Tufts Clinical and Translational Science Institute

Translational Research Day 2015:
Innovations in Clinical Trials
Participant Engagement

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Innovations in Clinical Trial Participant Engagement

November 10, 2015
8:30AM – 4:00PM

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Tufts Clinical and Translational Science Institute

Translational Research Day 2015:
Innovations in Clinical Trials
Participant Engagement

Harry P. Selker, MD, MSPH
Dean and Principal Investigator, Tufts CTSI

November 10, 2015

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Tufts CTSI's Mission & Purpose

- Our mission is to *stimulate and promote innovative clinical and translational research*, with the goal of improving the public's health
- We serve this objective by *facilitating, improving, and supporting others' research,* and through education and training
- A ***research services*** institute

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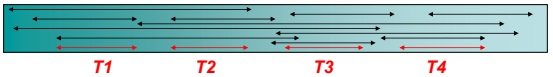
The Spectrum of Clinical and Translational Research: The Four Translational Steps



T1	T2	T3	T4	
Bench and animal research	*Clinical testing and trials*	*Testing in practice settings*	*Healthcare system delivery*	*Public health and health policy*

Clinical & Translational Science Awards

- **More than 60 NIH CTSAs (www.ctsaweb.org) are integrative academic homes for clinical and translational science to:**
  - **Train,** nurture and synergize multi- and inter-disciplinary investigators and teams
  - **Accelerate research** to catalyze the application of new knowledge and techniques to clinical practice
  - **Engage communities** in clinical research efforts

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Tufts CTSI Resources and Services

- Connections to collaborators and research projects
- Signature Programs: Comparative Effectiveness Research, Research Process Improvement, Stakeholder and Community Engagement, One Health
- Regulatory support
- Biostatistics, epidemiology, and research design (BERD Center)
- Informatics
- Clinical study support (Clinical and Translational Research Center)
- Pilot Studies Program
- Training and education
  - CTS Graduate Program
  - KL1 Career Development Awards & TL1 Fellowships
  - Professional Development

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Request CTSI Services at www.tuftsctsi.org

Get Connected: CTSI Happenings

- Weekly e-newsletter with news, professional development and funding opportunities, resources, and success stories.
- Issued every Monday at 8AM
- Sign up on our website or at http://eepurl.com/C4d9X

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http://ilearn.tuftsctsi.org/

Live seminars are recorded for our I LEARN site.
Seminar videos can be viewed at any time, and are free!

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Profiles: Researcher Networking

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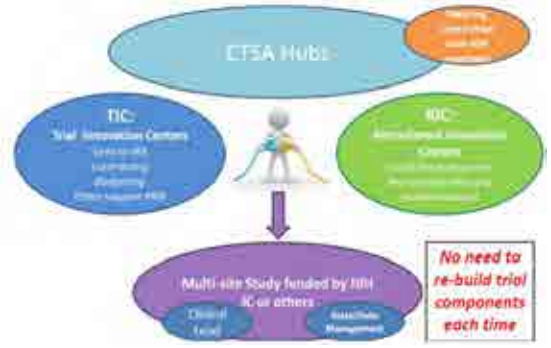
NIH NCATS Driving Streamlining of CTSA Consortium Trials

- Research training standards for all CTSA study sites
  - Good Clinical Practice
  - Education in translational research competencies
- A single IRB (IRBrely) for each multi-site trial
- Streamlined budgeting and contracting
  - Accelerated confidential disclosure agreement (ACDA)
  - Accelerated clinical trial agreement (ACTA)
  - Accelerated subcontracting

NCATS Transformation of CTSA Consortium Multicenter Clinical Studies



Tufts Clinical & Translational Research Center (CTRC): A Resource for Clinical Studies

Supports investigator-initiated and industry-initiated clinical research involving participants of all ages

- Services:
  - Clinical study unit
  - Nursing
  - Coordinator
  - Regulatory
- "CTRC-without-walls" supports studies in:
  - Tufts Medical Center inpatient and outpatient sites
  - Other Tufts CTSI hospitals and clinics

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Tufts CTSI Clinical Research Network

CTSI Research Network Hospitals:
- Baystate Medical Center
- Lahey Hospital & Medical Center
- Maine Medical Center
- New England Baptist Hospital
- Newton-Wellesley Hospital
- Tufts Medical Center and Floating Hospital for Children

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Tufts CTSI Clinical Research Network Goal: Multi-site Studies of *All Types*

Abbott · Lilly · Pfizer · ALLERGAN · SANOFI · BD · janssen · ConocoPhillips · MERCK · CARBERY · elan

NIH National Center for Advancing Translational Sciences

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Oh, what about those clinical trial participants??

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Americans and Clinical Research

- How important is clinical research? Great value 58%, Some value 38%, Not much value 4%
- Have you (or family member) participated in clinical research? Yes 15%, No 85%
- How likely are you to volunteer for clinical research? Very likely 30%, Somewhat likely 44%, Not likely 20%, Would not 6%
- ***Has your doctor ever suggested participating in a clinical study? Yes 6%, No 94%***

Research!America 2009

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Clinical Trial Access via Patient Portal

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Clinical Trial Access via Patient Portal

- Tufts Medical Center's patient portal provides online access to make appointment requests, view lab results, request prescription refills, etc.
- Tufts CTSI and Tufts Medical Center worked to put a link on the portal home page to the clinical trials web page
- This should result in greater visibility for, and patient participation in, Tufts Medical Center trials
- ***Trialists: Make sure your trials are listed!*** Complete Clinical Research Recruitment Website form (in packets) and submit to Doug Reichgott in Research Administration

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Oh, what about those clinical trial participants?? *Take it to the streets!*

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Thank You!

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Welcome

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The mPower App and Using Technology Tools for Participant Engagement in Clinical Trials

Karl Kieburtz, MD, MPH
Robert J. Joynt Professor in Neurology
Director, Clinical & Translational Science Institute
Senior Associate Dean for Clinical Research
University of Rochester School of Medicine

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Transforming Clinical Research
The Return of the House Call

Karl Kieburtz MD MPH
University of Rochester Medical Center
Director, Clinical & Translational Science Institute
Robert J Joynt Professor of Neurology
Senior Associate Dean, Clinical Research

Disclosures

Research Grants

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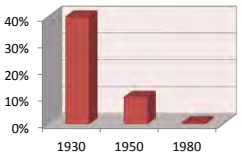
Consulting

US FDA, VA, NIH (NINDS), Acorda, Aptiv, Alnylam, AstraZeneca, Biogen-Idec, Biotie, Biovail, Britannia, CHDI, Civitas, Clintrex, Cynapsus, Genzyme, Impax, Intec, Ipsen, Isis, Lilly, Lundbeck, Melior, Neurmedix, Neuroderm, Novartis, Orion, Otsuka, Pharma2b, Phytopharm, Pfizer, Roche, Serina, Stealth Peptides, Synagile, Upsher-Smith, USworldmeds, Vaccinex, Vectura, Voyager, Weston Brain Institute, Xenoport

House calls were standard practice for physicians in the early 20th century

Brief history of house calls, 1930-1980
Proportion of patient-physician encounters that were in the home



Factors leading to the decline of the house call
- **Transportation –** Increasing availability of cars due to lower cost and improved roads
- **Technology** – Diagnostic and therapeutic technologies (e.g., x-rays, ECGs, labs) moved care from the home to more expensive institutions

Sources: Unwin BK, et al. House Calls. *Am Fam Physician* 2011; **83**: 925-38. Kao H, et al. The past, present, and future of house calls. *Clin Geriatr Med* 2009; **25**: 19-34. Photos: Moore J. What Sir Luke Fildes' 1887 painting The Doctor can teach us about the practice of medicine today. *Br J Gen Pract* 2008; **58**: 210-3; Ann Intern Med 2015;162:587-8

Telecommunications and technology are bringing the house call back

Proportion of American adults with broadband access, 2000 – 2010

Source: Pew `Research Center. http://www.pewinternet.org/2010/08/11/trends-in-broadband-adoption/

The result is the virtual house call …

Virtual house calls for episodic conditions

Source: Doctor on Demand. http://www.doctorondemand.com/medical

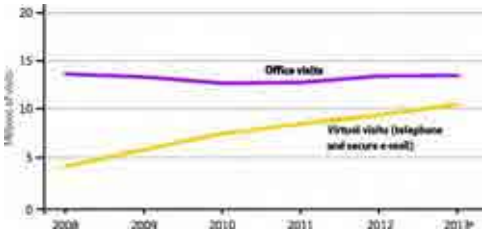
… that many organizations are now providing

Virtual house calls for episodic conditions

Source: Ann Intern Med 2015;162:587-9

Remote care will increasingly become the norm

Office vs. virtual visits at Kaiser Permanente Northern California, 2008-2013



"I expect that by 2016, with the expanded use of video, the number of virtual visits—including secure email, telephone, and video encounters—in KPNC will surpass the number of in-person office visits." – Robert M. Pearl, MD; Exec. Dir. & CEO – Permanente Medical Group

Source: Pearl R Health Aff 2014;33:251-257

Technology will reshape the way we deliver care

Mayo Clinic Plans for 2020

"How can we help patients everywhere? … Our board has approved our plan that by 2020 we will have meaningful interaction with 200 million people per year … [Ultimately], why wouldn't we at Mayo share what we know with people everywhere remotely."

Dr. John Noseworthy

Source: Nisen M. Mayo Clinic has a radical plan to expand its reach across the world. Business Insider. February 13, 2013. Available at: http://www.businessinsider.com/mayo-clinic-ceo-future-of-healthcare-2013-2.

