THE RARE DISEASES CLINICAL RESEARCH NETWORK AS A NESTED CULTURAL COMMONS

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- ***Case study applying our Commons framework***
- ***Work-in-progress***

- **IPSC 2008 @ Stanford**

- ***The University as Constructed Cultural Commons*, Wash.U. J. Law & Policy (2009).**

- ***Constructing Commons in the Cultural Environment*, Cornell Law Review (2010)**
  - Special issue dedicated to our article with commentary on the piece from Professors Thrainn Eggertsson, Wendy Gordon, Gregg Macey, Robert Merges, Elinor Ostrom, and Larry Solum, and our Reply to the comments
  - All together, a framework to work with …

- ***Convening Cultural Commons*, NYU School of Law, Sept. 23-24, 2011**
  - major interdisciplinary conference organized around research framework
  - ~ 30 participants, 15 papers including about a dozen case studies, comments on papers …

- ***Commons in the Cultural Environment* (Oxford University Press, forthcoming 2013).**

- **Bio/Medical Research Commons Conference at Pitt (Fall 2013)**
  - Same model: interdisciplinary, case studies + methodology, theory and other related papers
  - another book

- **Other events and conferences in the planning stages**
- **Funding, training, publication outlets, valuing descriptive work …**

Why this research area?
Why did we choose rare disease research?

- Somewhat new territory
- Privacy as a source of demand for boundaries around medical data commons
- **Rare disease research is a reasonably well-defined area / context**
- Nested / networked commons captured our attention

Rare disease research

- Rare diseases
  - <200,000 individuals
  - 5,000 – 8,000 rare diseases
- Rare disease research problems
  - *Small numbers*—research subjects for clinical studies
  - Funding, research protocols, trained researchers
- Commons as a solution?
  - Collaboration, cost-sharing / pooling resources
  - Community → patient recruitment

Our focus

- This case study:
  - Rare Diseases Clinical Research Network (RDCRN)
  - Urea Cycle Disorders Consortium (UCDC)

- Broader project
  - Other consortia, other rare disease research efforts outside RDCRN, PAGs, …

Our approach / methodology

- Use commons research framework (IAD-based) to structure inquiry, frame investigation, formulate sets of related questions (and identify questions we might otherwise ignore), categorize data
- Systematic approach is necessary for case study to meaningfully contribute to generalization and learning about commons

What we have done thus far

- **Literature review, using cultural commons framework to structure observations**
  - identify questions to investigate during interviews
- **Interviewed twelve professionals heavily involved with the UCDC**:

  (Ave. duration ~ 75-85 minutes)
  - Three NIH officials, including the head of ORD and the science officer for the UCDC;
  - Two of the three UCDC principal investigators; (Dr. Batshaw is also a site PI and currently the CMO at Children's National Medical Center);
  - UCDC Coordinator;
  - Site coordinator at Children's National Medical Center;
  - Neuropyschologist at Children's National Medical Center;
  - Lead attorney;
  - Pediatrician-researcher who is the PI at Children's Hospital, Philadelphia, PA;
  - Pediatrician-researcher who is the PI at the EMID site in Zurich; and
  - Director of Orphan Europe, a pharma company involved with UCD.
- **Attended a two-day conference**, one day focused on research and one day sponsored by the PAG involved researchers, medical professionals, patients, and families. We observed, took notes, met people, and had a few interviews.

What's next …

- **5-10 additional interviews**
- **A detailed questionnaire (email interview) for researchers and site coordinators we are not able to interview, and**
- **Possibly, short (~ 20 question) surveys as follow-ups**

1. to confirm or test hypotheses or observations from interviews
2. to dig a little deeper on certain observations

– E.g., leadership and collegiality ranked in all interviews as top two factors that influence success of UCDC

