

*William Coon Memorial Lecture*

## Making Informed Consent Count

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### Overview

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- ▣ The evolution of informed consent
- ▣ Informed consent as a process
- ▣ Evidence about informed consent and moving towards improvement

### The Evolution of Consent

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For Medical Treatment

- ▣ Patient litigation
- ▣ Laws and regulations

For Research

- ▣ Early consent practices
- ▣ Infamous research

### Medical Treatment and The Right to Liberty

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“Every human being of adult years and sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patient’s consent commits an assault for which he is liable in damages.”

*Schloendorff*

### Important Cases Refining the Doctrine

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“to disclose and explain to the patient in language as simple as necessary the nature of the ailment, the nature of the proposed treatment, the probability of success or of alternatives, and perhaps the risk of unfortunate results and unforeseen conditions within the body.”

*Natanson v. Kline*

### Important Cases Refining the Doctrine

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“[T]he patient’s right of self decision shapes the boundaries of the duty to reveal. That right can be effectively exercised only if the patient possesses enough information to enable an intelligent choice.”

*Canterbury v. Spence*

### Early Consent Practices for Research

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- ❑ Sometimes recognized as important for research with volunteers
  - Not necessarily free and voluntary
  - Lack of consent central to the problems in a litany of infamous experiments
- ❑ Not typically recognized as relevant for patients enrolled in research

### Two Senses of Consent

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- ❑ Autonomous authorization
- ❑ Social rules of consent

### Autonomous Authorization

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- ❑ Arises from a littered history
- ❑ Respect for persons/autonomy
- ❑ Liberty interests

### Social Rules

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- ❑ Consent of minors
- ❑ Special forms
- ❑ Witnesses

### The Process of Informed Consent

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- ❑ Threshold
- ❑ Information
- ❑ Consent

### Threshold

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- ❑ Decision making capacity
- ❑ Voluntariness

## Information

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- Disclosure
- Understanding

## Content of Disclosure

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- Nature of the proposed intervention
- Procedures and alternatives
- Potential risks and benefits
- Assurance that participation is voluntary
- Protection of confidentiality

## Information

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- Disclosure
- Understanding

## Authorization

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- An indication of agreement
- Consent forms
  - Consistent with disclosure
  - Readable

## An Empirical Imperative

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- Clinical research is predicated on the notion that we need data to determine 'truth' and facilitate sound decision-making
- Ironically, methods of clinical research, including those designed to protect participants such as informed consent, are introduced without data regarding safety or efficacy
- Where relevant we need to evaluate these protections as we would any proposed clinical intervention

## Recent and Current Efforts

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- Reviewing the literature
- **ACHRE SIS (Subject Interview Study)**
- Umbilical cord blood donation
- Early phase trials in oncology
- Proxy and research on dementia
- COINS (Conflict of Interest Notification Study)
- **EQUIC**

### Advisory Committee on Human Radiation Experiments

- Uncover the history of human radiation experiments between 1944 and 1974
- Examine cases of released radiation into the environment for research purposes
- Identify the ethical and scientific standards for evaluating these events
- Make recommendations to ensure that whatever wrongdoing may have occurred in the past cannot be repeated

### ACHRE's Empirical Projects

- Review federal agency policies
- Examine contemporary research documents and consent forms
- Interview patients receiving out-patient medical care about their understanding of and attitudes towards medical research

### Methods

- Part 1: Brief Survey
  - Interviewed 1,882 patients
  - From medical oncology, cardiology, and radiation oncology waiting rooms
  - Included 16 hospitals and 5 cities around the U.S.
  - To determine beliefs and attitudes about medical research and to ask if they were, or ever had been, participants in medical research
  - Paid \$5.00

### Methods

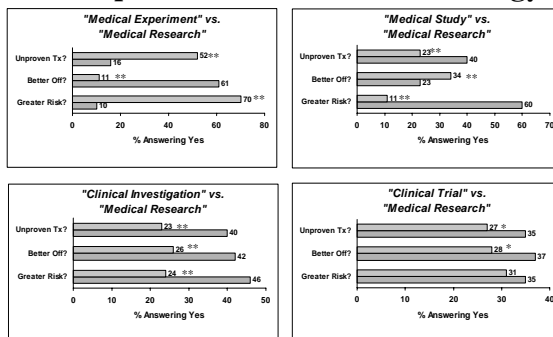
- Part 2: In-Depth Interview
  - Interviewed 103 patients
  - All reported in Brief Survey that they were or had been in medical research
  - To determine reasons for joining research and to describe their research experiences
  - Paid \$25.00

