented widely for over fifteen years to many IRBs throughout the country, and research ethics boards internationally, including Ireland, India, Finland, Canada, and Serbia, among others. In addition, she's presented to the Secretary's Advisory Committee to the Office for Human Research Protections on multiple occasions, and was a primary contributor to the SACHRP Recommendations on Internet Research. She has also been a keynote speaker for a number of Office for Human Research Protections Community Research Forums. Elizabeth is active in Public Responsibility in Medicine and Research, serving on the faculty roster since 2008 and serving on the Conference Planning Committee since 2012. She was the Conference Co-Chair of PRIM&R's SBER 2015 conference, and as of 2016, joined the Board of Directors.

Elizabeth Buchanan, PhD (continued)

Also, Elizabeth has been a member of the American Association for the Advancement of Science Committee on Scientific Freedom and Responsibility since 2012.

In addition to her work on Internet research, Elizabeth is currently PI on her fourth National Science Foundation grant. In her recent study, she is looking at the ethical implications of service learning programs, and specifically, Engineers without Borders. Recent publications include a briefing on algorithmic harms in *Data-Intensive Research in Education: Current Work and Next Steps;* an article in *Lecture Notes in Computer Science*, entitled "The New Normal: Revisiting Internet Research Ethics," an entry in the *Stanford Encyclopedia of Philosophy* entitled *Internet Research Ethics*, and a chapter on research ethics in the volume, *Research, Evaluation and Audit* (Facet Publishing). Elizabeth is the editor of one of the first anthologies of Internet research ethics (*Readings in Virtual Research Ethics,* 2004), and is author and/or co-author to numerous papers on research ethics and methods. Elizabeth is also primary co-author to the Association of Internet Researchers Ethics Guidelines for Internet Research. She holds BA degrees from Rutgers University, and her Master's and PhD from the University of Wisconsin-Milwaukee.

Is Facebook Hurting Your Study?

Ethical and Study Integrity Concerns Around Participant Use of Social Media

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Acknowledgments

- Dr. Lindsay McNair, WIRB
- Charlotte Coley
- Leslie Ray, Laura Munn
- UNC-CH
- NSF
- All of you!

Disclosure

I have no relevant personal/professional/financial relationship(s) with respect to this educational activity

Learning Objectives

- Review common social media tools and characteristics
- Discuss the benefits and challenges of study participant communication through social media platforms
- Explore implications to the study conduct and data validity when participants share study experiences
- Highlight areas for IRB considerations

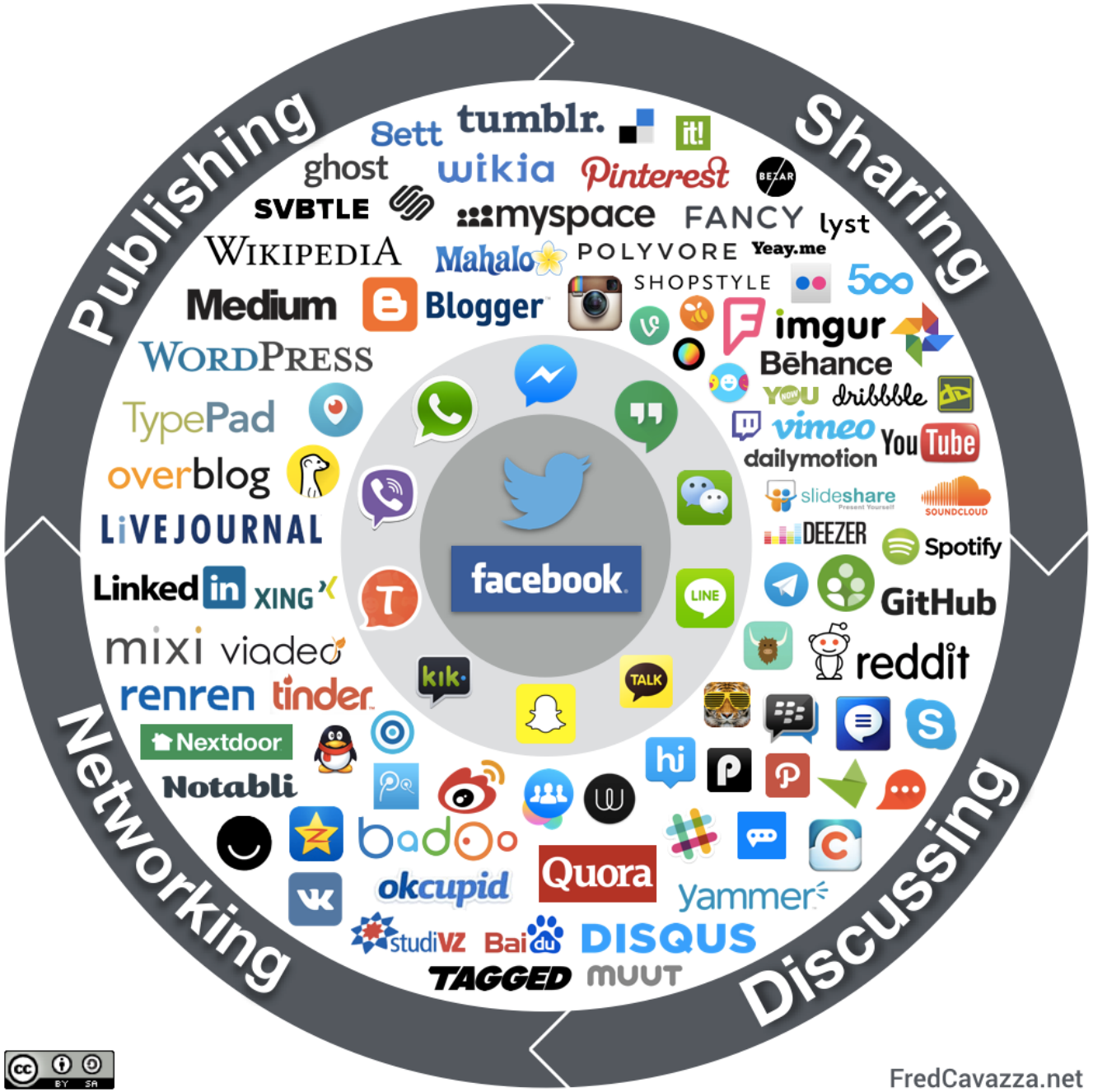
Internet Research Defined (SACHRP 2013)

- Research studying information that is already available on or via the Internet without direct interaction with human subjects (harvesting, mining, profiling, scraping—observation or recording of otherwise-existing data sets, chat room interactions, blogs, social media postings, etc.)
- Research that uses the Internet as a vehicle for recruiting or interacting, directly or indirectly, with subjects (Self-testing websites, survey tools, Amazon Mechanical Turk®, etc.)
- Research about the Internet itself and its effects (use patterns or effects of social media, search engines, email, etc.; evolution of privacy issues; information contagion; etc.)
- Research about Internet users—what they do, and how the Internet affects individuals and their behaviors
- Research that utilizes the Internet as an interventional tool, for example, interventions that influence subjects' behavior
- Others (emerging and cross-platform types of research and methods, including m-research (mobile))
- Recruitment in or through Internet locales or tools, for example social media, push technologies

Internet Research

- Internet-based research, broadly defined, is research which utilizes the Internet to collect information through an online tool, such as an online survey; studies about how people use the Internet, e.g., through collecting data and/or examining activities in or on any online environments; and/or, uses of online datasets, databases, databanks, repositories.
  - Internet as a **TOOL FOR** research or…
  - Internet as a **MEDIUM/LOCALE OF** research
- TOOL=search engines, databases, catalogs, etc…
- MEDIUM/LOCALE=chat rooms, MUDs, MOOs, newsgroups, web sites, MMORPGs, blogs, skype, social media, tweets, online course software, etc
- Increasingly, the line between tool and locale is blurring in the face of social media, mobile apps, and cellular devices