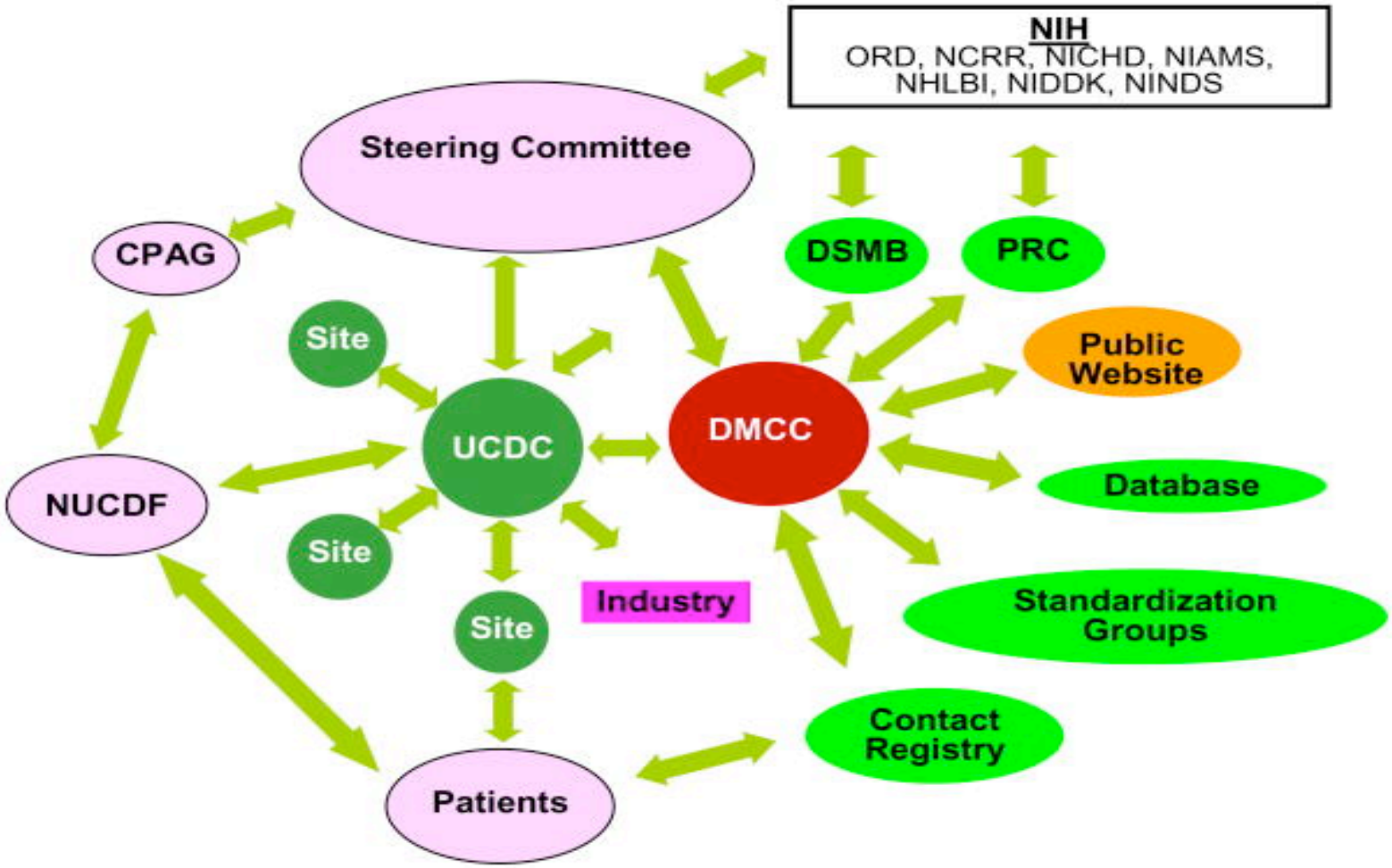
– Would be nice to confirm this with a survey instrument that reached a broader audience

– Also, would be nice to get more details about leadership characteristics or sources of collegiality

- **Once we have digested all of the interview notes!**

Background and Structure

- Many relevant background contexts to keep in mind
  - Nested commons—c.f., universities
- Complex relationships between NIH, research consortia, various communities (e.g., patients, health care)



Urea Cycle Disorders Consortium (UCDC) within the context of the Rare Diseases Clinical Research Network (RDCRN); DSMB-data safety and monitoring board; PRC-protocol review committee; CPAG-patient advocacy group; NUCDF-National Urea Cycle Disorders Foundation; DMCC-data monitoring and coordinating center.