### Demographic Characteristics

(N=1,882; Response Rate=94.7%)

Age > 59	53%
White	80%
African American	16%
Education	
High School Graduates	54%
College Graduates	25%

### How do patients understand terminology?



Slide courtesy of Dan Nelson

N= 470, Sugarman, et al, IRB 20:1-7, 1998

### EQUIC Goals

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- ❑ Create, field test, and validate an independent, real-time measure of the quality of informed consent encounters in actual clinical trials
- ❑ Develop specific interventions directed at improving the quality of informed consent
- ❑ Test interventions in CSP trials

### Expert Advisory Committee

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- ❑ Membership
  - Paul Appelbaum, MD
  - Marguerite Hayes, MD
  - Robert Pearlman, MD, MPH
- ❑ Findings
  - Independent measurement
  - Results confidential
  - Evaluate IC process and not experience
  - Not-interfere with research process
  - Minimal burden
  - Practical and simple

### EQUIC-Development Phase

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- ❑ Telephone interview after "parent" study consent
- ❑ Brief Informed Consent Evaluation Protocol (BICEP)
- ❑ Substrate for subsequent EQUIC studies

### EQUIC-DP Research Team

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- ❑ Maryann Boeger, MBA - Program Manager
- ❑ Andres Busette - Research Health Scientist
- ❑ Carole Cain, PhD – Interviewer
- ❑ Eric Crawford - Interviewer
- ❑ Robert Edson, MS – Statistician
- ❑ Madhulika Gupta, MS – Interviewer
- ❑ Phil Lavori, PhD – Co-Principal Investigator
- ❑ Patrick Nisco, MA- Interviewer
- ❑ Lee Pickett, MS – Interviewer
- ❑ Jeremy Sugarman, MD – Co-Principal Investigator
- ❑ Carmen Tumialan-Lynas, MS - Interviewer

### EQUIC-DP Parent Studies

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- |             |                  |
|-------------|------------------|
| 1. CSP 027  | FDG PET          |
| 2. CSP 403  | Shingles Vaccine |
| 3. CSP 410  | FeAST            |
| 4. CSP 424  | COURAGE          |
| 5. CSP 453  | HOST             |
| 6. CSP 494  | PTSD and Women   |
| 7. CSP 499  | SELECT           |
| 8. CSP 719B | Latent Prostate  |

### EQUIC-DP Participating Sites

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<b>Site</b>	<b>Study</b>	<b>Site</b>	<b>Study</b>
Ann Arbor, MI	CSP 424	Melbourne, FL	CSP 424
Birmingham, AL	CSP 403	Minneapolis, MN	CSP 403
Buffalo, NY	CSP 027	Northport, NY	CSP 403
Durham, NC	CSP 424	Northport, NY	CSP 499
Houston, TX	CSP 410	Northport, NY	CSP 719B
Houston, TX	CSP 424	Reno, NV	CSP 410
Indianapolis, IN	CSP 027	Seattle, WA	CSP 424
Lexington, KY	CSP 410	St. Louis, MO	CSP 499
Mayo Clinic	CSP 424	St. Louis, MO	CSP 719B

**13 VAMCs; 1 non-VAMC**

### EQUIC-DP Enrollment

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- Total: 632 interviews completed
- BICEP-1
  - 441 completed
  - 8/21/00-7/31/01
- BICEP-2
  - 191 completed
  - 8/1/01-7/2/02

### EQUIC-DP

#### Site Coordinators' Reports

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- 100% patient willingness to participate
- 98.9% "no difficulty with process"
- 99.5% "no difficulty with call"
- 95.4% "no difficulty reaching center"
- 98.4% "no interruption of clinic flow"
- 99.2% "no other difficulties"

### Degree of Disruption of Parent Study

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- None 66.3%
- Mild 32.8
- Moderate 1
- Severe 0

### Incremental Burden

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- Site coordinators
  - mean 14.2 min (std dev 9.6)
- Participants
  - mean 10.9 min (std dev 7.8)