Social Media Landscape 2015



FredCavazza.net

Types of Media Channels/Avenues

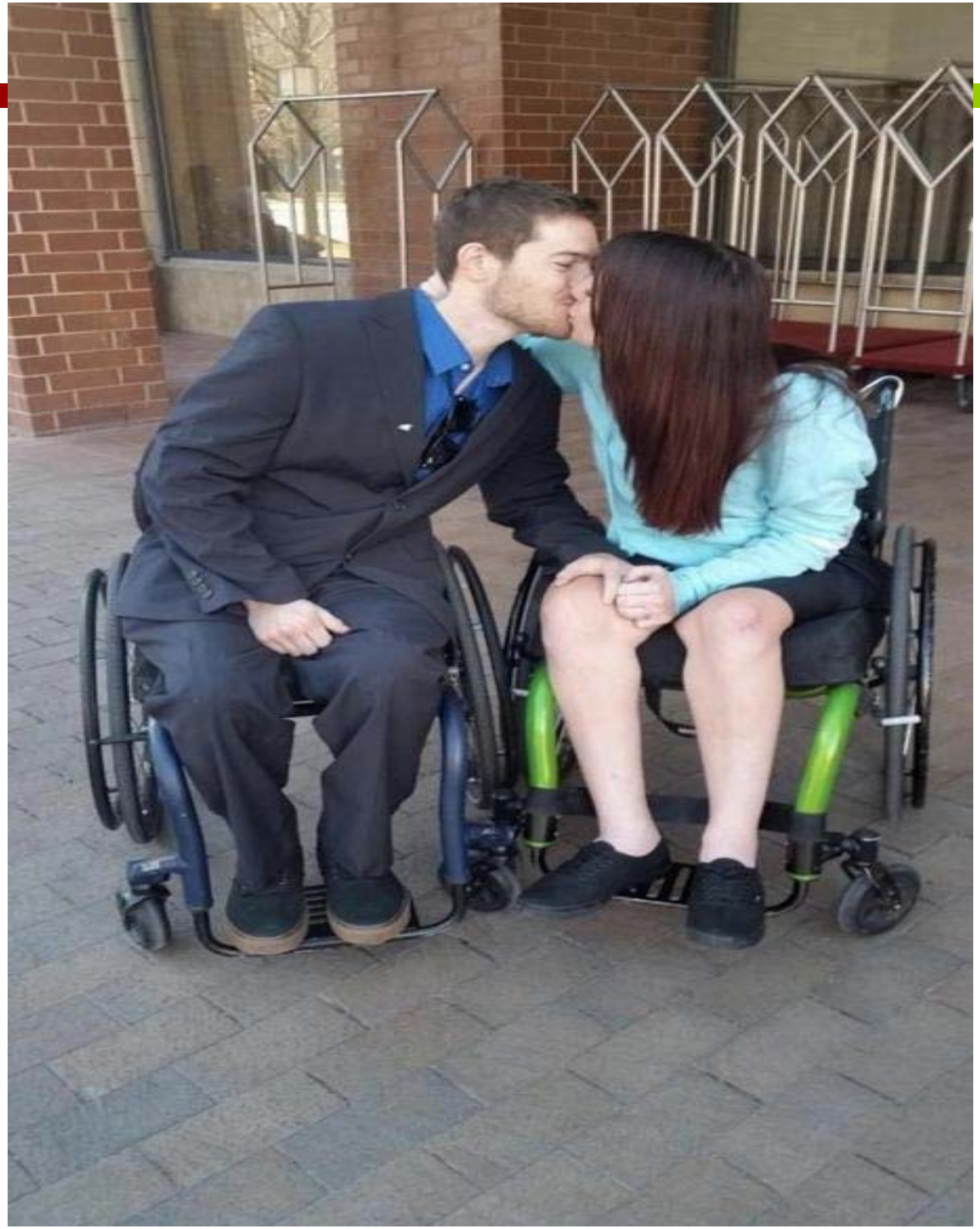
- Unidirectional, asynchronous: Email
- Bi/Multidirectional, asynchronous: Mailing Lists
- Bi/Multidirectional, synchronous: Chat rooms, Messaging
- Multidirectional, synchronous: Social Media, broadly conceived
  - Push technologies: “A data distribution technology in which selected data are automatically delivered to the user's computer or mobile device in real time or at prescribed intervals. E-mail messages, calendar updates and text messages are examples of data that are pushed to the user. Contrast with "pull technology," in which the user initiates a request for the data each time. Browsing the Web is an example of the pull model.
  - If data are sent to the receiving party at the moment they are generated, then the push technology is also real-time transmission.”

Common Ethical Considerations of Social Media Research

- Trackbackability/greased nature of social media data could generate unforeseen ethical challenges
- Uncontrolled following discussion among viewers/bloggers: interactive, not static
- Subsequent posts in effect add to posted information
- Must PI/IRB actively monitor social media sites used in research?
  - FDA Draft guidance released
  - FDA/OHRP has guidance on m-research and apps

Keeping Participants Engaged

- Interactive social media
  - Subjects often want to be able to discuss their experiences
  - Makes subjects feel like they are part of a community and their contributions are recognized: “We were looking for others to understand what we were going through. A trial is an isolating experience. We formed a bond” (Jeri Burtchell, 2014).



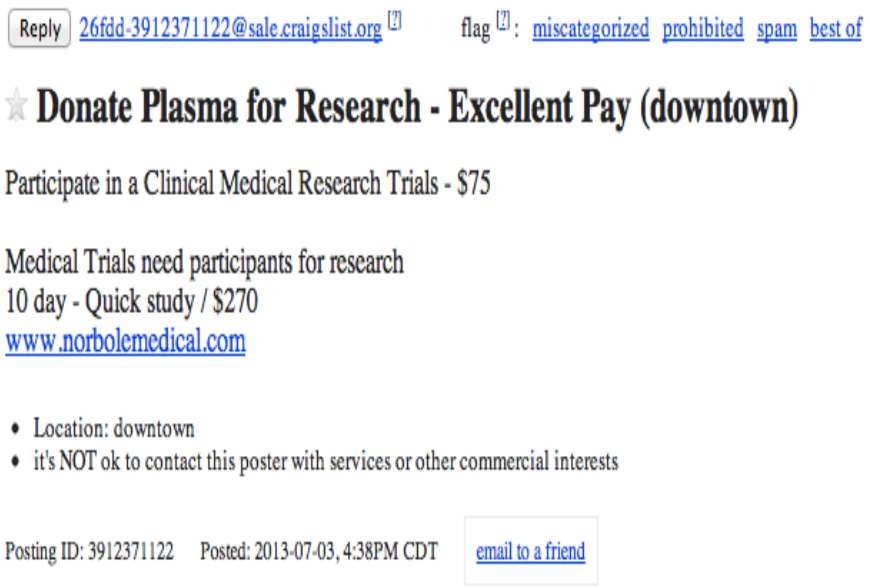
Are there downsides?

- Increasing recent attention on the potential complications
  - How to get around eligibility criteria
  - Breaking the blind
  - Sharing AE information
  - Encouraging/discouraging AE reporting
  - Premature efficacy assumptions
  - Misinformation

Subject recruitment

- OHRP considers subject recruitment part of informed consent
  - Recruitment plan must receive IRB review/approval prior to initiation

- Recruitment methods
  - Twitter apps
  - Blog postings
  - YouTube videos
  - “Push” methods
  - Robo calls, texts
  - Craigslist/BackPage



Reply 26fdd-3912371122@sale.craigslist.org [?] flag [?]: miscategorized prohibited spam best of

Donate Plasma for Research - Excellent Pay (downtown)

Participate in a Clinical Medical Research Trials - $75

Medical Trials need participants for research
10 day - Quick study / $270
www.norbolemedical.com

- Location: downtown
- it's NOT ok to contact this poster with services or other commercial interests

Posting ID: 3912371122 Posted: 2013-07-03, 4:38PM CDT email to a friend

Covance TWTB @testwiththebest · Oct 27

Recruiting for healthy males and females 18-45. Up to $5,800. bit.ly/1zdzlD8. #CovanceEvansville.

Covance TWTB @testwiththebest · Oct 17

New direct flights to Dallas being added over the next month! usat.ly/1vnEbuH Check out our current studies at bit.ly/1eHov92

Covance TWTB @testwiththebest · Oct 15

Looking for Healthy Non-Smoking Women, 18-45, for research study 8298-349. Up to $6,000. bit.ly/1sJQVL1 #CovanceDallas

1

Covance TWTB @testwiththebest · Oct 13

Healthy adults, age 18-55 needed for clinical research study 8302-509. Up to $2200 upon completion. Call 800-732-2528. #CovanceMadison

NovartisCancerUSOnly @NovartisCancrUS · Nov 13

Help spread the word about #NCT02069093, a phase II trial dedicated to researching
stomatitis & #breastcancer 1.usa.gov/1uEra0H #bcsm

NovartisCancerUSOnly @NovartisCancrUS · Nov 13

Committed to #CML #BCR-ABL #MMR research: Trial #ENEST-GOAL #NCT01744665
is an ongoing Phase II trial. Learn more: 1.usa.gov/1x6WeY5

mProve Health @mprovehealth · Jul 29

Recruiting patients for clinical trials? Try text messaging! Join us for a Shire case study presentation: bit.ly/1t9H8vD

2

Study Scavenger Email Blast

Frontage In NJ has a New Study Posted...

Frontage seeks non-smoking healthy adults, between 18 and 55.

The study requires up to 12 consecutive overnight visits and 10 outpatient visits, depending on study group.

Participants must weigh 110 lbs (60kg) and have a body mass index (BMI) between 18 and 30 kg/m^2

Compensation up to $2950 for completing all study procedures.

To find out if you qualify, call 877-298-9071, apply online: www.frontagelab.com/enroll-in-a-study.asp:

Or email: recruiting@frontagelab.com

Check it out on Study Scavenger now:

http://www.studyscavenger.com/Content/ViewStudy.aspx?SiteID=31d3d095-cabe-4171-a20f-0ac77d189fcbated web page...

Call Today !! 877-298-9071

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Welcome!

Thanks for visiting Just Another Lab Rat!, your one stop guide for learning how to volunteer for a clinical research study and the best resource for veteran volunteers.

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Just Another Lab Rat has joined forces with Study Scavenger Smart Phone App for Subject Recruitment to form a network serving the research community. For more information click here.
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Available on the iPhone App Store

ANDROID APP ON Google play

If this is your first time here, please check out the **Guide To Clinical Research**
The major Phase I clinics are listed below. If you're not healthy, there may be a patient clinic near you.
In order to sign up for a clinic, you must call or sign up through the clinic directly. This site is only a resource guide and is does not directly recruit volunteers. Please mention you found out about studies from this site!

Major Phase I Clinics in the US

All studies are subject to capacities, change and or cancellation.