Outline

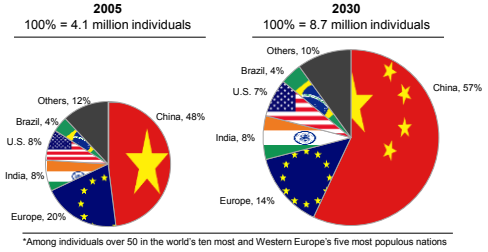
- Access challenge for Parkinson disease
- Virtual visits for Parkinson disease
- Smartphone application for objectively measuring symptoms in Parkinson disease

Outline

- **Access challenge for Parkinson disease**
- Virtual visits for Parkinson disease
- Smartphone application for objectively measuring symptoms in Parkinson disease

The burden of chronic conditions such as Parkinson disease is growing globally

Distribution of individuals with Parkinson disease by country from 2005 to 2030*



*Among individuals over 50 in the world's ten most and Western Europe's five most populous nations

Source: Neurology 2007;68:384-6

However, access to neurological care is limited in the United States

Proportion of Medicare beneficiaries with PD who do not see a neurologist

Source: Dorsey ER, George BP, Leff B, Willis AW. The coming crisis: obtaining care for the growing burden of neurodegenerative conditions. Neurology 2013; 80:1989-96

Outline

- Access challenge for Parkinson disease
- **Virtual visits for Parkinson disease**
- Smartphone application for objectively measuring symptoms in Parkinson disease

We are using simple, inexpensive technology to reach patients around the world

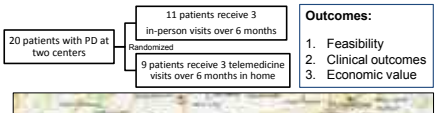
Novel application of existing technology

Equipment

- Internet-enabled device
- Web cam, microphone
- Encrypted software

- In-home care
- Remote patient monitoring
- Remote study participation

We completed a randomized, controlled trial of virtual house calls for Parkinson disease



Outcomes:

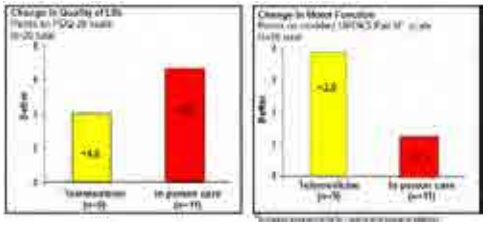
1. Feasibility
2. Clinical outcomes
3. Economic value

Sponsors: Google Excellus

Source: JAMA Neurol 2013;70:565-70

Patients in both arms had similar clinical outcomes

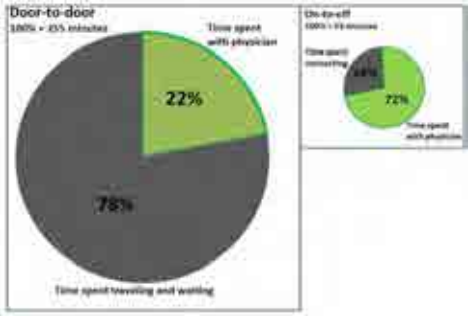
Clinical outcomes



Source: JAMA Neurol 2013;70:565-70

Virtual visits flip the care paradigm

Patient time spent on in-person versus telemedicine visits



Source: JAMA Neurology 2013;70:565-70.

Virtual visits offer patients care, convenience, and comfort

Feedback from patients and families

Care	•"We had a good family crying moment after the appointment from just pure joy of finally having the opportunity for him to see a (Parkinson disease) specialist" •"The (Parkinson disease) literacy was amazing"
Convenience	•"It's great not having to drive the 2 hours … having the added expense of my wife missing an entire day of work, [and] saving on gas for the car, tolls, [and] parking" •"I could have access to a movement specialist, which I currently don't where I live"
Comfort	•"I liked the interaction being personal despite the 3000 mile distance…it felt somehow protected by the veil of technology, which enabled the exchange to be more honest" •"I am more relaxed in my home setting"

Source: Neurol Clin Pract. 2014;4(2):146-152.

We have completed enrollment in a national randomized controlled trial of telemedicine for Parkinson disease

In collaboration with:

PARKINSON FOUNDATION pcori SBR HEALTH Deliver Care Anywhere patientslikeme Vidyo

Connect.Parkinson.org

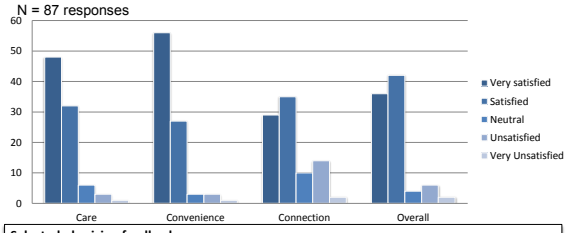
Interest in the study has been very high

Source: Google Analytics. Map of Connect.Parkinson.org site visitors from 2/23/2014-3/23/2014. Accessed 6/30/2014

Physicians are generally satisfied but have concerns about the quality of the connection

Initial clinician feedback

N = 87 responses



Selected physician feedback

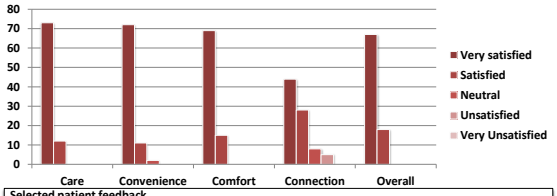
- "Visit interaction was great, but it was very difficult to determine actual ratings for rapidly alternating movements."
- "Video quality, particularly for rating Unified Parkinson's Disease Rating Scale is frustrating."
- "I think it is fine for the interview part, and maybe for clinical follow-ups."

Source: Connect.Parkinson Study

Patients are very satisfied with the telemedicine visits

Initial patient feedback

N= 85 responses



Selected patient feedback

- "I learned more in one visit than all the information provided by other physicians over a period of years!!!"
- "I felt it was a great doctor's visit. Better than many I've had face to face."
- "It was so good to not have to ride 45 minutes in a handicapped van each way to see a (movement disorder specialist)."
- "On a cold rainy day it was so nice not to have to worry about getting a ride and getting from the car to the office. I could concentrate on what I wanted to ask and the info the doctor provided."

Source: Connect.Parkinson study

With 23andMe, we assessed the phenotype of individuals who know their genetic information

Study's aims

1. To assess feasibility of recruiting participants for a remote research study
2. Assess ability to collect data remotely
3. Assess validity of self-reported data from individuals with Parkinson disease

Methods

One-time remote standardized assessment of individuals with self-reported Parkinson disease who live in the U.S., have high speed internet access, and may have at least one genetic risk variant for Parkinson disease

Outcome measures

1. Motor and non-motor characterization of participants
2. Validation of self-completed 23andMe Parkinson's disease baseline survey

Sponsor

biogen idec 23andMe

We conducted remote assessments with 50 participants in 23 states in 3 months

Results

- All study participants with self-reported PD were judged by neurologists to have PD (k=1.00)
- Also had high level of agreement for age of onset (k=0.97) and presence of family history (k=0.85)
- 95% of participants indicated interest in future virtual research visits
- This study sets the stage for larger scale studies targeting genetic sub-populations

Map of participants

Source: Digital Health available at: http://dhj.sagepub.com/content/1/2055207615592998

We performed a similar study with Fox Trial Finder and connected remotely to over 160 participants in 39 states

Map of participants

This study provided some valuable insights

Virtual research visits

Methods
•Fox Trial Finder participants provided consent by phone, completed baseline surveys, downloaded video conferencing software, and received a web camera.
•After a test connection, participants underwent a remotely assessed cognition and had a virtual research visit to:

(1) Review their history
(2) Perform MDS-UPDRS (modified to exclude assessments of rigidity and balance).
(3) Confirm whether PD was the most likely diagnosis,
(4) Solicit feedback on their experience

Results
•81.4% individuals from 39 states completed the visits

•On average, participants were:
(1) 61.6 years old
(2) Had Parkinson disease for 8.0 years
(3) Scored 26.5 on the Montreal Cognitive Assessment
(4) Had modified UPDRS motor score of 22.8.
(5) Parkinson disease was most likely diagnosis in 97.0% of cases.

•Overall satisfaction with the visits was 79% (satisfied or very satisfied) among neurologists and 93% among participants.

Transforming face-to-face clinical research

- Individuals can accurately self-identify illnesses, sometimes using direct to consumer testing
- Individuals endorse 'research from home'
- Researchers endorse remote evaluations, but feel some constraints with technology
- Researchers in one location can access and evaluate potential participants in a national and perhaps global distribution
- The model of an academic clinical research site with a local reach is actively being 'disrupted'

New tools and technologies can foster disruption in clinical trials

21st century tools and methodologies

Source: JAMA Neurol. doi:10.1001/jamaneurol.2014.4524

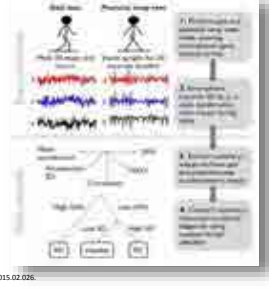
Outline

- Access challenge for Parkinson disease
- Virtual visits for Parkinson disease
- **Smartphone application for objectively measuring symptoms in Parkinson disease**

Movement disorders have external manifestations that smartphones can assess

Figure 1: Picture of Android smartphone and software application.