### Mean Timing of Interviews

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- Completion of parent study IC and EQUIC IC: 19.8m (sd 28.0)
- EQUIC IC and call initiation: 8.4m (sd 11.7)
- Duration of call: 8.8m (sd 3.6)
- Interview length: 7.7m (sd 2.9)

### Respondents' Reports about Parent Study IC Process

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- 95.1% received "just right" amount of information
- 99.3% remember signing consent form
- 99.8% "felt no pressure to consent"
- 98.4% "made a good decision to participate"
- 89.1% "completely satisfied with the IC process"

### Taking a Deeper Look

- Verbatim responses to selected items
  - What is the primary purpose of the [parent study]?
  - When can you stop participating in the [parent study]?
- Coding developed and refined during BICEP-1

### “What is the primary purpose of [parent study]?” (n=191)

<u>Code</u>	<u>Percent</u>
Addresses a research question?	80
Directed at an outcome to ultimately benefit others?	59
Directed at an outcome to ultimately benefit self?	6
Other?	1

### “When can you stop participating in the [Parent Study]”

<u>Code for clear appreciation of voluntariness</u>	<u>Percent</u>
Yes	55
No	45

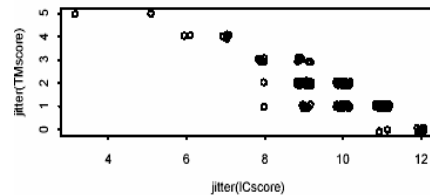
### IC Aggregate Score (Mean=9.8; sd=1.29)

- | <u>Positive</u>             | <u>Negative</u>                         |
|-----------------------------|---|
| □ All information needed    | □ Pressure to participate               |
| □ Sign form                 | □ Not participating affect medical care |
| □ Aspirational benefit      | □ Direct benefit                        |
| □ Satisfaction              | □ Ultimately benefit self               |
| □ Address research question | □ Uncertainty about signing form        |
| □ Ultimately benefit others |   |
| □ Voluntariness             |   |

### TM Aggregate Score (Mean 1.62; SD=.93)

- | <u>Positive</u>           | <u>Negative</u>                 |
|---------------------------|---------------------------------|
| □ Direct benefit          | □ Aspirational benefit          |
| □ Ultimately benefit self | □ Addresses a research question |
|                           | □ Ultimately benefit others     |

### IC vs TM Score



### Lessons

- ▣ BICEP is well-tolerated, by participants and staff
- ▣ BICEP imposes minimal burden
- ▣ Patients who consent are uniformly satisfied with the process, but inspection of verbatims reveals considerable room for improvement, especially in the “therapeutic misconception”
- ▣ Innovations have scope to work

### EQUIC-SM

- ▣ Aim to develop and test the effectiveness of a self-monitoring “check-list” (the SMQ) to be used by the person obtaining informed consent
- ▣ Assumes that persons obtaining informed consent have sufficient knowledge, interest and ability to obtain meaningful informed consent, but that in the context of a busy clinical environment the process or parts of it may be treated superficially

### Hypothesis

- ▣ The use of an explicit approach to self-monitoring will focus the attention of the person obtaining consent, and prompt them to attend to each aspect of the informed consent process in greater detail and thereby improve the quality of informed consent

### Methods

- ▣ Parent studies recruited
- ▣ Sites recruited and cluster randomized to Control or Experimental arm (SMQ)
- ▣ Following informed consent for the parent trial, participants asked for oral consent to complete the BICEP
- ▣ Interviewers were masked with respect to site assignment
- ▣ Person obtaining consent in the Experimental arm completes the SMQ and faxed it to the coordinating center

### Respondents

- ▣ 943/1049 agreed to participate
- ▣ 83-100% agreement rates across studies
- ▣ 938 BICEP interviews completed

### Parent Studies, Sites and Assignment

Study/Site	CTL	SMQ
DITPA/Cleveland	0	4
Host/Boston	9	0
Host/Northport	0	2
RadArt/Birmingham	0	9
RadArt/Houston	0	9
RadArt/Little Rock	17	0
RadArt/Minneapolis	0	10
SEL/Boston	112	0
SEL/Central Baptist	0	18
SEL/Hines	0	38
SEL/Kansas City	68	0
SEL/LomaLinda	42	0
SEL/Minneapolis	114	0
SEL/Northport	0	1
Smoke/New Orleans	2	0
ThINRS/Bufalo	50	0
ThINRS/Denver	0	28