AZ *Tempe*	Celerion	NJ *Eatontown*	Clinilabs
CA *Cypress*	WCCT Global	NJ *Hackensack*	Frontage
CA *Glendale*	Parexel	NJ *Marlton*	PRA

Recently Updated Studies:

All studies are subject to capacities, change and or cancellation.
To view all studies, download the APP to the left!
Or click here to view online.

Worldwide Clinical Trials
Location: San Antonio, TX
Health Condition: *Healthy Patient Studies

PAREXEL
Location: Baltimore, MD
Health Condition: *Healthy Patient Studies

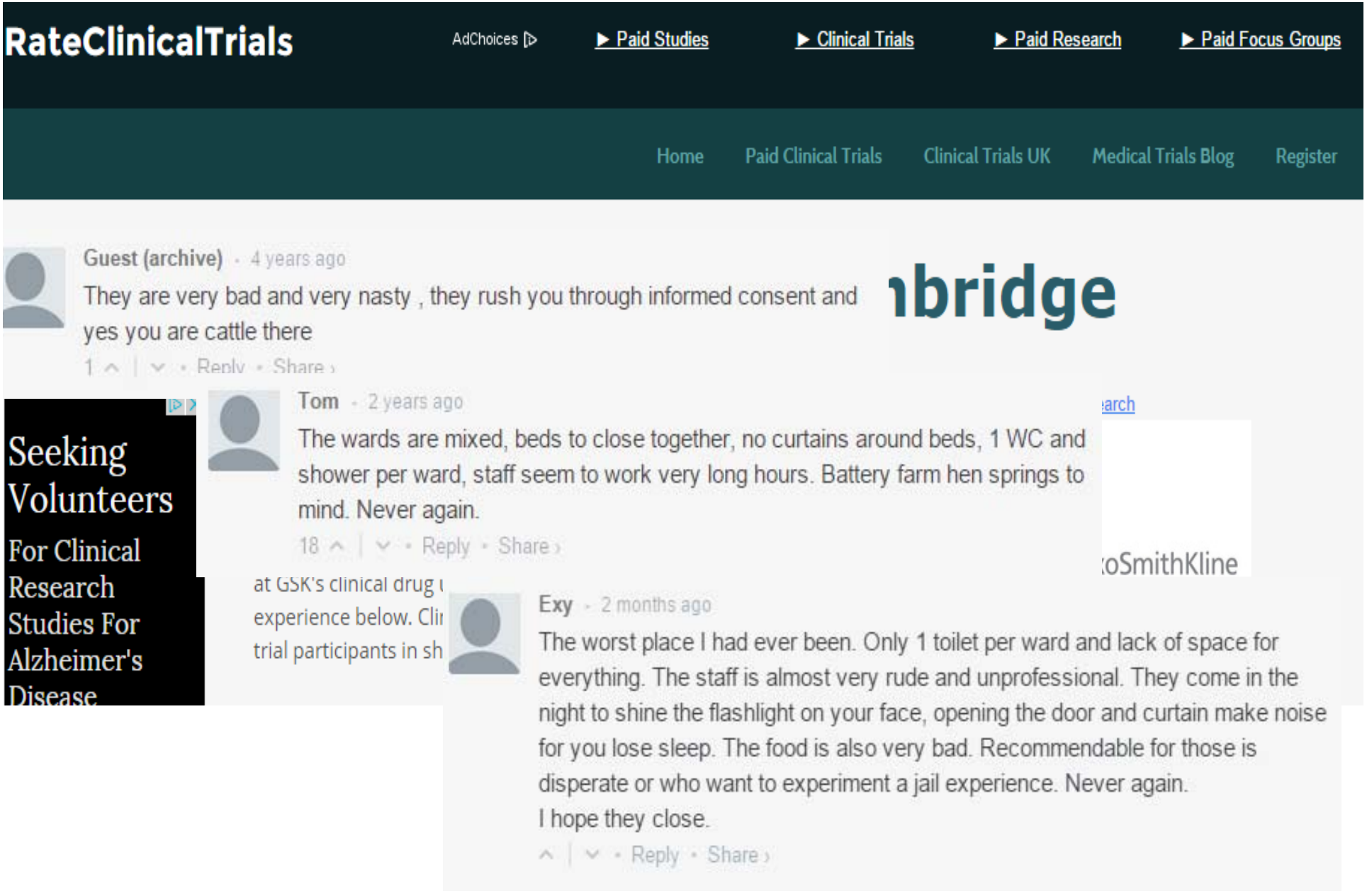
PAREXEL
Location: Baltimore, MD
Health Condition: *Healthy Patient Studies

PAREXEL
Location: Baltimore, MD
Health Condition: *Healthy Patient Studies

Covance Madison
Location: Madison, WI
Health Condition: *Healthy Patient Studies

TKL Research
Location: Fair Lawn, NJ
Health Condition: *Healthy Patient Studies

PAREXEL
Location: Baltimore, MD


RateClinicalTrials
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▶ Paid Research
▶ Paid Focus Groups
Home
Paid Clinical Trials
Clinical Trials UK
Medical Trials Blog
Register
Guest (archive) · 4 years ago
They are very bad and very nasty , they rush you through informed consent and yes you are cattle there
1 · Reply · Share ›
Tom · 2 years ago
The wards are mixed, beds to close together, no curtains around beds, 1 WC and shower per ward, staff seem to work very long hours. Battery farm hen springs to mind. Never again.
18 · Reply · Share ›
Seeking Volunteers
For Clinical Research Studies For Alzheimer's Disease
Exy · 2 months ago
The worst place I had ever been. Only 1 toilet per ward and lack of space for everything. The staff is almost very rude and unprofessional. They come in the night to shine the flashlight on your face, opening the door and curtain make noise for you lose sleep. The food is also very bad. Recommendable for those is disperate or who want to experiment a jail experience. Never again.
I hope they close.
· Reply · Share ›

yelp

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Anaheim Clinical Trials

Write a Review | Add Photo | Share | Bookmark

J T.
Garden Grove, CA
65 friends
9 reviews

6/13/2013

Only been there once and it was thanks to Nina Tran who helped me out with the process. She's a great coordinator. Thanks Anaheim Clinical Trial, hope to do business with you again.

Was this review ...?
Useful | Funny | Cool

Annette T.
Irvine, CA
19 friends
12 reviews

6/13/2013

Staff was very friendly and professional. Howard was very helpful with the process.

Was this review ...?
Useful 1 | Funny 1 | Cool

William K.
Diamond Bar, CA
112 friends
8 reviews

6/13/2013

First to Review

I was a research patient at Anaheim clinical trials and I wanted to give a quick review of my experience. The staff was very professional and courteous. One of the staff that stood out above the rest was Inho Lee. I enjoyed the entertainment rooms with the big screen tvs and Netflix. I was completely comfortable. I will definitely do another study with them.

Was this review ...?
Useful | Funny | Cool

Add Photo

Henry L.
Lake Elsinore, CA
0 friends
8 reviews

Share review
Compliment
Send message
Follow Henry L.

8/1/2014

If I could give a negative star I would.

This place is just foul. I responded to a Craigslist ad for a study. After showing up and spending over 2 hours at the clinic; giving blood and other test I was told that if I passed the first phase I would be call to start the second phase. This was supposed to happen in the next 2 weeks. After waiting and receiving no call back I assumed my test results came back negative thus I was not going to proceed to the next phase.

I was Ok with this but then today I received a call from 714-399-3897. The lady said since I did not show up to the 2nd phase trial that I could participate on another.
I told her wait a minute, I was not told that I had passed to the second phase. She said that someone should have called me and let me know, but maybe I needed to check my voicemail. This really got me upset because I always answer my phone and if I'm unable to answer I check my voicemail constantly. I NEVER RECEIVED ANY CALL OR

Consider…

- How subjects will be contacted
  - Access may be through moderator or member in internet locale

- When and where the subjects are approached about participation
  - How to avoid misrepresentation by researcher?
  - Outside of formal study space?

Communication between subjects

"… And my pills are very bitter and nasty tasting. I've also cross referenced my taste experiences with others who I know are getting the (study drug) and we all agree on the flavor…"

"… If you can suck it without gagging and it tastes vaguely neutral then it's the placebo."

"….can you describe your pills in more detail? Like a more complete description of what they look like, how they react when they get wet, what their texture is, how long do they last in the mouth after being swished around, and a more complete description of the taste."

- Thread included much discussion about how and when to get certain lab tests outside the study to determine whether subjects were on placebo, so they could drop out of study if not on the investigational agent

Tue, 25 Mar 2014 22:19:29 18

I am starting cycle 12. They have added some side effects to the list. Edema and fatigue are most common, along with something else which I can't remember... And nausea, diarrhea, constipation are less common. No mention of the acne like skin or hair loss.
My nurse today was distracted by having to fill the pump. So distracted that I didn't notice she forgot my labs!! lol
And I have the beginnings of a UTI so I'm on Cipro. So in 2 months my meds have doubled! We talked about the edema and the fact that I can't seem to take a day off: the swelling comes right back, not that it goes away completely. But kidneys look good so I will keep taking it.
Scan yesterday shows nothing new. And stability. So I'm happy there. CA19-9 is up a bit to 39. Guess I gotta lay off the meat for a bit.
All in all, a good day!