Seminara et al (2010)

Hierarchy - levels

1. NIH
2. RDCRN, CPAG, DMCC, others
3. Rare disease research consortia
4. (i) research sites, (ii) patient advocacy groups, and (iii) professional health care communities.
5. Patients, families, … public

Resources

- Level 2 – shared across consortia (DMCC)
  - *Patient registry*
  - *Informatics protocols, standards and data management practices*
  - *Secure web-based platforms for data collection*
  - *Communications platform*
  - *Conferences – shared experiences, knowledge, etc.*
  - *Research methods and protocols tailored to the acute problems of rare disease research*

Resources

- Level 2 – shared across consortia (DMCC)
  - *Patient registry (not really)*
  - *Informatics protocols, standards and data management practices (to an extent, but mainly via DMCC itself)*
  - *Secure web-based platforms for data collection (available, but not effective for UCDC*)*
  - *Communications platform*
  - *Conferences – shared experiences, knowledge, etc. (yes, and monthly conference calls)*
  - *Research methods and protocols tailored to the acute problems of rare disease research (possibly, but may be untapped potential)*

Resources

- Level 3 – shared within specific RDR community
  - Research Subject Registries
  - Research participants (patients)
  - Research Methodology, including Tacit Knowledge
  - Longitudinal Study
  - Data and biological materials relevant to or produced by ongoing clinical research studies
  - Information to support the design of future clinical trials
  - Information about the results of completed clinical studies
  - Authorship credit
  - Information about ongoing clinical studies and experimental treatments for potential participants
  - Diagnostic tools
  - Educational materials
  - Information about support groups, coping, and experiences of others
  - Funding

Participants and Roles

- Rare Disease Researchers
- Information Technology and Informatics Specialists and Researchers
- Treating Physicians / Health Care Personnel
- Patients and Families
- Patient Advocacy Groups

Goals and Objectives

- Collaborative clinical research in rare diseases, including longitudinal studies of individuals with rare diseases, clinical studies and/or phase I , II and II/III trials;
- Training of investigators in clinical research of rare diseases;
- Pilot/demonstration projects; and
- Access to information related to rare diseases for basic and clinical researchers, academic and practicing physicians, patients, and the lay public. (Website resource for education and research in rare diseases)

Goals and Objectives

- Looks to us like the central goal is:

Patient recruitment

  - Seems to have implications for analysis / evaluation of institutional design
    - Building trust relationships is key
    - Privacy protection is important
    - PAGs and health care providers play role

Goals and Objectives

- Looks to us like the central goal is:

Patient recruitment

- **It is. But it is part of the collaborative research project.**
  - Genuine connection to PAG, patients, and families; could see it strongly when they were together at the PAG reception and during the conference.
  - Parents were incredibly knowledgeable about the science and ongoing research

Openness

- Closed to nonmembers
- 19 out of thousands
- Not clear from public documents if data is shared within research consortia
  - Interviews suggest that data is openly shared among researchers and other members of consortia; some (minor) gatekeeping;
  - also, accessible to outsiders, such as outside metabolic researchers or even pharma, with approval …

Activities and Governance

- Not much detailed info is publicly available
- Need to dig deeper
- Host of issues where potential conflict can arise (e.g., publication credit)

Activities and Governance

- Many interesting interview discussions
  - Informal
  - Consensus based voting, except sometimes majority -- no written rules
  - Hierarchical
  - Many decisions made by Executive Committee, but some just by head PI (even if formally there is a vote)
  - Conflict resolution
    - Informal, personal, negotiation
    - *Ask about conflicts and interviewee sits back in chair**

Outcomes / Evaluation

- Metrics?
  - Development of new treatments
  - Accelerated research results
  - Improved recruitment of patients for clinical studies
  - Improved infrastructure and methodology for rare disease research

Outcomes / Evaluation

- Metrics?
  - Development of new treatments
    - Pharma interest / activity
    - 1 is better than 0
  - Accelerated research results
  - Improved recruitment of patients for clinical studies
  - Improved infrastructure and methodology for rare disease research

Additional questions

- Selection of Winners?
  - What is the relationship with thousands of other rare diseases?
- Experiment in institutional design?
  - According to NIH official, yes
- Development of shared infrastructure for (rare) disease research? Possibly
- Relevance to (1) future of pharma industry & personalized medicine, and (2) treatments for subjects with very rare genetic disorders potentially useful for population with not so rare genes who suffer similar disorders / symptoms when in stressed environment (e.g., during surgery)

Personal Note

- Case study research is difficult; it requires attention to methodology and a willingness to (re)learn how to do research, to work with folks in other disciplines, to deal with IRB, …

- But it is really fun and interesting.