Study/Site	CTL	SMQ
ThINRS/Detroit	0	7
ThINRS/Durham	0	40
ThINRS/Kansas City	25	0
ThINRS/Loma Linda	0	66
ThINRS/Palo Alto	38	0
ThINRS/Syracuse	69	0
ThINRS/West Haven	0	43
ThINRS/West LA	7	0
WPTSD/Albuquerque	0	15
WPTSD/Atlanta	0	27
WPTSD/Baltimore	10	0
WPTSD/Boston	20	0
WPTSD/Cincinnati	5	0
WPTSD/Dallas	0	15
WPTSD/New Orleans	18	0

### Data Reduction

- Exclusion of data from late entering parent studies (N=2) and non-randomized arm of 1 parent study excluded leaving
  - 836 participants
  - 5 parent studies
- 15 Control Sites/15 SMQ sites
  - CTL (508, 61%) and SMQ (328, 39%)

### Compliance

- 302/328 completed SMQs
- 92.1% overall compliance
- Range 84% to 100% over parent studies

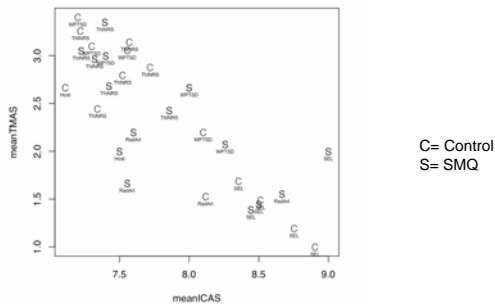
### Summary Scores

- Mean ICAS score was 7.9 (out of a possible 10)
  - 11% had a 'perfect' score
  - 16% had a score of 6 or less
- Mean TMAS mean was 2.2 out of a maximum (worst) score of 5
  - 15% had a 4 or 5, indicating a substantial degree of therapeutic misconception
- Correlation of the two scores is -0.8

### Results

- Mixed effect analysis reveals a non-significant (and near zero) negative effect of SMQ on the ICAS (P=0.73, effect= -0.034, std err= 0.099) and TMAS (P=0.97, effect = -.005, std err = 0.137) after adjusting for parent study and including a random effect for site.
- The permutation test shows a total P-value=0.89 for the observed -0.04 ICAS effect (0.49 in the left tail and 0.40 in the right) and a total P-value=0.91 for the observed TMAS score of 0.04 (0.39 in the left tail and 0.52 in the right).

Mean TMAS and ICAS Scores  
(by site and parent study name)



### Discussion

- Sample too heterogeneous?
- Underpowered?
- Invalid or unreliable measures?

## Implications

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- ❑ There is room for improvement in the quality of consent
- ❑ It is possible to field randomized trials of informed consent
- ❑ Not all interventions, however plausible, are effective underscoring the need to for empirical testing of approaches

## Concluding Comments

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- ❑ To do the ethical work assumed in regulations and guidelines, informed consent must be considered as a process that goes well beyond completing consent documents
- ❑ Efforts directed at enhancing informed consent need to be evaluated rigorously
- ❑ Similar empirical work should be directed at other procedures and processes employed in the research enterprise to help ensure that we meet the promise of ethical principles to protect the rights and interest of research participants

## Bibliography

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- ❑ Lavori PW, Sugarman J, Hays MT, Feussner JR. Improving informed consent in clinical trials: a duty to experiment. *Controlled Clinical Trials* 1999; 20:187-193.
- ❑ Sugarman J, Kass NE, Goodman SN, Perentesis P, Fernandes P, Faden RR. What patients say about medical research. *IRB* 1998;20: 1-7.
- ❑ Sugarman J, Lavori PW, Boeger M, Cain C, Edson R, Morrison V, Yeh SS. Evaluating the quality of informed consent. *Clinical Trials* 2005; 2:1-8.
- ❑ Lavori P, Wilt T, Sugarman J. Quality assurance questionnaire for professionals fails to improve the quality of informed consent. *Clin Trials* 2007; 4: 638-649.