Jeri Burtchell @FingoHead · Nov 7
Back where it all began. #clinicaltrial checkup for extension of Gilenya study. Leaving with 6 mo. of pills.

mremeet Jul 21, 2008

The placebos were sweetish to neutral tasting.That's how all placebo people interpreted their pills. Nearly everyone who was later actually proven to be getting VX950 described it as a gagging bitter taste. But Vertex has been monitoring our chats here all along (including placebo detection), so they may have wised up by now and bittered their placebos. However, I can't believe they're still testing a group that does not get ribavirin? I'd look into that carefully, I seriously doubt they are dumb enough to keep doing that. That would be a waste of money and also be horribly unethical based on what happened to the others here already. But against all odds, if they are including a ribaless group - I wouldn't enroll in the trial if I were you.

susan400 ★★★★ Jul 19, 2009

To: all

One could conceivably get a viral load outside of the trial, (at their own cost), at about the 2 week mark and see if their viral load had gone just about undetected (if not undetected) and be able to tell in that way. A previous non-responder is not going to clear the virus on standard SOC in 2 weeks time.

I did not go outside of my trial because I knew right from the beginning that I was actually getting Telaprevir, because Group C was the only group in Prove 3, that did not receive RIBA...., Group C got Telaprevir and Pegasys, Period, end of story, no placebo for Group C. This was the group I got randomized into. At week 5, after my week 4 blood draw results came back, they called me up and told me that I would not be allowed to continue because I had rebound on my virus. But, because I was double-blinded, they would not release my viral loads reports. I had to wait until 24 weeks had passed until I was able to get all of my past viral loads from screening through week 5.

So, my advice would be that if you choose to go into a Telaprevir trial, plan on going to outside of the trial for a viral load at week 2 and that would be a good indicator. I am not worried about getting into trouble with the Vertex people since they have already told me that I'm not allowed to participate in any more Telaprevir trials. Jerks! They wouldn't even give us Group C people a chance to retreat w/all 3 drugs!!! I know because I wrote them a letter and begged for the chance and was told by the VX rep, NOPE.

So, that is my opinion for what it's worth!

Good luck to you all.

Susan400

Patients posting structured data on efficacy & safety on investigational drug to public / social sites

Patients | Treatments | Symptoms | Research | FAQ

Filter by: All | Please type at least 3 letters to choose a condition | patients

Home > Evaluations from Patients who take Fingolimod clinical trial

Evaluations from Patients who take Fingolimod clinical trial

Category: Others

Most Popular Types: FTY720, TRANSFORMS CFTY720D2302, CFTY720D2309 (Show all)

See also: Fingolimod

Overview | **Individual Patient Evaluations**

6 patient evaluations for Fingolimod clinical trial

MS: 4 yrs

MS: 12 yrs

by **shenannigans99**

See shenannigans99's full Fingolimod clinical trial history

Purposes: MS (Multiple Sclerosis) and Transplant rejection prevention (Started Oct 27, 2008)

Date	Dosage	MS (Multiple Sclerosis) Efficacy	Transplant rejection prevention Efficacy	Side Effects	Adherence	Burden

Purpose: Participate in clinical trial (Started Oct 29, 2007)

Date	Dosage	Efficacy	Side Effects	Adherence	Burden
Aug 03, 2010	**0.5 mg** Daily	Moderate	None	Always	Not at all

Advice Tips Aug 03, 2010

I LOVE not having to do injections anymore. I am in my 2nd year and was told at my last visit that my visits will continue until drug approval or if I should have a major reaction that has been reported, such as macular degeneration. So far, this has been wonderful!!

Cost: monthly

1 helpful mark

MS: 26 yrs

by **cobebu8**

See cobebu8's full Fingolimod clinical trial history

Purpose: MS (Multiple Sclerosis) (Started Nov 18, 2008)

Date	Dosage	Efficacy	Side Effects	Adherence	Burden
Sep 01, 2009	Daily	? Can't tell	Severe	Always	Not at all

0 helpful marks

MS: 8 yrs

by **Singer**

See Singer's full Fingolimod clinical trial history

Purpose: Other (Started Apr 08, 2003)

Date	Dosage	Efficacy	Side Effects	Adherence	Burden
Jun 01, 2009	**1 mg** Daily	None	Moderate	Always	Not at all

Latest side effects: Slowed heart rate

0 helpful marks

Communication between subjects

"… The (study drug) is causing the [side effect] ….. and it must be removed ….(1) Stop the (study drug) and get it out of your system; (2) Go to a dermatologist …(3) Get them to start you on a prednisolone taper starting at 40 mg first day, then 30mg for 4 days, then 20mg for 4 days and then 15mg for one day…..

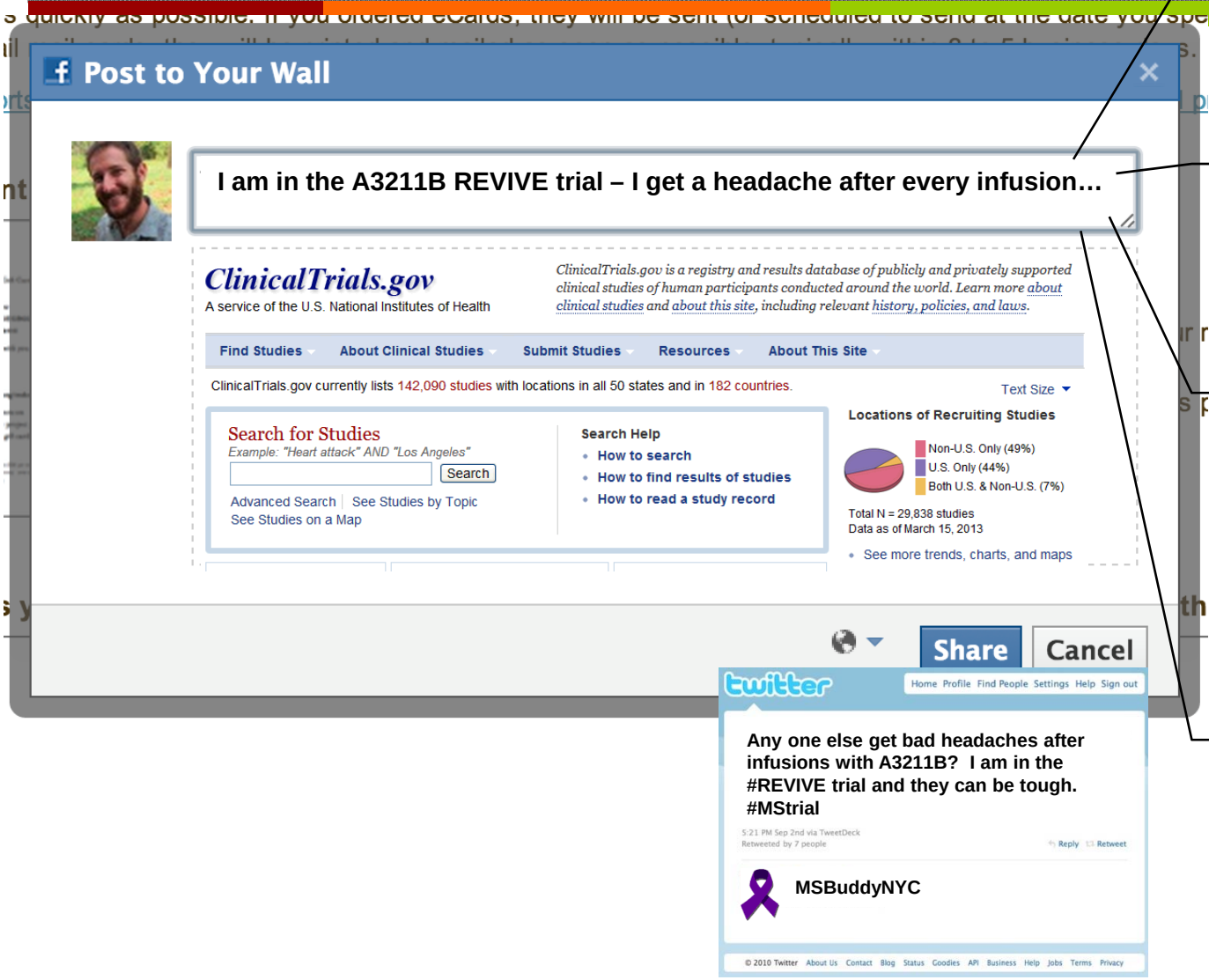
[if that is not successful] try 125mg iv of Solu-Medrol. ..don't let some jive-talking doctor try and tell you it's the same thing… I'm the resident expert on the subject at this point. So yeah, I'm gonna … assert you should stop the (study drug)! And no I'm not a doctor..."

Communication between subjects

- Major concerns from Sponsor and PIs that information could bias the conduct of study
  - May affect safety reporting
    - Subjects may talk to others online and not inform investigators
    - May change frequency of reporting some events
- Non-subjects were publishing conclusions about results while the study was still ongoing (e.g., “10/20 subjects report online that they have responded, response rate is 50%…”)

Unconfirmed Spontaneous Reports

How would sponsor or FDA use this data?



Is he really in the study?

Is he on active or control?

Is the safety event already captured by the PI and in the safety database?

Did he post the same safety event with other profiles on other social media sites?