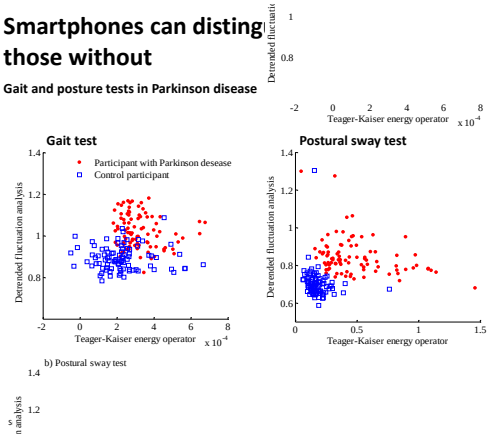
Figure 2: Procedure for collecting voice recordings, finger tapping, and passive sensor data from gait and postural sway test



Source: Parkinsonism & Related Disorders, http://dx.doi.org/10.1016/j.parkreldis.2015.02.026.

Smartphones can disting[illegible] n those without

Gait and posture tests in Parkinson disease



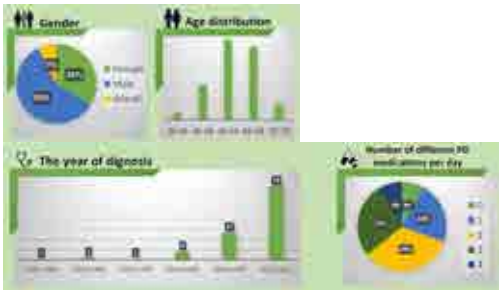
We have recently launched a 2000 person smartphone study in PD

https://foxtrialfinder.michaeljfox.org/trial/3861/

Smartphones allow for global participation anytime anywhere

Geographical representation of study participants (N=653)

Most participants were recently diagnosed



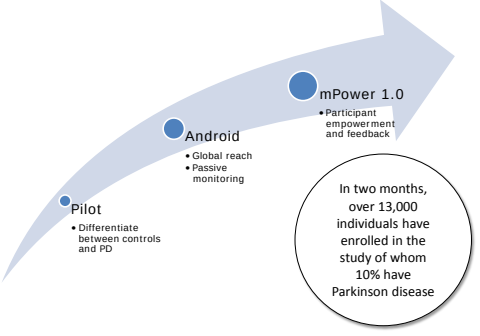
In March Apple announced the release of smartphone applications for medical research

mPower smartphone application for Parkinson disease

mPower includes surveys, structured tests of cognition, speech, speeded taps, speed and gait

This technology is currently being used in clinical trials to capture objective measures of Parkinson disease

We plan to have new generations of mPower with greater functionality



Questions?

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Thank You!

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Participant Engagement: Why Participate in Research?

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Participation in Clinical Research: Motivations and Perspectives

Julia Farides-Mitchell, MA
Project Manager
The Center for Information & Study on
Clinical Research Participation (CISCRP)

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Participation in Clinical Research
Motivations and Perspectives

Julia Farides-Mitchell, MA

Project Manager
Patient Engagement and Communication Programs
The Center for Information & Study on Clinical Research Participation (CISCRP)

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Learning Objectives

- Explain why Patients participate in clinical research
- Describe how Patients feel about their participation in Clinical Research

Key Topics to Discuss

- Why Patients participate in clinical research
- How Patients Feel about their participation in Clinical Research
- Assessment of where clinical trials may be falling short in patient engagement

Types of Patients Involved in Clinical Research

- **Patients can be separated into a few different groups**
  - General Public
    - Lay Public not actively looking to participate in clinical research
  - Perspective Patient
    - Lay Public actively looking for clinical trials to participate in
      - Healthy Patients
      - Patients seeking condition-specific trials
  - Participating Patients
    - Lay Public who have participated, and may participate again, in clinical research

J. Farides-Mitchell
November 2015

Why Patients Participate…

- ~~**General Public**~~
- **Perspective Patient**
  - Healthy Patients
    - Altruism
    - Monetary Gain
  - Patients seeking condition-specific trials
    - Varied treatment options
    - Suggestion from their doctor/friend/family
    - Altruism
    - Monetary Gain/Free care
- **Participating Patients**
  - Repeat participants
    - Positive experience in previous trials

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Patients and Their Participation

- **Patients Understand the Importance of their participation, but…**
  - It often lacks personal relevance
  - They feel as though they are gambling with their health
    - i.e. they are "guinea pigs"
    - They question the quality of care they will receive
  - They lack knowledge about clinical research
  - Clinical research has no "public face"
    - Clinical research is a very large unknown to many patients, and has many misconceptions in the general public
  - They do not feel engaged in the process
    - Clinical research may feel alienating
    - Clinical research often lacks critical follow-up to inform patients about results of their trials

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November 2015

Improving Patient Engagement

- **Before the trial**
  - Putting a face to clinical research
    - Education about clinical research provides patients with a sense of personal relevance and informs patients at the same time
    - Engaging previous participants to talk to prospective participants
  - Patient Advisory Boards
    - Engage patients before the protocol is finalized to provide feedback on ease of participation, patient-centered accommodations, and patient experience with their condition
    - Contributes to increased relevance
- **During the trial**
  - Addition of more patient-centered initiatives and accommodations
- **After the Trial**
  - Providing patients the results of their trial brings closure to their participation
  - Increases relevance of their participation

J. Farides-Mitchell
November 2015

Questions?

Thank You!

Challenges and Rewards of Engaging Pet Owners in Clinical Trials in Veterinary Medicine

Andrew Hoffman, DVM, DVSc, Diplomate, ACVIM

Professor, Large Animal Medicine
Director, Regenerative Medicine Laboratory
Cummings School of Veterinary Medicine
Tufts University

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Learning Objectives

- Discuss the major objectives of clinical trials in veterinary patients
- Identify the major issues impending participant engagement
- Describe ethical incentives and solutions that will help to increase participant engagement
- Explain major challenges that may be faced in the future

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Demographics in Veterinary Medicine (www.avma.org)

- **Dogs (70M), Cats (74M), Horses (4.8M), Birds (8M)**
- **Veterinarians: 102,583 (AVMA 2014 data)**
- **University Teaching Hospitals: 30 (2014)**
  - e.g. Caseload @ Cummings School – Tufts = >40,000/yr
- **Specialists: 11,761**
  - Cardiology, Dermatology, Ophthalmology, ECC, Neurology, Nutrition, Oncology, Pathology, Internal Medicine, Virology, Bacteriology/Microbiology

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Companion Animal Diseases (And Models of Human Conditions)

Cardiac	Myxomatous mitral valve disease (Mitral valve prolapse)
	Arrythmogenic right ventricular cardiomyopathy
	Dilated cardiomyopathy
	Hypertrophic cardiomyopathy
Neurologic	Intervertebral disc herniation
	Epilepsy
	Canine cognitive dysfunction syndrome (Alzheimer's Disease)
	Degenerative myelopathy (ALS)
Gastrointestinal	Inflammatory bowel disease
	Peri-anal fistulas (fistulizing Crohn's disease)
Dermatologic	Atopic dermatitis
	Pemphigus foliaceous
Musculoskeletal	Osteoarthritis
	Hip dysplasia
Ophthalmologic	Auto-immune uveitis, Glaucoma
	Keratoconjunctivitis sicca

Kol, Arzi, et al. *Science* 2015

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Dual Benefit of Many Companion Animal Studies

Kol, Arzi, et al. *Science* 2015

Past examples (selected):

Keratoconjunctivitis Sicca (KCS):	Restasis Lifitegrast
Non-Hodgkins's Lymphoma:	Ibrutinib
Osteosarcoma	Limb-sparing surgery (ped, adult)
Mandibular reconstruction	rhBNP2

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Companion Animal Study Paradigm

Companion animal disease model (CADM) →
- **Innovative strategy**
- **Pre-CADM safety testing**
- **PoC**
- **Long-term safety**
- **Clinical trial simulation**
- **Optimization**
- **Personalization**
- **Reproducibility**

→ **Human clinical studies**

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Examples

http://sites.tufts.edu/vetclinicaltrials/regenerative-medicine-stem-cell-trials/

- **Wharton's Jelly mesenchymal stem cell transplantation**
  - Mitral valve dysplasia with congestive heart failure
  - Arrhythmogenic right ventricular cardiomyopathy
  - Atopic dermatitis
  - Inflammatory bowel disease
  - Perianal fistulas/fistulizing Crohn's Disease
  - Immune complex glomerulonephritis
  - Intervertebral disc herniation
- **exRNA biomarkers**
  - Plasma biomarkers post-CPR
  - Plasma and urinary biomarkers for mitral valve disease
  - Plasma biomarkers for ARVC

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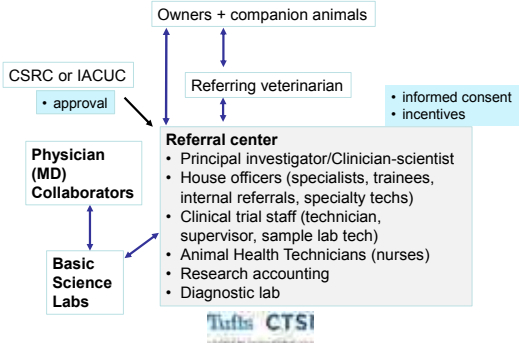
Participants