The Potential Influence of Internet-based Social Networking on the Conduct of Clinical Research Studies

Seth W. Glickman
University of North Carolina, Chapel Hill (USA)

Sam Galhenage
Fremantle Hospital (Australia)

Lindsay McNair
Equipoise Consulting, LLC (USA)

Zachry Barber
Vertex Pharmaceuticals Inc. (USA)

Keyur Patel and Kevin A. Schulman
Duke University (USA)

John G. McHutchison
Gilead Sciences, Inc. (USA)

ABSTRACT: the rapid growth of internet usage has led to an explosion of social networking sites for discussion of health issues. This provides a forum for subjects to communicate with one another during the course of the studies. Previous studies have raised concerns about the quality of health information on social networking sites, although none have evaluated content related to ongoing clinical trials. We reviewed material posted in virtual communities by self-identified clinical trial participants. We identified material posted in online health forums that could

Received: April 4, 2011; revised: October 10, 2011

The rapid growth of internet usage has led to an explosion of social networking sites geared towards discussion of health issues. The sites are increasingly used to recruit subjects to clinical trials and provide a forum for subjects to communicate with one another during the course of the study. Although these sites are an important resource for patients, the information shared between subjects during the course of a clinical trial has the potential to influence the outcome of the study. In this article we provide an overview of the role of social networking Internet sites in clinical research, provide specific examples of how information posted in social networking could affect the integrity of ongoing clinical trials, and discuss key challenges this phenomenon presents for research subjects, investigators, research sponsors, and regulatory agencies.

Since the mid-1990s, the Internet has had a growing influence on the daily lives of people worldwide. According to a recent report from the Nielson Company (2011) more than 80% of Americans now have a computer in their homes, and of those, almost 92% have Internet access, according to a detailed study on home

nature medicine

OPINION

Engage with research participants about social media

Craig H Lipset

A growing number of participants in clinical trials are sharing information about their health online. It's time that the drug development community starts to examine how this social media use might compromise the integrity of research studies and how it might also offer new opportunities.

Pfizer

Not long ago, the likelihood of clinical trial participants socializing and sharing information was limited to the clinic waiting room. As such, the risk of conversations among patients leading to the unblinding of experimental treatments in research studies was generally viewed as minimal. Over time, this has changed. During the HIV/AIDS crisis of the 1980s and 1990s, patients to share health data to support their ability to select treatment options for optimal outcomes. In addition to sharing perceptions of efficacy and safety for approved products, patients can also track and share data for investigational medicines during clinical trials. PatientsLikeMe used data posted by patients with amyotrophic lateral sclerosis who participated

THE WALL STREET JOURNAL.

U.S.

Researchers Fret as Social Media Lift Veil on Drug Trials

Online Chatter Could Unravel Carefully Built Construct of 'Blind' Clinical Trials

Jeri Burtchell at home in East Palatka, Fla. *BOB CROSLIN FOR THE WALL STREET JOURNAL*

By AMY DOCKSER MARCUS

22 COMMENTS

July 29, 2014 10:30 p.m. ET

On her first day in a clinical trial for an experimental multiple sclerosis drug, Jeri Burtchell was convinced she was getting the new drug, not the standard therapy that some patients were randomly assigned to receive.

When she bumped into the trial's lead investigator in the elevator that day, she told him,

Waiting for p<0.05 (A publication of PLM)

11/06/2012

By: Robert A. Goldstein

	Lithium carbonate	NP001	KNS-760704 (dexpramipexole)	Sodium chlorite
Total N of reported trial from ClinicalTrials.gov	Various	105	943	N/A
N of patients/matched controls meeting our data criteria on PatientsLikeMe	78 / 390	28 / 280	29 / 319	17 / 85
Duration of PatientsLikeMe observation window	12 months	6 months	12 months	2.5 months
Baseline rate of decline for all patients	0.91 (0.04)	0.93 (0.07)	0.96 (0.05)	0.87 (0.30)
Change in rate of decline for patients reporting intervention or study participation	-0.02 (0.10)	-0.21 (0.21)	-0.13 (0.16)	0.69 (0.67)
Placebo effect [fixed offset for any report <=2 months]	-0.45 (0.17)	-0.54 (0.17)	-0.44 (0.26)	-0.38 (0.29)
Model confidence that treatment slows progression to a clinically significant degree across all study participants [combination of treatment/placebo arms]	5%	55%	36%	12%
Estimated effect size if PatientsLikeMe has same balance between treatment/placebo arms as actual trial	-0.02 (0.10)	-0.32 (0.26)	-0.27 (0.23)	0.69 (0.67)
Model confidence that treatment slows progression to a clinically significant degree, for patients in treatment arm(s) using estimate from above	5%	69%	64%	12%

Patients posting structured data on efficacy & safety on investigational drug to public / social sites

Data may be aggregate in attempt to predict outcome of trials still underway

http://figshare.com/articles/Waiting_for_p%3C0.05/96802

Communication between subjects

What should researchers do?

- Be aware of where participants are getting information
- Educate participants about potential impact of communication
  - In person
  - In informed consent documents
  - Through other media (CISCRP)

Assessing risk to studies

- Things to consider
- Is there an active advocacy community?
  - Is the community is identifiable online locations?
- Study design:
  - Sample size; large or very small?
  - Blinded or open-label?
  - Endpoints: subjective or objective?

Approaches to Successful Social Media Communications

- Set up private chat rooms, boards, groups for trial participants
- Have a moderator
- Consider eliminating synchronous communications so a moderator can preview before posting
- Provide examples of appropriate and inappropriate messages (Bookbinder, 2014)

Addition to Consent Form

"In all clinical studies, it is important that the people participating in the study (doctors, nurses and subjects) do not make any conclusions about what the results of the study might be, until all the data has been collected and reviewed. If there are rumors about how many subjects have side effects, or about whether the drug is working or not working, it may affect the study. If the data from the study might be affected by early conclusions, it could cause the study to have to be repeated.

…….

Addition to Consent Form

….If you participate in this clinical study, you should feel free to discuss the study with your family and with other people who are close to you. You should also tell any health care providers who treat you that you are in the study. However, to help make sure that the data from the study is as accurate and reliable as possible, please do not discuss information about the study in public places while the study is in progress. Public places may be situations like support groups, or may be places like internet message boards. If you have questions about side effects, please talk to your study nurse or study doctor."

For More Information

Elizabeth Buchanan
715 232 2477
buchanane@uwstout.edu

If there is time…

SPEAK OUT, BUT SPEAK SMART.

ABOUT US

ABOUT CLINICAL TRIALS IN GENERAL

LINKS

CONTACT

VIDEO GALLERY

THE SURPRISING EFFECTS OF WORDS ARE POWERFUL

Words are powerful. That's why talking about a **clinical study** can change its results. For example, talking to someone on the same study about how you're feeling or your experience of the study can change:

- The way they feel (e.g., hearing about a headache can cause you to develop a headache)
- The way they think about the study (e.g., your opinions could color their own)

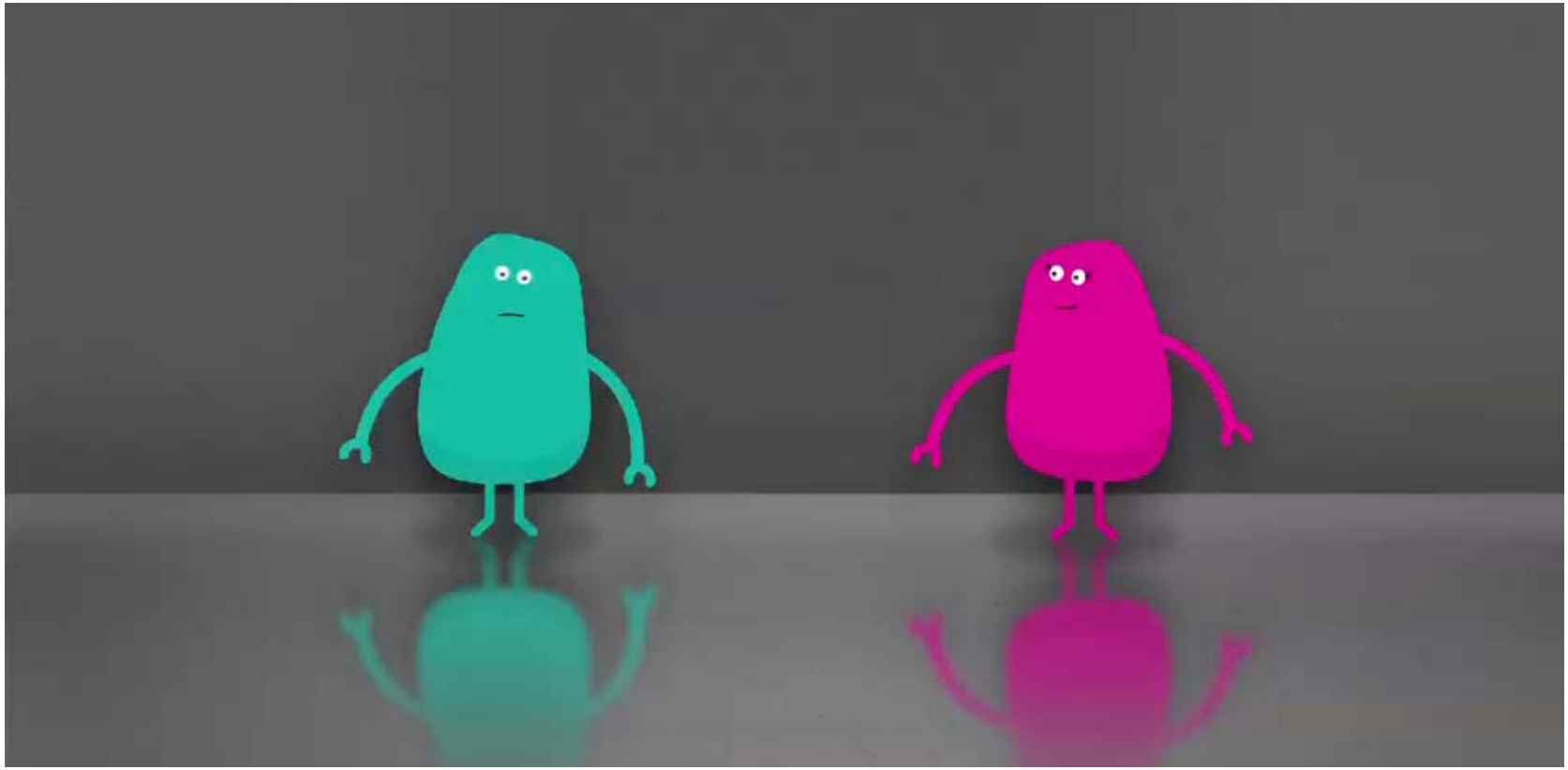
Please watch our short films to learn more.

“Speak Up but Speak Smart”

- Shire contacted CISCRP with an interest in developing educational materials for study participants, about the impact conversations can have on study integrity
- CISCRP and Shire connected with Langland (communications company)
- Langland and CISCRP developed and produced the program (funded by Shire)

Slipping Through Screening

Slipping Through Screening



Slipping Through Screening

Placebo/Nocebo Effects

- Placebo effect:
  - Positive effect from an inactive "treatment"
- Nocebo effect:
  - Negative effect from an inactive "treatment"

REVIEW ARTICLE

Nocebo Phenomena in Medicine

Their Relevance in Everyday Clinical Practice

Winfried Häuser, Emil Hansen, Paul Enck

SUMMARY

Background: Nocebo phenomena are common in clinical practice and have recently become a popular topic of research and discussion among basic scientists, clinicians, and ethicists.

Methods: We selectively searched the PubMed database for articles published up to December 2011 that contained the key words "nocebo" or "nocebo effect."

Results: By definition, a nocebo effect is the induction of a symptom perceived as negative by sham treatment and/or by the suggestion of negative expectations. A nocebo response is a negative symptom induced by the patient's own negative expectations and/or by negative suggestions from clinical staff in the absence of any treatment. The underlying mechanisms include learning by Pavlovian conditioning and reaction to expectations induced by verbal information or suggestion. Nocebo responses may come about through unintentional negative suggestion on the part of physicians and nurses. Information about possible complications and negative expectations on the patient's part increases the likelihood of adverse effects. Adverse events under treatment with medications sometimes come about by a nocebo effect.

Conclusion: Physicians face an ethical dilemma, as they are required not just to inform patients of the potential complications of treatment, but also to minimize the likelihood of these complications, i.e., to avoid inducing them through the potential nocebo effect of thorough patient information. Possible ways out of the dilemma include emphasizing the fact that the proposed treatment is usually well tolerated, or else getting the patient's permission to inform less than fully about its possible side effects. Communication training in medical school, residency training, and continuing medical education would be desirable so that physicians can better exploit the power of words to patients' benefit, rather than their detriment.

► Cite this as:
Häuser W, Hansen E, Enck P: Nocebo phenomena in medicine: their relevance in everyday clinical practice.
Dtsch Arztebl Int 2012; 109(26): 459–65. DOI: 10.3238/arztebl.2012.0459

Words are the most powerful tool a doctor possesses, but words, like a two-edged sword, can maim as well as heal.", Bernard Lown (e1).

Doctor–patient communication and the patient's treatment expectations can have considerable consequences, both positive and negative, on the outcome of a course of medical therapy. The positive influence of doctor–patient communication, treatment expectations, and sham treatments, termed placebo effect, has been known for many years (e2) and extensively studied (1). The efficacy of placebo has been demonstrated for subjective symptoms such as pain and nausea (1). The Scientific Advisory Board of the German Medical Association published a statement on placebo in medicine in 2010 (2).

Method

The opposite of the placebo phenomenon, namely nocebo phenomena, have only recently received wider attention from basic scientists and clinicians. A search of the PubMed database on 5 October 2011 revealed 151 publications on the topic of "nocebo," compared with over 150 000 on "placebo." Stripping away from the latter all articles in which "only" placebo-controlled drug trials were reported left around 2200 studies investigating current knowledge of the placebo effect. In comparison, the data on the nocebo effect are sparse. Of the 151 publications, only just over 20% were empirical studies: the rest were letters to the editor, commentaries, editorials, and reviews (*Figure*).

Our intention here is to portray the neurobiological mechanisms of nocebo phenomena. Furthermore, in order to sensitize clinicians to the nocebo phenomena in their daily work we present studies on nocebo

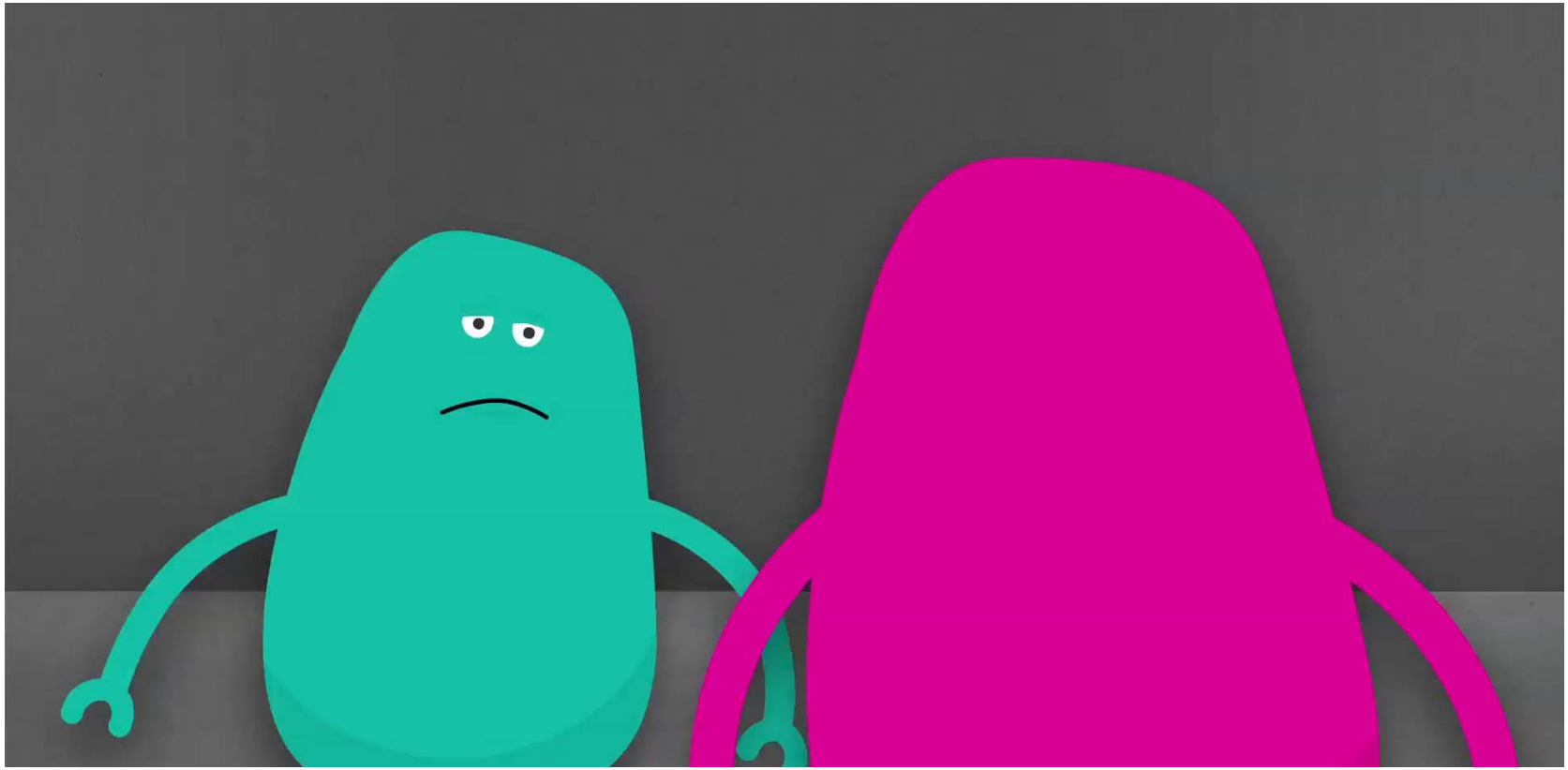
TWO WEEKS INTO Ted Kaptchuk's first randomized clinical drug trial, nearly a third of his 270 subjects complained of awful side effects. All the patients had joined the study hoping to alleviate severe arm pain: carpal tunnel, tendinitis, chronic pain in the elbow, shoulder, wrist. In one part of the study, half the subjects received pain-reducing pills; the others were offered acupuncture treatments. And in both cases, people began to call in, saying they couldn't get out of bed. The pills were making them sluggish, the needles caused swelling and redness; some patients' pain ballooned to nightmarish levels. "The side effects were simply amazing," Kaptchuk explains; curiously, they were exactly what patients had been warned their treatment might produce. But even more astounding, most of the other patients reported real relief, and those who received acupuncture felt even better than those on the anti-pain pill. These were exceptional findings: no one had ever proven that acupuncture worked better than painkillers. But Kaptchuk's study didn't prove it, either. The pills his team had given patients were actually made of cornstarch; the "acupuncture" needles were retractable shams that never pierced the skin. The study wasn't aimed at comparing two treatments. It was designed to compare two fakes.