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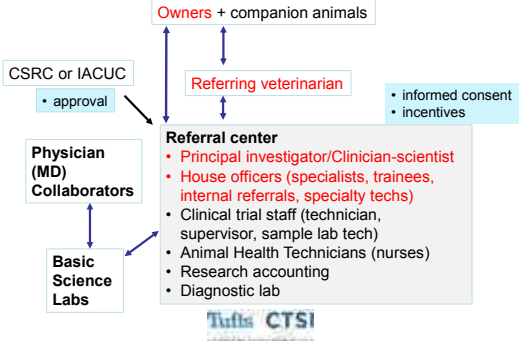
Challenges



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Deterrents for Owners

- Painstaking protocol – loss of work or vacation time
- Safety risks to animal
- Have to change food (or any behavior)
- Trials with no incentives
- Stress of procedures (e.g. extra blood draws)
- Owners during stressful time
- Placebo controlled studies
- Insufficient incentives to offset $$ of SOC
- Stress of leaving animal behind or being without animal
- Fear of research (depends on *relationship* with doctors)
- Insufficient $$ in reserve for complications
- Confusing consent forms (unusual)
- Stem cells (general fear)
- Warnings on consent forms (depends on explanation)
- Xeno products

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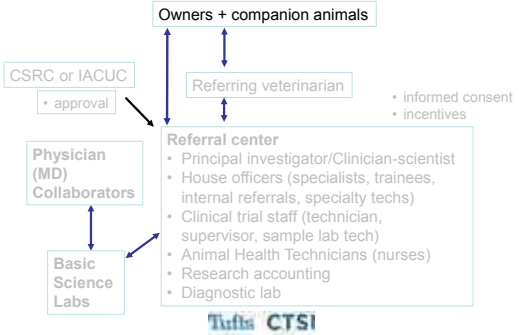
Financial or Equivalent Incentives



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Current Incentives to Owners

n=72/75 open trials at Tufts Veterinary Medical Center

- Screening and/or repeated lab work
- Imaging (CT, MR, Ultrasound, Fluoro)
- Offset surgical costs (disc herniation)
- ECG monitoring (home)
- Biopsies
- Recheck exams
- $300 toward purchase of cyclosporine
- 25% bill up to $1500
- $500 (to be spent on patient within 1 year)
- $150 gift card (if study completed)
- $1250 toward radiation
- Parking fee reimbursement

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Deterrents for RDVM & Clinicians

- **Do not know about clinical trials (n=75)**
- **Insufficient time to participate (especially after hours)**
- **PI not driving clinical trial**
- **Other…**
  - Teaching burden
  - Inadequate staffing to triage eligible cases
  - Time-consuming EMR that does not serve clinical trials
  - Work does not benefit promotion
  - Perceived need more investments in clinical trials
  - Overemphasis on bottom line by hospital administration

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Clinicians- Actual Support

- **Digital white board in middle of hospital**
- **Study protocols icon/list *on every computer***
- **Bi-Monthly newsletters (clients, RDVM, and H-Officers)**
- **Visits to RDVM hospitals**
- **Research seminars for House Officers with food**
- **Other…**
  - Promotion incentives for collaboration
  - Student/Intern/resident orientation
  - Internal RFAs supporting research
  - Laboratory support
  - Clinical trial technicians (2 FTE) and super (0.5 FTE)
  - Clinical trial website
  - Website – inquire by email – daily checked

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Future Directions

- Apps for identifying clinical trials
- EMR working for clinical trials (flagging)
- Staff to identify eligible cases
- PI more aggressive information campaign
- Incentivize house officers equitably (all trials)
- Focus on ER
- Better predictions of caseload
- More stringent criteria for trial failure
- Multi-center approach

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Tufts University | Cummings School of Veterinary Medicine

Regenerative Medicine Laboratory
Vicky Yang, Research Assistant Professor, Assistant Director
Alisha Gruntman, Assistant Professor
Kristen Thane, Post-Doctoral Scholar
Sarah Crain, PhD Candidate
Airiel Davis, Research Assistant
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Kerry Loughran, Veterinary Student Researcher

http://vetsites.tufts.edu/rml/

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Collaborators
Saumya Das, MD, PhD (Beth Israel Hospital)

Support

Shipley Foundation | NIH National Heart, Lung, and Blood Institute | Morris Animal

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Questions?

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Thank You!

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Challenges in Consenting Pregnant Women, Children and Neonates

Jonathan Davis, MD
Vice-Chair of Pediatrics for Academic Affairs
Chief of Newborn Medicine
The Floating Hospital for Children at Tufts Medical Center
Professor of Pediatrics
Tufts University School of Medicine
Director of Regulatory Affairs
Tufts CTSI

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Disclosures

- **I have no conflicts of interest to disclose**
- **I am funded by NIH and FDA to study new and existing agents to improve neonatal outcome**
- **I Chair the Neonatal Advisory Committee in the Office of the Commissioner at the FDA. My presentation reflects my own opinions and does not necessarily represent the opinions of the FDA**
- **I am a Director of the International Neonatal Consortium through FDA/EMA/Critical Path Institute**

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Learning Objectives

- Identify important issues when conducting research on vulnerable populations
- Explain the challenges when consenting pregnant women or their infants
- Discuss the unique challenges of conducting research on premature infants (e.g. blood sampling, outcomes)

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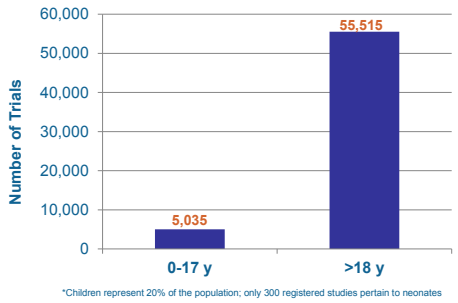
Registered Trials in ClinicalTrials.gov*



*Children represent 20% of the population; only 300 registered studies pertain to neonates

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Why has Drug Development for Pregnant Women, Children and Neonates Been so Difficult?

- Small markets
- Rare diseases
- High risk - significant liability
- Appropriate animal models?
- Difficulty with study design/outcome measures
- May need to wait to determine outcome
- Hard to establish safety – prenatal exposure, postnatal exposure, environmental influences
- Hard to establish efficacy

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Ethical Considerations

- Human subject protections at 21 CFR Part 50
- Additional safeguards found at Subpart D – is there prospect of direct benefit?
- Does the study represent a minor increase over minimal risk?
- Should we consent pregnant mothers prior to labor, in active labor, or after delivery when we know the neonate meets criteria? How about mothers <18 years old?
- Assent of minor for older children

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Informed Consent

- System designed to protect research subjects while educating them on why they should participate in a research study
- Inconsistency in approach, especially when conveying risk (physical, mental, privacy)
- Time and resource intensive – especially with language and cultural barriers
- Consent forms can be >20 pages – do patients truly "understand" what they agreeing to?
- Limited evidence that this actually improves human subjects protection (especially for multisite studies)

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Informed Consent

- Establish consistency with structure and format
- Introduce a hierarchy of information – short form
  - Executive Summary
  - Current condition along with expected risks and alternatives if not in the study
  - Study purpose and design
  - Integrated risks and benefits
  - Expectations and responsibilities
  - Appendices with additional information

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Developing Drugs for High Risk Populations: National and Global Efforts

- Studies require attention to many details
- Designing these studies requires "Team Science" – investigators, pharmacologists, statisticians, bioethicists, regulators, support staff, foundations, families
- Better communication/collaboration among Regulatory Agencies, Funding Agencies, Industry, CROs, and Academia
- Global network initiatives most promising

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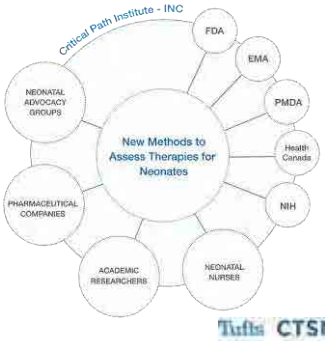
Members Spanning the Globe



- **Neonatal Nurses**
  - NANN
  - COINN
- **Founding Companies**
  - AstraZeneca
  - Jannsen
  - Lilly
  - Novartis
  - Pfizer
  - Sanofi
  - Shire
- **Families/Advocacy**
  - Graham's Foundation
  - March of Dimes

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Why the Clinical Path Institute?

- **Acted as a trusted, neutral third party**
- **Convene scientific consortia of industry, academia, and government for sharing of data/expertise**
  - The best science
  - The broadest experience
  - Active consensus building
  - Shared risk and costs
- **Enable iterative EMA/FDA/PMDA participation in developing new methods to assess the safety and efficacy of medical products**
- **Official regulatory endorsement of novel methodologies and drug development tools**

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Questions?

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That's All Folks!

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Panel Discussion

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15 Minute Break

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Innovative Recruitment Strategies

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Using Social Media for Participant Engagement in Clinical Trials: A Pilot Study

Laura Blaisdell MD, MPH, FAAP

Center for Outcomes Research and Evaluation
Maine Medical Center Research Institute

Learning Objectives

- Identify how different social media platforms can support research recruitment and retention
- Explain humans subjects protection considerations when using social media in the research setting

National Children's Study

- **Was planned as a long-term study of children's health and development ever to be conducted in the U.S.**
- **To examine**
  - Health and development of more than
  - 100,000 children across the United States,
  - Following them from before birth until age 21.
- **Sponsored by the Eunice Kennedy Shriver National Institute for Child Health and Human Development of the NIH and other federal agencies including NIEHS, CDC and EPA**

NCS Study Model

- Sample of women 18-49 years reflecting the diversity of America
- Enrolled before or during pregnancy
- Follow them and their children prospectively
- Observational, not interventional study
- Collect environmental, genetic and biological samples
- Collect physical and behavioral outcomes data

NCS Study Locations

Vanguard Study

- **Vanguard (pilot) Study**
- **Test methods and procedures for Main Study**
- **Initially housed at 40 centers, then in 4 Regional Operating Centers**
- **Recruitment ended 2013**
  - Enrolled 5,000 children

The Main Study

- NIH Director decided to close the NCS on December 12, 2014 following the advice of a review group.

Community Engagement in NCS

- **Engaging community in research increasingly important.**
  - Door-knocking requires community preparation.
  - Using it since Framingham.
- **Many clinical trials are now using social media to engage participants.**
- **Young Adults and women of childbearing age are a particularly difficult demographic to recruit.**

Ubiquitous Web & Social Media

- **What does this mean?**
  - The first information source
  - Essential for credibility of some
  - Erases geographic differences between people (and study sites)
  - Omnipresent (mobile devices)
  - Cost Effective
- **Little is known about how best to use social media platforms for research.**

Use of Social Media in Highly Restricted Environments

- **Goal's are Different**
  - Credibility? Ads? Information dissemination?
- **Policies are essential**
  - Confidentiality & Privacy Policies
  - Who is your company/Study Center's voice?
  - Proprietary issues of accounts
- **Institutional Review Board**

Use of Social Media in Highly Restricted Environments

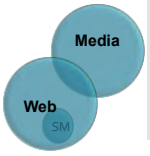
- **General Engagement vs. Participant Engagement**
- **Content may be interpreted as an extension of informed consent.**
  - Avoid overpromise benefits or underestimation of risks
- **Posting frequency and real-time nature of social media creates considerable burden for IRBs.**
  - Without timeliness and relevance, the impact of social media is reduced.
  - Forge new processes with IRBs?

Web & Social Media Strategy

- Goals
- Tools to Meet the Goals
- Tricks to Do it the Best

Plan Components

- **Goal**
  - Create awareness, trust and retained interest for the NCS using social media & web.
- **Tools:**
  - Website, Blog, Email Marketing, Facebook, Twitter
- **Tricks**
  - Search Engine Optimization, Key Word Matrix & Blog
  - Optimizing Facebook
  - Link, Link, Link & RECYCLE



Search Engine Optimization (SEO)

- **Improving the visibility of a website in search engines via un-paid search results.**
- **Earlier & frequently viewed in the search results list results in more visitors to a page.**
- **Considers:**
  - How search engines work
  - What people search for
  - The actual search terms or keywords typed into search engines &
  - Which search engines are preferred by the targeted audience

Search Engine Optimization (SEO)

Sample relevant terms provided by Study Center	Search Engine Optimization (Examples of over 2000 terms)
•Children's health	•Health problems
•Environment	•Autism in children
•Cumberland County, Maine	•Gluten-free recipes
•Research	•Type 2 diabetes
•Community	•What is child health
•Health, growth, development	•What is cholera
•National	•Articles about health
•Physical, social, family	•What foods are gluten-free
•Participation	•Obesity in the USA
•Recruitment	•Treatments for ADHD
•Pregnancy	•Signs of autism
•Support	•Nutrition for kids
•Privacy, confidentiality	•Childhood diseases
	•Food tolerance
	•Mental health child
	•Infant nutrition
	•Gluten free milk
	•Famous people with aspergers

Search Engine Optimization

Keyword	Competition	National Monthly Searches	Global Monthly Searches
is aspergers genetic	0.04	880	1300
famous people with adhd	0.07	4400	6600
most common diseases in children	0.07	1000	1600
common childhood illnesses	0.09	1300	3600
main stages of child development	0.1	36	480
celiac disease recipes	0.5	720	1600
can adhd be cured	0.52	260	390
toys for autistic children	0.89	3600	5400
facts about type 2 diabetes	0.81	880	1300

OK	Better	Best
Comp > 0.75	Comp = 0.5 -0 .75	Comp < 0.5
Searches < 300	Searches = 301 - 999	Searches > 1,000

Blog

- Use SEP generated Key Word Matrix to create content
- Again, content must be carefully considered prior to posting

Facebook

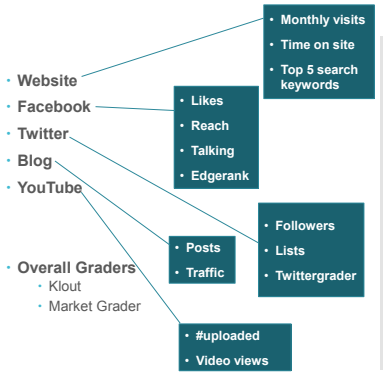
- Landing page
- Posting schedules
- Posts that engender engagement
- Get your base talking

Link, Link, Link and Recycle

- Facebook and Blogs can be linked
- Twitter - same content but requires customizing
- YouTube - new mobile cameras make YouTube easy to do in high quality.

Measuring Effects of Social Media Platforms

SM Metrics Measured

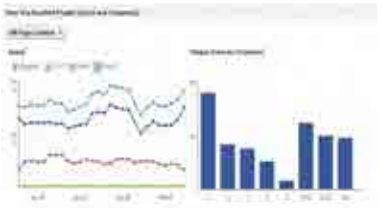


Facebook Insights

- **Data on:**
  - Demographics
  - Geography

Facebook Insights

- **Data on:**
  - How people came to be on your page
    - Organic, paid, viral



Facebook Insights Data

- **Exists on Two Levels:**
  - Page level data
  - Post level data

Insights Page Level Data

- **Facebook Page Level Data**

We used these

- **Lifetime Total Likes**: Lifetime The total number of people who have liked your Page. (Unique Users)
- **Daily Friends of Fans**: Daily The number of people who are friends with people who liked your Page (estimated). (Unique Users)
- **Daily Page Engaged Users**: Daily The number of people who engaged with your Page. Engagement includes any click or story created. (Unique Users)
- **Daily Total Reach**: Daily The number of people who have seen any content associated with your Page. (Unique Users)
- **Daily Total Impressions**: Daily The number of impressions seen of any content associated with your Page. (Total Count)
- **Daily Logged-in Page Views**: Daily Page Views from users logged into Facebook (Total Count)
- **Daily Reach of page posts**: Daily The number of people who saw any of your Page posts. (Unique Users)
- **Daily Total Impressions of your posts**: Daily The number of impressions that came from all of your posts. (Total Count)
- **Daily Total Consumers**: Daily The number of people who clicked on any of your content. Clicks generating stories are included in "Other Clicks." Stories generated without clicks on page content (e.g., liking the page in Timeline) are not included. (Unique Users)
- **Daily Page consumptions**: Daily The number of clicks on any of your content. Clicks generating stories are included in "Other Clicks." Stories generated without clicks on page content (e.g., liking the page in Timeline) are not included. (Total Count)

And this…

Insights Post Level Data

- **Facebook Post Level Data**
  - **Lifetime Post Total Reach**: Lifetime The number of people who saw your Page post. (Unique Users)

We call this "Views"

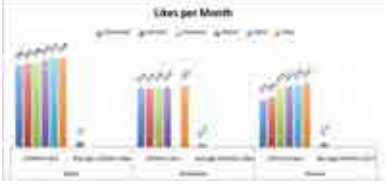
  - **Lifetime Talking About This (Post)**: Lifetime The number of unique people who created a story about your Page post. (Unique Users)

We call this "clicks"

Basic Facebook Metrics

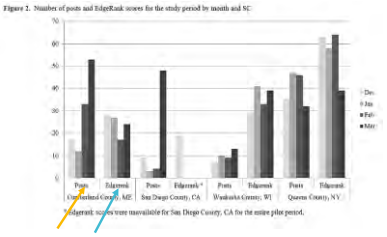
Likes Per Month

Likes can be accumulated quickly, regardless of how many months a page was live

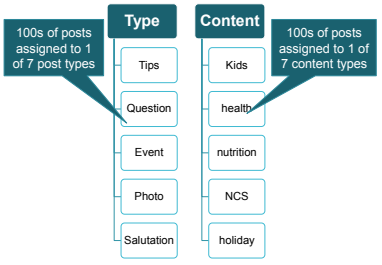


Basic Facebook Metrics

- Number of posts
- Edgerank

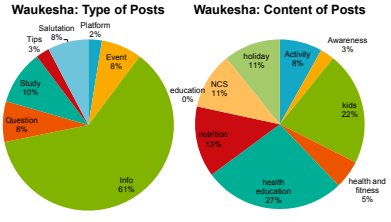


Post Analysis: Type and Content



Type & Content of Posts At One Study Center

- **TYPE**
- **CONTENT**

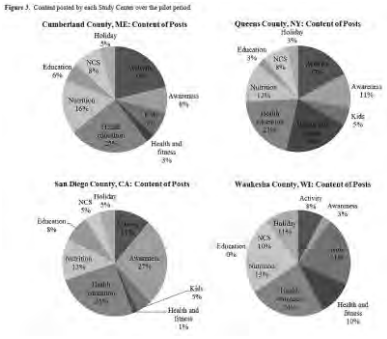


December to March Average

Individual SC Posting Trends

- **In May, the FB pages in Queens and Waukesha posted less information posts (green) and more platform posts (blue)**

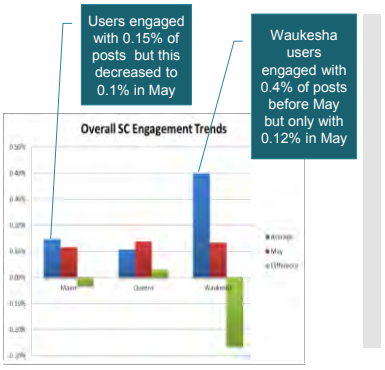
Content Posted By Each Study Center Over Pilot Period



That's great but so what?

- **So we can tell how much we posted, including knowing what type of post it was and what the content was….**
  - But what we really care about is **posting stuff that people will share, click and view**
    - So how can we tell if people engaged (share, click view) with our posts?
      - Better yet, how can we tell what type and content of posts people **really** engaged with so we can do more of that and less of the stuff that people ignored.

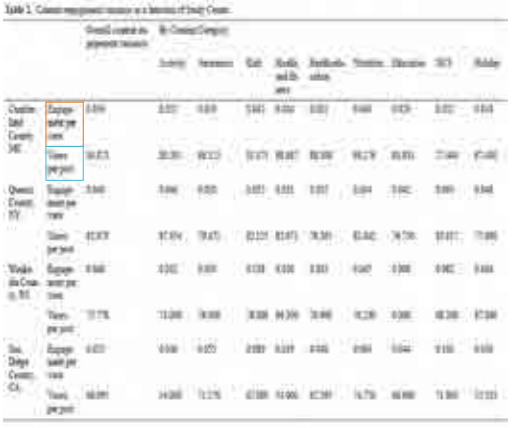
Engagement Analysis



Engagement Metrics

$$\bar{E}_{Maine,Queens,Waukesha} = \left(\frac{Clicks}{Views} \middle/ \#Posts\right)^{\{May - \bar{X}_{dec-mar}\}}$$

$$E\text{¢}_{c} = \left(\frac{PcClicks}{PcViews} \middle/ \#PcPosts\right)^{\{May - \bar{X}_{dec-mar}\}}_{Maine,Queens,Waukesha}$$



Highest Raw Engagement Score

Table 2

	Maine		Queens		Waukesha	
	Type	Content	Type	Content	Type	Content
December	study	NCS	event	activity	info	health education
January	event	activity	event	NCS	info	kids
February	event	activity	study	NCS	info	health education
March	event	activity	study	NCS	salutation	NCS
May	study	NCS	salutation	activity	study	holiday

Stats: Significant Results

Posting Trends

- Significant difference for Queens for Type posts between May and the Dec-March average

Type	Fisher extended exact test, a=.05
Maine	0.7842
Waukesha	0.512
Queens	1.29E-13

Content	Fisher extended exact test, a=.05
Maine	0.705
Waukesha	0.14
Queens	0.6653

Engagement

- Significant difference for Waukesha for post content engagement between May and the Dec-March average

Type	Fisher extended exact test, a=.05	p-value
Maine	0.776	0.453
Waukesha	-2	0.068
Queens	**0.79**	0.445

Content	Unpaired T-test, a=.05	p-value
Maine	-1.17	0.261
Waukesha	-2.23	0.04
Queens	-1.28	0.219

Review

- Social Media is Increasingly Used in Research with growing data to demonstrate its effectiveness.
- Not all platforms are the same, reach the same demographic and they change monthly.
- Human Subjects Protections must be considered when using social media.
- Measuring effect of social media on recruitment and retention is possible.

Questions?

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Thank You!

Acknowledgements to the MMCRI Social Media Team!

Eva Farina-Henry, Leo Waterston, MJ Benson and Peg Gagnon

Laura Blaisdell MD/MPH
blaisl@mmc.org

Recruitment in Social Behavioral Research (Dear Abby and More)

Debra Lerner, MS, PhD
Professor, Departments of Medicine and Psychiatry,
Tufts University School of Medicine
Sackler School of Graduate Biomedical Sciences
Director
ICRHPS Program on Health, Work and Productivity
Director, Tracking and Evaluation
Tufts CTSI

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Learning Objectives

- List recruitment methods for field research
- Explain the pros and cons associated with using social media

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A Definition

"Social media has been broadly defined to refer to the many relatively inexpensive and widely accessible electronic tools that enable anyone to publish and access information, collaborate on a common effort, or build relationships.''

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Murthy, Dhiraj (2013). Twitter: Social Communication in the Twitter Age. Cambridge: Polity. pp. 7–8. ISBN 978-0-7456-6510-8.

Recruitment

- **The goal is, using ethical methods, to locate the right people and motivate them to move through the entire process of:**
  - Learning about the study
  - Giving permission for us learn more about them
  - Helping them decide whether to participate
  - Making it official
- **Social media provide new tools**

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Recruitment Approach Considerations

- **Research Objectives**
- **Design Requirements** (rigor of sampling)
- **Known Sample Characteristics** (e.g., health, demographics, location)
- **Budget** (cost per enrollment)
- **Timeframe**
- **Practical Matters**

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IRB Considerations for Recruiting With Social Media

- Required, even if exempt
- Include samples of each communication
- Include information about target population
- May need letters from collaborating sites
- Detail data security and confidentiality protocols

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When Does Use of Social Media Make the Most Sense?

- Large sample, limited time
- Hard-to-find sample
- Desire technology users
- Subjects preferring social distance
- Subjects with access or travel barriers
- Survey research

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Social Media Recruitment Tools

- **Many studies require multiple tools and approaches**
  - Email
  - Website (augmented with chat function)
  - Social Networks (chat groups)
  - Blogs
  - Twitter
  - Texting

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Pros of Using Social Media for Recruitment?

- Current
- Efficiency
- Reach
- 24/7
- Tailoring
- Graphic
- Adaptability of Technology
- Modifiability
- Link-ability
- Feedback
- Tracking
- Anonymity

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Challenges to Using Social Media for Recruitment

- Technical
- Security
- Users
- Fraud, Abuse
- Denominator
- Biases (selection)
- Control
- Study Sections

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Caregivers of Individuals With Schizophrenia

- National survey to identify demands on unpaid caregivers, supports and unmet needs
- Also focused on the degree to which caregivers are employed and difficulties managing a job and career in addition to being a caregiver
- Sponsored by Janssen Scientific

by Abigail Van Buren
Share on FacebookShare on TwitterContact Dear AbbyPrint Article

DEAR ABBY: My ex-husband and I have been back together for eight months. We were divorced for two years, during which time he remarried. We stayed in contact during his second marriage and he says he still loves me, so he left her.

He's now back with me after living on his own for a few months. I'm frustrated because he won't commit to me again. He says he has forgiven me for what broke up our marriage, but he will never consider remarrying me.

He says he has lost faith in all women. He says one marriage to me was enough and that he's confused. He told me it's fine with him if I put my rings back on. He introduces me as his wife when we're out together, but won't divorce his second wife.

I know I'm coming on too strong and pressuring him to be the man he used to be. I just don't think it's right that he should get all the benefits of having his wife and children back with none of the commitment. Should I back off and give him time to heal, or am I trapping myself in a hopeless relationship that's going to leave me a divorcee?

– HOPELESS IN MISSOURI

Recruitment Methods

- Dear Abby Electronic and print column posting
- Research Opportunities portion of advocacy organization websites
- E-newsletters of advocacy organizations
- Tweets to followers of advocacy organizations
- Postings in Reddit chat groups
- Website with Chat and Toll-Free Line

Some Unexpected Results

Who's Responding?

"On the Internet, nobody knows you're a dog."

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Some Unexpected Results

$$$Fat Wallet$$$

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Summary

- Social media offer new choices for recruitment
- Pilot-test content, media performance, user interface and security
- Each approach must be considered carefully and fully evaluated
- Watch carefully for problems, glitches and unanticipated events

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Questions?

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Thank You!

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Using an Expert Panel to Randomize Patients in a Cervical Spondolytic Myelopathy Clinical Trial

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Clinical Equipoise Panels Increase Patient Consent to Randomization in Surgical Trials

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Tufts CTSI's Translational Research Day 2015
Tufts University School of Medicine
Boston, MA
November 10, 2015

Lahey Hospital & Medical Center

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Learning Objectives

- Discuss the meaning of clinical equipoise as it relates to the ethics of conducting randomized clinical trials
- Explain the importance of enrolling the majority of eligible patients into randomized clinical trials.
- Describe how expert clinical panels might increase patient acceptance of randomization.
- Identify the logistics of setting up an expert clinical panel to review cases for enrollment in clinical trials.

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Does Spine Surgery Work?

Ask Your Patients

Judgment
Satisfaction Outcome

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If it was only that simple . . .

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With Access to Big Data . . .

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Equity Markets: Benchmarks

Finance: Assess Portfolio Performance
Spine: No System to Measure Outcome

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Government and Payers: Criticism/Pressure

- **US complex spinal fusion ⬆15–fold 2002–2007, with increasing major complications and costs**
- **Mean hospital charges**
  - **Fusion = $80,888**
  - **Decompression = $23,724**

  Deyo et al., *JAMA*. 2010;303:1259-1265.
- **US cost of spine care ≥ $86 billion/year, with >300,000 spinal fusions/year**
- **(Cost of Cancer in US = $89 billion/year)**

  Martin et al., *JAMA*. 2008;299:656-664.

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Spinal Fusion: Where is the Evidence?

Lumbar fusion guidelines*: "Grade B: Lumbar Fusion or a comprehensive rehabilitation program incorporating cognitive therapy are recommended as treatment alternatives for patient with chronic low back pain . . ."*

– Resnick et al., *J Neurosurg: Spine*. 2014;21:42–47

- 3rd party payers limit patient access to lumbar spinal fusion, citing lack of evidence
- Institute of Medicine: Low back pain and cervical spondylotic myelopathy (CSM) among top 100 CER priorities

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Why do we need Evidence?

Contemplation between material wealth and pure knowledge

Rembrandt's Aristotle and the Bust of Homer

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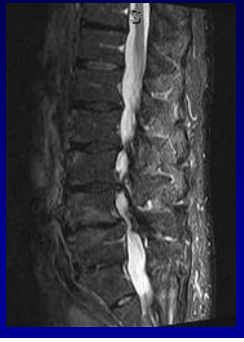
First…Do No Harm



75 year-old cardiologist with spinal stenosis and neurogenic claudication

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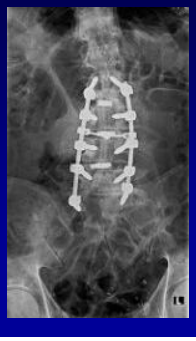
First…Do No Harm



Cardiologist with spinal stenosis treated with multi-level fusion resulting in significant blood loss, transfusions, ICU management and a prolonged 1 year recovery

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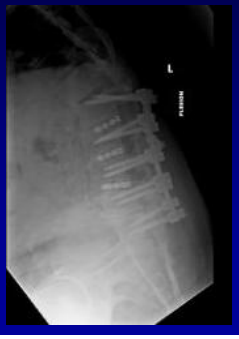
First…Do No Harm



Cardiologist with spinal stenosis treated with multi-level fusion resulting in kyphotic deformity that ended his practice

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First…Do No Harm

Cardiologist with spinal stenosis treated with multi-level fusion resulting in kyphotic deformity "addressed" with T10-Sacrum fusion

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Who can we help and to what degree?

The Doctor 1891 - Sir Luke Fildes

- **Surgery**
- **Outcomes**
- **Trials/ Registries**

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Barriers to Generating Rigorous Comparative Effectiveness Evidence

- **Cost**
- **Infrastructure**
- **Equipoise**

Generalizability?

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Generating Rigorous Comparative Effectiveness Evidence

Assess intervention *efficacy*: RCT

- "Gold standard" for ***efficacy***; causality (random treatment allocation protects *internal* validity)
- High data reliability, reproducibility
- Lack of equipoise, cross–overs, limited generalizability reduce enthusiasm

Assess intervention *effectiveness*; who benefits, who does not or is harmed: Registry

- Random probability sample selection protects *external* validity
- Reduced data completeness

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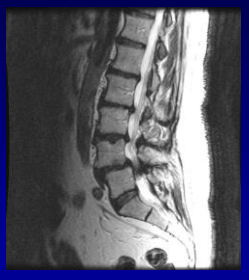
Grade I Degenerative Spondylolisthesis (Spinal Stenosis)



- Most frequent indication spinal surgery patients >65
- 40% degenerative slip
- 20% re–operated in 5 years
- Lack of data RE: utility of fusion vs. laminectomy

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Spondylolisthesis: Payer Perspective

Cost/case:	$ 12,000	$ 35,000
Volume/yr:	150,000	150,000
Total Cost:	$1.8 billion	$ 5.3 billion

Bundled payment

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Hypothesis: Fusion Will Result in Superior Outcome if Laminectomy Alone Destabilizes the Spine

Stable

Unstable?

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SLIP Study RCT Design

Surgical Treatment

66 patients randomized

- Lumbar laminectomy alone (N=35)
- Laminectomy with pedicle screw fixation and posterolateral fusion (n=31)

No Interbody Devices; No BMP

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Randomization Requires Trust/Equipoise

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SLIP Study - Randomization

130 pts screened
106 pts enrolled

- 66 Randomized (Target 64)
- 40 Not–Randomized

62% randomized

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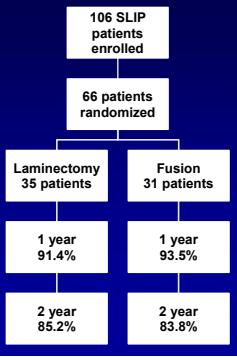
SLIP Study Execution



- 130 patients screened
- Baseline characteristics comparable
- Follow-up: >80% at 2 years

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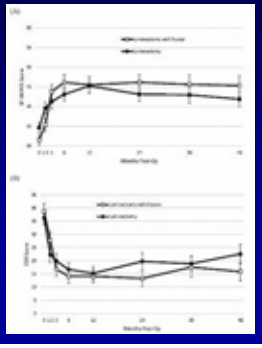
Comparative Outcomes: Fusion vs. Laminectomy Alone



PCS (SF–36)
(Higher Score is Better)
2 year – P=0.046
3 year – P=0.02
4 year – P=0.02

Both Laminectomy alone and Lami/Fusion had comparable reduction in ODI – with greater improvement after fusion

P=0.05

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Patient Consent to Randomization: Major Barrier to Conducting Surgical RCTs

If establishment of clinical equipoise is necessary for randomization to be ethical, could a group of doctors build trust?

- What if each patient being considered for a randomized clinical trial could:
  - Comprehend the uncertainty among treatment options?
  and
  - Obtain value added to their care by participating in an RCT?

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Crowd Intelligence

http://www.nauticed.org/sailing-blog/yacht-club-intelligence-nauticed-sailing-school-press-release/crowd-intelligence/

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Construction of Clinical Equipoise Panel

- **Panel = 10 experts**
  - Experienced and skilled in both options
  - Published outcome studies on techniques
  - Equipoise between various options
- **50% panel – not enrolling investigators**
- **Experts blinded to voting results**
- **No Equipoise if >80% vote for one strategy**
  Ghogawala et al, Ann Surg, 2015

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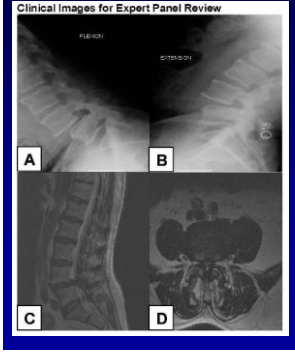
Spinal Equipoise Panel



- **76 y.o. male neurogenic claudication and L4/5 spondylolisthesis)**
- **Accepted randomization after 7 of 8 expert spine surgeon panel votes favored randomization**

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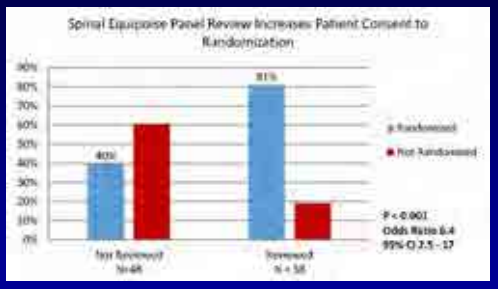
Spinal Experts Network



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"Dose Response" Effect? # of Experts Voting Against Randomization

Number of Votes Against Randomization	Average Number of Votes for Randomization#	Randomization Acceptance Rate*
0 or 1	6.48 (4–9)	95% (40/42)
2	5 (4–6)	75% (3/4)
3 or 4	3.44 (1–5)	20% (1/5)

* P<0.001 for trend
[Values represented as the mean (range)

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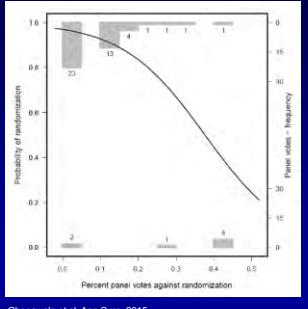
Spinal Experts Network



Ghogawala et al, Ann Surg, 2015

As experts vote against randomization, patient consent to enrollment also goes down

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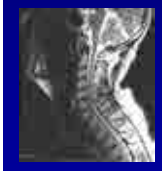
Cervical Spondylotic Myelopathy Case Presentation



- 55 year-old Dean of a law school in Boston
- Active tennis player
- 3 months tingling R hand
- Recent falls on tennis court
- Felt "zingers" in both arms in dentist's office
- Exam – pathological hyperreflexia, bilateral Hoffman's, full strength

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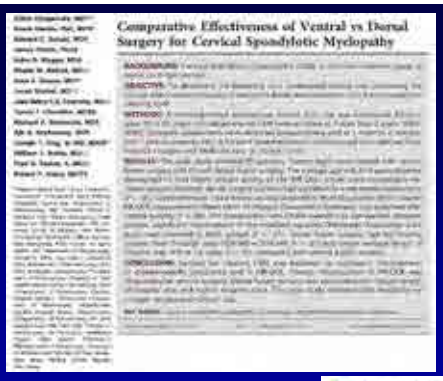

Comparative Effectiveness of Ventral vs Dorsal Surgery for Cervical Spondylotic Myelopathy

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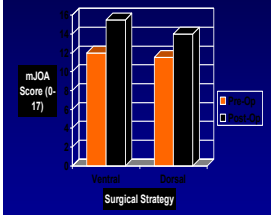
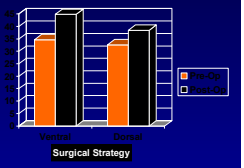
CSM Pilot Study Procedure – Specific Outcomes





P<0.05

Complications:
Ventral – Dysphagia
Dorsal – Pain, C5 weakness

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NIH-PCORI CSM-S Trial


Cervical Spondylotic Myelopathy Surgical Trial (CSM-S Trial)

RCT – 159 patients

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Spinal Experts Panel

Panel Vote

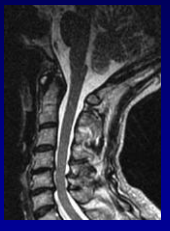
Vote	Strategy
Enroll	anterior discectomy
Enroll	laminoplasty
Enroll	anterior discectomy
Do Not Enroll	laminoplasty
Enroll	anterior discectomy
Enroll	anterior discectomy
Enroll	anterior discectomy
Enroll	posterior
Enroll	laminoplasty
Enroll	anterior discectomy
Enroll	laminoplasty
Enroll	laminoplasty
Enroll	laminoplasty
Enroll	anterior discectomy
Enroll	laminoplasty

Votes

Enroll	14
Do Not Enroll	1
Anterior	7
Posterior	8

Clinical Equipoise

Patient Randomized



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Spinal Experts Panel

Panel Vote

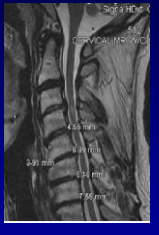
Vote	Strategy
Do Not Enroll	posterior laminectomy with fusion
Enroll	anterior discectomy
Enroll	anterior discectomy
Do Not Enroll	posterior laminectomy with fusion
Do Not Enroll	
Enroll	anterior discectomy
Enroll	posterior laminectomy with fusion
Do Not Enroll	posterior laminectomy with fusion
Enroll	anterior discectomy
Do Not Enroll	laminoplasty
Do Not Enroll	anterior discectomy
Enroll	posterior laminectomy with fusion
Enroll	laminoplasty
Enroll	laminoplasty
Enroll	posterior laminectomy with fusion

Votes:

Enroll	9
Do Not Enroll	6
Anterior	5
Post Fusion	6
Laminoplasty	3

Clinical Equipoise

Patient Randomized



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Spinal Experts Panel

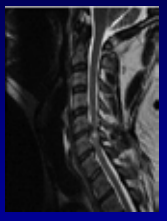
Panel Vote

Vote	Strategy
Enroll	anterior discectomy
Enroll	anterior discectomy
Enroll	anterior discectomy
Enroll	anterior discectomy
Enroll	anterior discectomy
Enroll	anterior discectomy
Enroll	anterior discectomy
Enroll	anterior discectomy
Enroll	anterior discectomy
Enroll	anterior discectomy
Enroll	anterior discectomy
Enroll	anterior discectomy
Enroll	anterior discectomy

Votes:

Enroll	**13**
Do Not Enroll	**0**
Anterior	**13**
Posterior	**0**

No Clinical Equipoise Patient NOT Randomized



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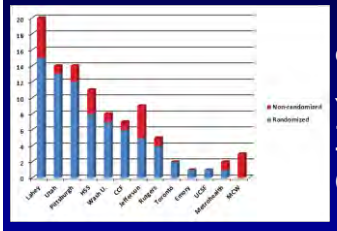
NIH-PCORI CSM-S Trial



Current Trial Progress

Year 1:
103 enrolled
78 randomized (73%)
(3.8% crossovers)

Goal – 159 patients

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Equipoise Panels: Summary

- **Hypothesis-driven clinical science – RCTs**
- **Key Points**
  - Innovative strategies are needed to increase patient consent to randomization in trials
  - Clinical equipoise panels represent one novel approach
  - Equipoise panels preserve the ethics of randomization and provide value added for study participants

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Questions?

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Thank You!

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Panel Discussion

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Summary Remarks: Future of Participation Engagement in Clinical Trials

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Evaluations

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Lunch & Poster Session

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Challenges in Participant Engagement

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Using Research Process Improvement to Solve Recruitment Challenges

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Tufts University School of Medicine
Director, Research Process Improvement Program
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Human Nutrition Research and Center on Aging
Tufts University

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Learning Objectives

- **Delineate components of process improvement**
- **Describe potential applications of process improvement methods to research studies.**
- **Identify process improvement methods useful in addressing participant recruitment.**
- **Identify a process improvement tool that could be used to address a current research challenge.**

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Research Process Improvement Program

- **Build the capacity of researchers to use process improvement methods to resolve the most frequent or important barriers to successful studies**
  - Project start-up
  - Team communication and collaboration
  - Participant recruitment and retention
  - Data collection and analysis
  - Project management

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- **Quality Assurance**
  - monitoring active research protocols to ensure the protection of human subjects
  - confirm that research is conducted in compliance with federal regulations and organizational policies
- **Quality by Design**
  - systematic, prioritized, risk-based approach to trial design, conduct, and monitoring

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Process Improvement Framework

Model for Improvement, Lean Six Sigma, Results Based Accountability

1. **What outcome do we want to achieve?**
2. **How will we know when we reach it?**
3. **How close are we to reaching it?**
4. **What's the story behind our current progress?**
5. **Who are our partners in getting there?**
6. **What actions can we take to do better?**
7. **What do we propose to do next?**

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Question 1.
What outcome do we want to achieve?

Participant recruitment and retention goals:

- Efficiently recruit and retain 20 participants by 6/30/2016
- Remain within recruitment budget of $$

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Question 2.
How will we know when we reach it?

- What measures or metrics are we using?
- Add types of metrics

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Question 3
How close are we to reaching it?

- **What do we know about our current performance?**
- **What was our previous performance in a similar trial?**
- **What is the trend if we do nothing?**

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Question 4
What's the story behind our current progress?

- Who can we ask?
- What information can we collect?
- What process improvement tools can we use?

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Process Improvement Tools

- Process map, flow chart
- Swim lane diagram
- Cause and effect diagram
- 5 Whys

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Question 5
Who are our partners in getting there?

- Who are the obvious people working with us?
- Who needs to champion the actions we take?
- Who are we dependent on to make things work?
- How can we involve other stakeholders in the improvement process?
- How can potential or actual participants help us improve?

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Question 6
What actions can we take to do better?

- What are some no cost, low cost actions we can take today?
- What are some out of the box solutions?

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Question 7
What do we propose to do next?

- What action are we going to take tomorrow
- Who, what, when, where, for how long?
- How will we judge if the action is working?

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Role of MicroRNAs on Age and Contraction-induced Skeletal Muscle Growth

- Objective - determine the mechanistic role(s) of PR-miRs in skeletal adaptation to anabolic stimulation
  - Participants: healthy young, sarcopenic older, and age and functionally matched non-sarcopenic older males and females.

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Role of MicroRNAs on Age and Contraction-induced Skeletal Muscle Growth

- **Recruitment and enrollment of at least 30 participants who will undergo a series of 4 study visits.**
  - **#1 -** medical history and testing to determine eligibility.
  - **#2 -** evaluation of muscle strength to determine the intensity of future exercise for the study
  - **#3 -** baseline muscle biopsy (overnight stay)
  - **#4 -** acute resistance exercise intervention and repeat muscle biopsies.

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MicroRNA Study

1. Outcome we want to achieve:

1. Recruit and retain adequate # of participants
2. Obtain **usable** muscle biopsy samples

2. How will we know when we reach it?

- What will it look like? (measures, experiences, stories)
- Measures related to recruitment (# screened, # eligible, # enrolled) and # who complete study
- Measures about tissue samples (# biopsies with adequate amount and type of tissue, # appropriately handled)

3. What is our current progress in getting there?

- Measures, data
- What was our previous experience with similar studies

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MicroRNA Study

4. What is the story behind our current progress?

- What are the barriers to recruitment and retention?
- What could happen during the biopsy to make the tissue unusable?
- How do we accurately inform participants about length of study visits.

5. Who are our partners/team members in getting there?

- Co-Is, research staff, recruitment staff, patients, stakeholders, nursing staff, lab staff

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MicroRNA Study

6. **What actions can we take to do better? What works?**
   - Identify and be prepared to effectively address participants concerns at pre-screening
   - Make each visit as efficient as possible.
   - Reduce the team learning curve for handling biopsy tissue

7. **What do we propose to do next?**

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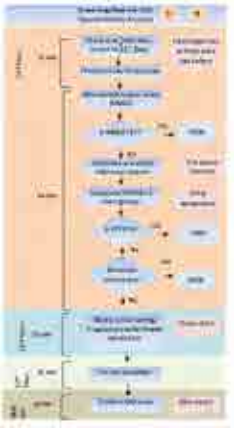
Study Start-Up			Recruitment and Enrollment			Study Visits		
Protocol	IRB	Other Start-up Activities	Pre-screening	Enrollment	Screening visit	Visit #1	Visit #2	Visit #3

- **Process map study visits**
- **Simulate visit for flow and efficiency**
- **Practice assessments and procedures**
- **What changes can we test to improve flow?**



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Metrics

1. Time from first contact to enrollment
2. # telephone screened
3. # screening visits
4. # eligible
5. # declining to participate (reason)
6. # enrolled
7. # completed 4 visits

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Metrics

7. # not completing 4 visits and reason
8. Drop outs/exclusions by visit #
9. Length of time for screening visit
10. Length of time from completion of screening visit to enrollment decision
11. Length of time for visits #1, #2, #3/4
12. Other participant related metrics?

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Potential barriers to recruitment

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Questions?

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Thank You!

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Interactive Group Session: Challenges and Solutions

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Table Exercise

2:30 – 3:15

- **A study team wants to reduce the time from notice of grant award to first patient, first visit. Based on their previous experience, their study start-up and participant recruitment processes and not efficient.**
- **Using the process improvement framework, and your knowledge about the research process, identify actions the team can take.**

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Report Back/Panel Discussion

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Research Process Improvement Services

- Consultation services are currently available to Pilot Award Program awardees, K Scholars, and T awardees and CTSI-housed clinical research services (Clinical and Translational Research Center, CTRC)
- Other information available through ILEARN

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Summary Remarks

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Evaluations

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Tufts Clinical and Translational Science Institute

Translational Research Day 2015:
Innovations in Clinical Trials
Participant Engagement

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