KEYWORDS
Harvard Medical School, health and medicine, placebos, Ted Kaptchuk

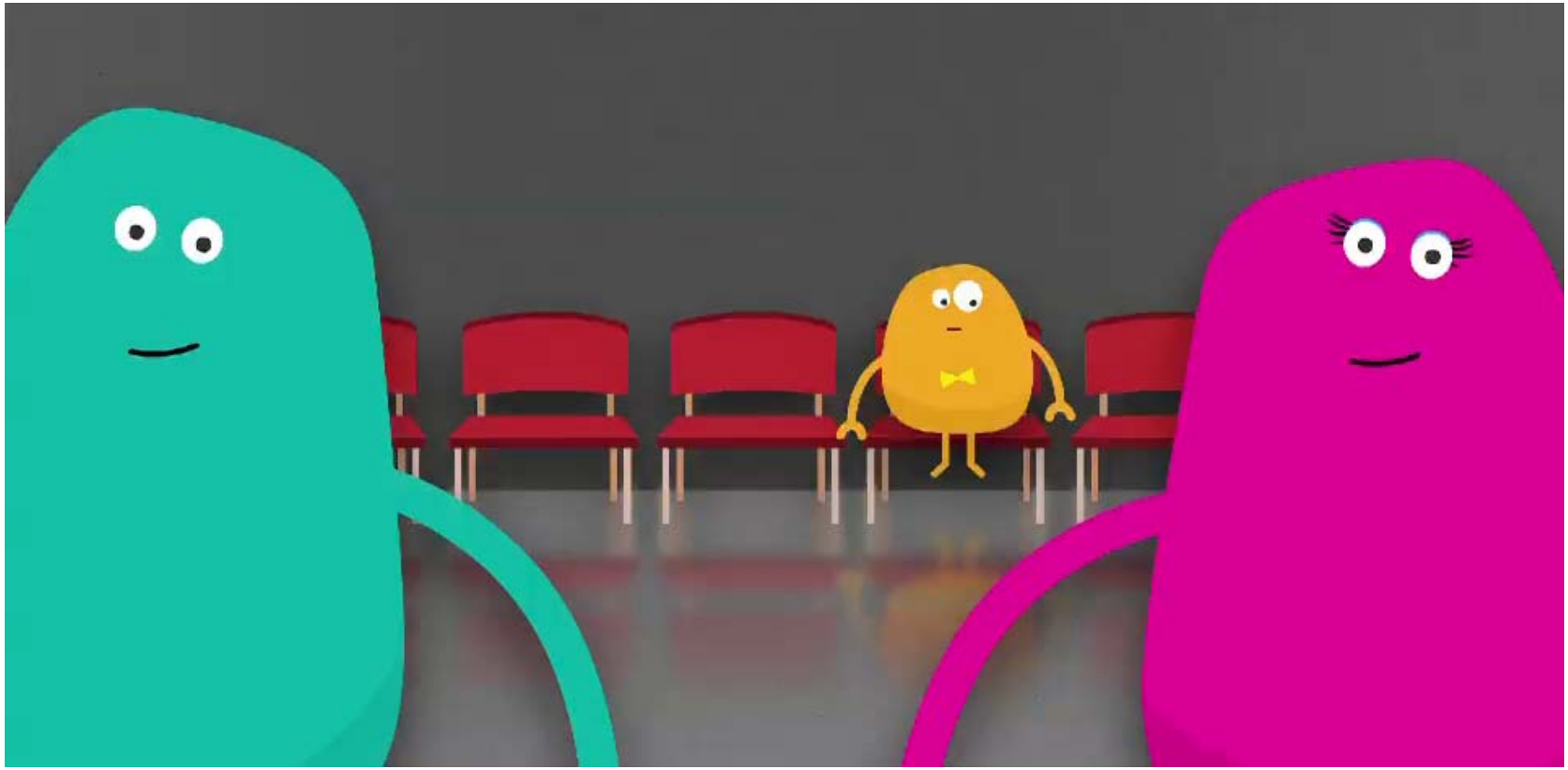
"The Placebo Phenomenon, Harvard Magazine. Nov-Dec 2014.

When is a Side Effect Not a Side Effect?

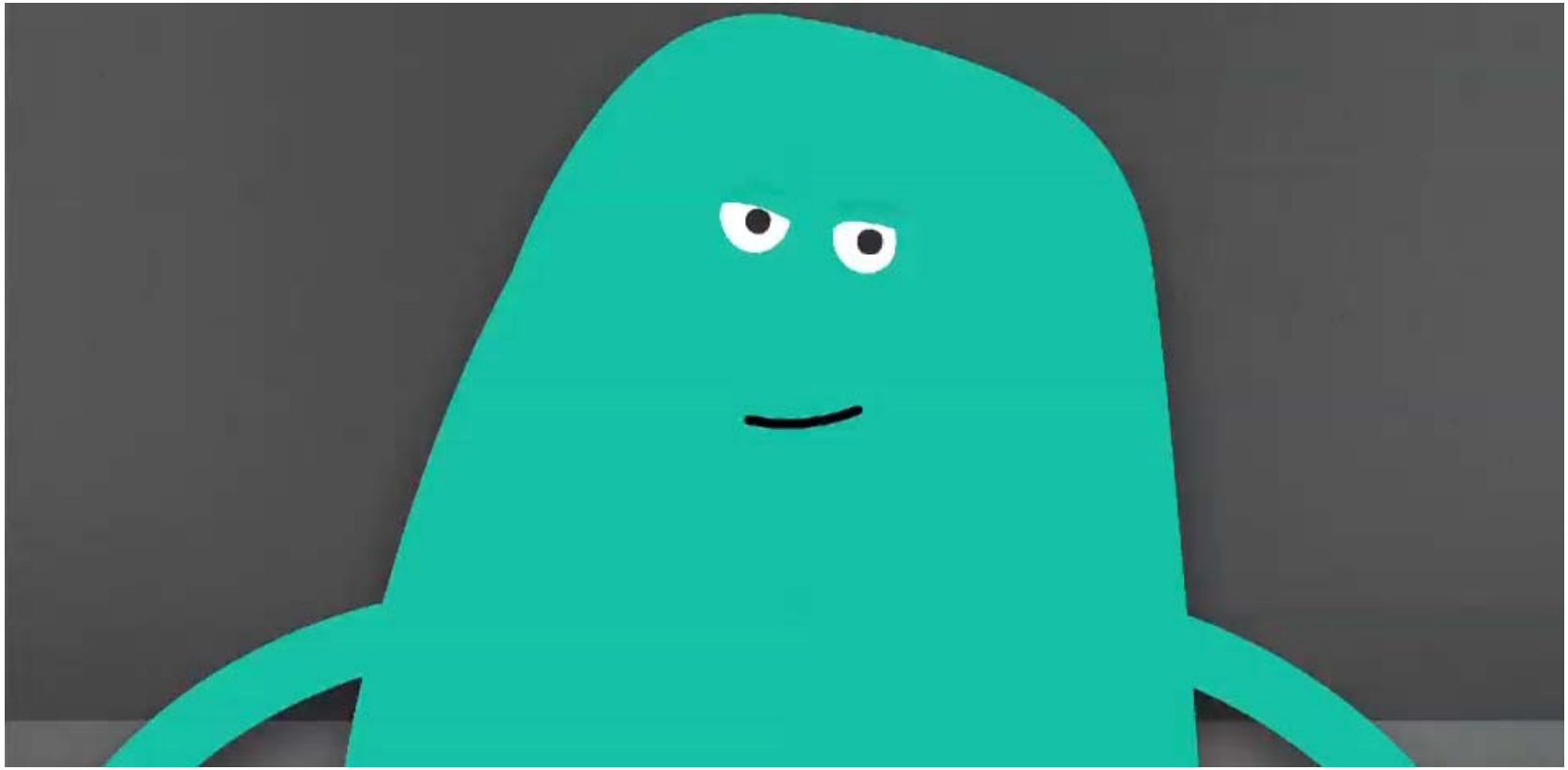
When is a Side Effect Not a Side Effect?



When is a Side Effect Not a Side Effect?



The Placebo Effect



The Placebo Effect

The Placebo Effect

“Speak Up but Speak Smart”

- Feedback has been very positive, with more visibility than expected
- Approximately 30-40 sponsors and CROs provide links or access to the site
  - Donations requested from companies that use/show the site
  - Some clinical sites are using it but hard to track how many
- Refinements of content planned for 2015

BREAK

Be Back at 10:00 Sharp!

BREAK

Be Back at 2:45 Sharp!

BARBARA ENTWISLE, PHD

Vice Chancellor for Research

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

David Resnik, JD, PhD

Dr. Resnik has an M.A. and Ph.D. in philosophy from the University of North Carolina at Chapel Hill and J.D. from Concord University School of Law. He received his B.A. in philosophy from Davidson College. Dr. Resnik was an Associate and Full Professor of Medical Humanities at the Brody School of Medicine at East Carolina University (ECU) from 1998-2004, and an Associate Director of the Bioethics Center at ECU and University Health Systems from 1998-2004. Dr. Resnik was Assistant and Associate Professor of Philosophy at the University of Wyoming (UW) from 1990-1998, and Director of the Center for the Advancement of Ethics at UW from 1995-1998. Dr. Resnik has published over 200 articles on various topics in philosophy and bioethics and is the author of 8 books. He serves on several editorial boards and is an Associate Editor of the journal Accountability in Research. Resnik is also Chair of the NIEHS Institutional Review Board.

National Institute of Environmental Health Sciences

SHARING GENOMIC DATA AND SAMPLES: ETHICAL AND REGULATORY ISSUES

David B. Resnik, JD, PhD

Bioethicist, NIEHS/NIH

This research was supported by the intramural program of the NIEHS/NIH. It does not represent the views of the NIEHS, NIH or federal government.

Genetics/Genomics

- More and more research studies today incorporate some type of genetic/genomic analysis.
- Epidemiology
- Pharmacogenomics/genetics
- Gene therapy
- Genetic test development
- Biobanking
- Genome-wide association studies
- Whole genome sequencing
- Clinical trials

Sharing

- The ethics of openness is a key part of the scientific ethos.
- Openness (sharing of data, samples, methods) promotes scientific progress
- NIH policies require the sharing of genomic data https://gds.nih.gov/03policy2.html

Confidentiality

- Protecting confidentiality is an important part of ethical research with human subjects.
- The Common Rule requires that there are adequate provisions for protecting the privacy and confidentiality of human research participants (45 CFR 46.111a7).
- The proposed revisions to the Common Rule require investigators to protect the confidentiality, security, and integrity of biospecimens and identifiable private information. The HHS Secretary will publish a list of reasonable and appropriate safeguards.
-

De-identification

- At one time, removal of identifiable private information from genomic samples or data was regarded as an effective way of protecting confidentiality when sharing.
- Two types of de-identification:
- Coded data/samples: data/samples are marked with a code; investigator retains a key that links the code to identifiable private information, but does not share the key.
- Anonymous/samples: the samples/data have no personal identifiers; if they were coded at one point, the key has been destroyed.

Re-identification

- In the past 10 years, statisticians have developed methods for re-identifying de-identified genomic data in a database. These include:
- Using a sample of the person's sequenced DNA to re-identify them in the database. Samples could be obtained from a variety of databases (criminal, military, health care). Homer et al. PLoS Genetics 2008; 4(8):e1000167.
- Reconstructing identity based on genotypic, phenotypic, and demographic information available in various databases. Lin et al. Science 2004; 305(5681):183. Lowrance and Collins. Science. 2007 Aug 3;317(5838):600-2.

Controlled Sharing of Genomic Data

- Before re-identification became possible, investigators shared human genomic data on publicly available websites.
- The NIH required funded researchers to deposit human genomic data on DbGaP or NCI sites. Data were publicly available.
- NIH changed its policy in 2009 so that most human genomic data will be available only under data use agreements.
- Data use agreements have become standard practice for sharing genomic data.

Data Use Agreements

- Data use agreements have become standard practice for sharing genomic data.
- These usually describe what will be shared, how it will be shared, used, etc.
- Recipients agree not to share data without permission, to protect confidentiality, and not to try to re-identify de-identified data.
- You could use these agreements to share identified genomic data.

Material Transfer Agreements

- MTAs used for sharing research materials (biological samples, etc.).
- Use an MTA for sharing genomic samples.
- The MTA spells out what is shared, conditions for sharing, confidentiality, storage, use, etc.

Technology Transfer

- Tech Transfer Office usually handles MTAs and data use agreements.
- They work with the IRB to make sure the sharing that takes place through these agreements is consistent with what the subjects consented to.

Breaches of Confidentiality

- Investigators should disclose breaches of confidentiality or security to the institutional review board (IRB).
- The IRB can decide how to deal with the situation, e.g. whether to amend the protocol, conduct education/training, submit a report to OHRP, etc.
- Investigators should inform subjects about breaches and whether these place them at any increased risk of harm.
- Examples: samples delivered to the wrong place; investigator mistakenly receives identified samples or data, theft of computer with private human subjects data; private information sent to an unsecure email account.

Waiver of Confidentiality

- Some studies deal with the problem of potential loss of confidentiality by asking subjects to waive confidentiality/privacy protections.
- In the Personal Genome Project (Harvard Medical School), subjects agree to make their identifiable genomic, medical, and demographic data available on a public website.
- Subjects are presumably motivated by a desire to help advance science through open data sharing and are not too concerned about loss of confidentiality/privacy. The PGD was piloted on subjects with an MS or PhD in genomic science but expanded to include others.

PGP consent, page 9.

“By signing this consent form, you authorize the PGP to publish your specimen analysis data and other personal information you have submitted to the PGP. This means that the PGP may publish this data and information without legal restriction and without your being asked to provide any additional consent. The PGP will publish the data and information on a publicly accessible website and database. It may also publish the data and information in other formats and/or media. Your ability to withdraw your consent once the PGP has published all or some of this data and information is limited, and is described in Article X of this consent form. There may be risks to you associated with the publication of this data and information. Those risks are described in Article X of this document.”

Waiver of Confidentiality/Privacy

- Will subjects understand the implications and risks of waiving confidentiality/privacy? The PGD consent form is complex and 24 pages long.
- What about risks to family members who do not consent to this sharing—might they be identified? The PGD prohibits monozygotic twins from participating unless both consent, but what about other family members?
- The decision cannot be effectively reversed once data are made public.
- The PGD appears to be a unique study; I know of no other studies that asks subjects to waive confidentiality protections.

Informed Consent

- Informed consent is a fundamental principle of ethical research with human subjects.
- The federal regulations require investigators to obtain consent from the subject or representative (45 CFR 46.111a4), but the IRB may waive consent requirements for minimal risk research that could not be carried out without a waiver (45 CFR 46.116d). The waiver must not impact the subject's welfare or rights and they must be provided with additional information after participation, if appropriate. For example, if the consent form a subject signed said nothing about sharing data or samples, the IRB might waive consent to allow sharing de-identified data or samples.

Informed Consent

- Consent is not necessary for activities deemed to be not human subjects research or exempt human subjects research. For example, the federal regulations do not require that consent be obtained to use anonymous tissue leftover from clinical tests or procedures or to share de-identified samples.
- The proposed changes to the Common Rule will practically eliminate all sharing of human biological samples without consent.
- A human biological specimen is a defined as a human subject, which eliminates sharing of leftover tissue without consent.
-

Informed Consent

- The proposed changes allow subjects to sign a short consent form for general sharing of their data/samples, which could be done on admission to a hospital or clinic. The regulations specify the content of the short form; HHS will develop a template.
- The proposed changes permit a waiver of consent for the use of biological samples if the research cannot be conducted without a waiver but prohibit a waiver of consent if the subject has refused to share samples.

Informed Consent

- The proposed changes also include some specific language pertaining to consent for biospecimen use, i.e. whether specimens will be used for commercial purposes and whether subjects will share in the profit; return of clinically relevant research results; re-contacting for future studies.

Informed Consent Approaches

- Specific consent: subjects must consent for each use of biosamples or data.
- Broad consent: subjects consent to general (broad) use of samples or data.
- Tiered consent: subjects are presented with a range of options for use of samples/data, including broad use, specific use, no use, and use for specific purposes, e.g. for research related to the subject's disease or condition, only for non-commercial research, not for producing embryonic stem cells or human-animal chimeras, etc.

Re-consent

- May be ethically appropriate if the research changes significantly or when pediatric subjects reach the age of majority.
- Re-consent could take place by signing a new consent form or an addendum.

Withdrawal of Samples/Data

- Subjects should be informed about how to withdraw from a study including removal of samples or data.
- Samples could be destroyed, data removed.
- Removal of samples or data may be limited if they have already been shared.

Community Consultation

- Community consultation is becoming more important in all types of research, including research involving the collection, use, and sharing of genomic samples and data.
- Community members may provide advice on research design, survey design, data/sample collection, recruitment, consent, data sharing, and publication.
- Investigators may share information about the progress of research through newsletters, letters, etc.

Havasupai Case

- In 1990, researchers from Arizona State University (ASU) collected 200 blood samples from members of the Havasupai American Indian tribe.
- Although the consent form stated that the samples and data would be used for research on behavioral and mental illnesses, the researchers had told tribal leaders that the study would focus on the genetics of diabetes.
- Members of the tribe later learned that the investigators had used the samples and data to study diseases other than diabetes and shared these samples with other researchers. They strongly objected to sharing the samples and data and using them to study schizophrenia, inbreeding in the tribe, and the tribe's evolutionary and genetic origins.
- The tribe filed a $50 million lawsuit against ASU and the investigators, alleging that the use of the samples and data violated the informed consent provided by the participants. In April 2010, ASU and the tribe agreed to settle the lawsuit out of court. As part of the settlement, ASU formally apologized to the tribe, returned the samples, and paid the tribe $700,000, which was divided among forty-one participants,
- Members of the tribe said they felt betrayed and would no longer participate in any ASU studies.

Havasupai Case

- Illustrates the importance of paying careful attention to consent issues concerning the use and sharing of samples and data.
- Illustrates the importance of developing and maintaining good relationships with the community and finding out whether they have any special needs or concerns related to the research.

Questions?

MARK KOYANAGI

LUNCH IN THE DINING ROOM

On the 1st. Floor, directly below this room

Turn left at the bottom of the stairs

THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL