Encouraging Comparative Effectiveness Research While Protecting Privacy: Can We Develop A Research Safe Harbor for CER?

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Outline

- The promise of comparative effectiveness and other information-based research: Doug Peddicord
- How HIPAA and the Common Rule regulate the use of health information : Doug Peddicord
- The impact of HIPAA and Common Rule restrictions (practices) on health information use by research and other health care organizations : Tina Grande
- The view from the IRB: Felix Gyi
- Proposing a new framework (a Safe Harbor) for CER and other health information-based research: Ann Waldo

ACRO
ASSOCIATION OF CLINICAL RESEARCH ORGANIZATIONS

Doug Peddicord, Ph.D.
Executive Director

Comparative Effectiveness Research (CER)

A non-profit Patient-Centered Outcomes Research Institute is tasked to spur studies that determine which drugs, devices, and medical procedures work best

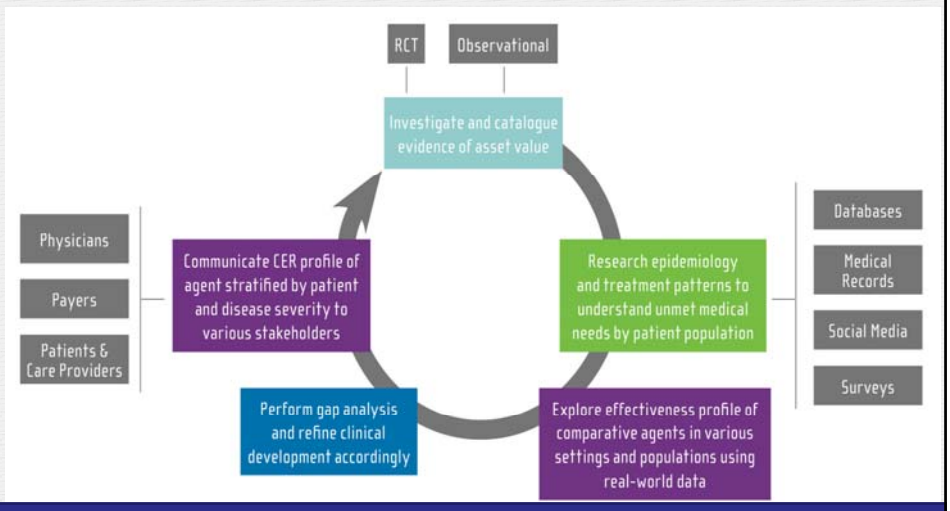
The Institute will be in charge of setting a national agenda for the studies, as well as providing more money and disseminating results

- The organization will be run by a 19-member board of governors with three representatives of drug, device and diagnostic- testing companies as well as patient advocates, doctors and the National Institutes of Health

The $500 million annual funding in the health care reform law builds upon the $1.1 billion approved by Congress previously for comparative effectiveness research

Source: Bloomberg. *Health Law Surprise Is Page 1,617 Demanding Which Drugs Work*, March 2010

The Vision: A CER Evidence Development Cycle



An 'EBM' ecosystem is supported by data and analytics to transform raw healthcare data into analytic tools, services and insights to guide care decisions

So where will the data for CER come from?

- Randomized clinical trials (RCT) – small data sets [identifiable data, informed consent]
- Observational studies - e.g., registries, large simple trials - large data sets [identifiable data, informed consent]
- Medical records - paper, EHRs, PHRs – very large data sets [identifiable and not, with and without consent]
- Claims and other payer systems - hospital, physician, pharmacy – very large data sets [identifiable and not, with and without consent]
- Physician reported – [identifiable and not, with and without consent]
- Patient reported – [identifiable or not]
- Consumer reported – [identifiable or not]
- Surveys and other – [identifiable or not]

What rules govern the use of health information for research purposes?

- HIPAA – 45 CFR part 164
- The Common Rule – 45 CFR part 46

How Does HIPAA Define Health Data?

- **Health Information**: any information… that "relates to the past, present or future physical or mental health or condition of an individual"….
- **Individually Identifiable Health Information**: a subset of health information, including demographic information, that identifies the individual or with respect to which there is a reasonable basis to believe the information can be used to identify the individual… when transmitted or maintained electronically or in any other form this individually identifiable info is **protected health information** (PHI)
- A **limited data set** removes direct identifiers, prohibits re-identification and is used for public health or research (and, though less than fully identifiable, is still considered PHI)
- **De-identified** data is at "very small" risk of being re-identified (safe harbor and statistician methods) and may be freely used for research or other purposes without regard to the requirements of HIPAA

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And what does the Common Rule say ?

- At 46.102 – A human subject means a living individual about whom an investigator… conducting research obtains data through intervention or interaction with the individual… or **identifiable private information.** The section goes on to say, **Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects**
- In outlining certain exemptions from research subject to IRB review under the Common Rule, Section 46.101 stipulates an exemption **if the information** [about the subject] **is recorded by the investigator in such a manner that subjects cannot be identified directly or through identifiers linked to the subjects**

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More On The Common Rule

- In the criteria for IRB approval of research at 46.111 (7) the Rule notes that **When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data**
- So, that's pretty much what the Common Rule has to say about privacy: that the **subject has to be readily identifiable or can be linked to through identifiers and that there are adequate provisions to protect privacy**.

Use of PHI/identifiable information for Research

- Both the Common Rule and the HIPAA Privacy Rule permit the use and disclosure of PHI/identifiable health information for research -
  - with individual authorization, **or**
  - without individual authorization, under limited circumstances

Research Use and/or Disclosure of PHI with HIPAA Authorization

- Authorization signed by the individual required for:
  - ➢ research by a covered entity that creates or receives 'new' PHI - e.g., clinical trials
  - ➢ research that creates or receives existing PHI - e.g., medical records research (unless IRB or Privacy Board waiver obtained)

Research With Patient Consent

Common Rule	Privacy Rule
↓	↓
IRB review/ Informed Consent	Patient Authorization

Research Use/Disclosure of PHI /identifiable Information *Without* Individual Consent

- Obtain IRB (or Privacy Board) waiver
- Obtain representation from researcher that use/disclosure is solely for research on PHI of decedents [HIPAA]
- Use a "limited data set" that does not include 'direct' identifiers, with a "data use agreement" that prohibits re-identification of or attempts to contact individuals [HIPAA]
- Obtain representation that use/disclosure is necessary to prepare a research protocol or similar purposes *preparatory* to research, with provision that PHI may not be removed from the entity [HIPAA]
- Disclose information "for the purpose of activities related to the quality, safety or effectiveness of" FDA-regulated products [HIPAA]

Research Use of PHI/Identifiable Health Information Without Patient Permission

Common Rule	Privacy Rule
IRB review *(4 waiver criteria)* •no more than minimal risk •will not adversely affect rights and welfare • could not practicably be carried out • information provided afterward if possible	• IRB/Privacy Board Review *(3 waiver criteria)* • decedents • limited data set • preparatory to research

For CER and other information-based research

- Informed Consent (HIPAA Authorization) may be expensive, time-consuming and impracticable for **non-interventional** research that accesses very large data sets to compare treatments, assess quality, etc.
- But mechanisms – e.g., IRB and Privacy Board waivers; use of limited data sets and de-identified data – for obviating individual consent seem to be in place….
- So, **what is in the way** of CER and other information-based research… and **how might we solve the problem?**

HEALTHCARE LEADERSHIP COUNCIL

Tina Olson Grande, MHS
Senior Vice President for Policy

Translating Policy into Practice: How does HIPAA affect research in the real world?

Healthcare Leadership Council

Multi-sector association of hospitals, pharmaceutical companies, university medical centers, health plans, medical device manufacturers, and others

HLC members highlighted in information-based research:

Mayo Clinic
New-York Presbyterian Hospital
Marshfield Clinic
Cleveland Clinic

Translating Policy into Practice: How does HIPAA affect research in the real world?

Overarching concerns regarding regulatory restrictions include:

- Misinterpretation of HIPAA (over-interpretation)
- Patient/subject recruitment
- Administrative burden

- *State privacy laws*

Translating Policy into Practice: Mayo Clinic

Rochester Epidemiology Project (REP)

- Began in 1966
- Unique data resource that allows investigators to conduct long-term population-based studies of disease incidence, prevalence, risk and protective factors, outcomes, health services utilization, and cost effectiveness
- Each medical care site that participates in the REP solicits and documents permission from individual patients for their records to be used in research
→Currently, 95% of patients have granted research permission

Translating Policy into Practice: Mayo Clinic – *cont'd*

HIPAA Authorization Form (HAF) Study

- Surveys play key role in health research
- Authorization form required by HIPAA to use and disclose protected patient information
- Study evaluated the effects of including a HAF on multiple measures of survey performance
  -Half of participants received survey + HAF; other half, no HAF
- Elements of HAF that adversely affect willingness to participate in health surveys:
  1) Erroneous belief that signing the form means respondents' PHI will no longer be protected
  2) Many HAFs require participants' signatures, which negatively affects willingness to participate
-

Translating Policy into Practice: Mayo Clinic – *cont'd*

HIPAA Authorization Form (HAF) Study

→RESULTS: The inclusion of a minimally burdensome version of the HAF (1 page) reduced survey response rates by up to 15% points – statistically significant

- Loss of sample size decreases relative precision of estimates
- Loss in statistical power translates to more expensive survey protocols to achieve necessary confidence levels
- Administrative and cost burdens to administer HAFs

Translating Policy into Practice: New-York Presbyterian Hospital

- **Increasing costs of research**
  -Hiring consultants/lawyers
  -Added layers of personnel
  -Costs related to overregulation
  -Security safeguards

- **Knowledge gap**
  -Researchers are not privacy and security experts
  -Consequences of mishandling information / breach risks
  -Paralyzes research – "We are mortally afraid"

Translating Policy into Practice: New-York Presbyterian Hospital – *cont'd*

- **Misinterpretation of HIPAA**
- **Information restrictions**
  -Privacy and security rules so strict, "researchers [can't] even get to the data"

→**END RESULT: Disincentives for researchers;** moving away from research-related sensitive data

Translating Policy into Practice: Marshfield Clinic

- **Screening for eligible research subjects**
  -Preparatory to research problems
  -Research support staff limitations
- **Authorization for future research**
  -Example: Personalized Medicine Research Project
  -Subsequent contact raises concerns among patients
  Result: Seek authorization waivers from IRB
- **Accounting of Disclosures**
  -Applies to all research; have to track any disclosure per HIPAA
  -Cost and administrative burden

→**END RESULT: Researchers have quit because of obstacles posed by HIPAA;** deterrent to clinicians who might otherwise be interested in research

Translating Policy into Practice: Cleveland Clinic

- **Long-term follow-up**
  -Can't anonymize data if planning to conduct long-term patient follow-up
- **Data sharing restrictions**
  -Can't share data across institutions; continual loss of data as time goes on
- **Comparative Effectiveness Research (CER)**
  -Need for prospective data
- **Patient Recruitment**
- **Transparency**
  Example: 97% of patients agreed to their tissue samples being used. "It's OK if you [use my data], but I want to know."

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Translating Policy into Practice: The Big Picture

- The value of health data
- Payment and delivery system reform
- Electronic healthcare infrastructure

"*Health care data represent a precious resource that must be used to the fullest possible extent to promote the public health, while the rights of patients and consumers are protected.*"

Developing the Sentinel System — A National Resource for Evidence Development
N Engl J Med 2011; 364:498-499
February 2011

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IRB Services • Consultation • Education

Felix Khin-Maung-Gyi, PharmD, MBA, CIP, RAC
Chief Executive Officer

Comparative Effectiveness Research:

- The IRB's role in balancing society's mandate to protect rights and welfare of research subjects while advancing science

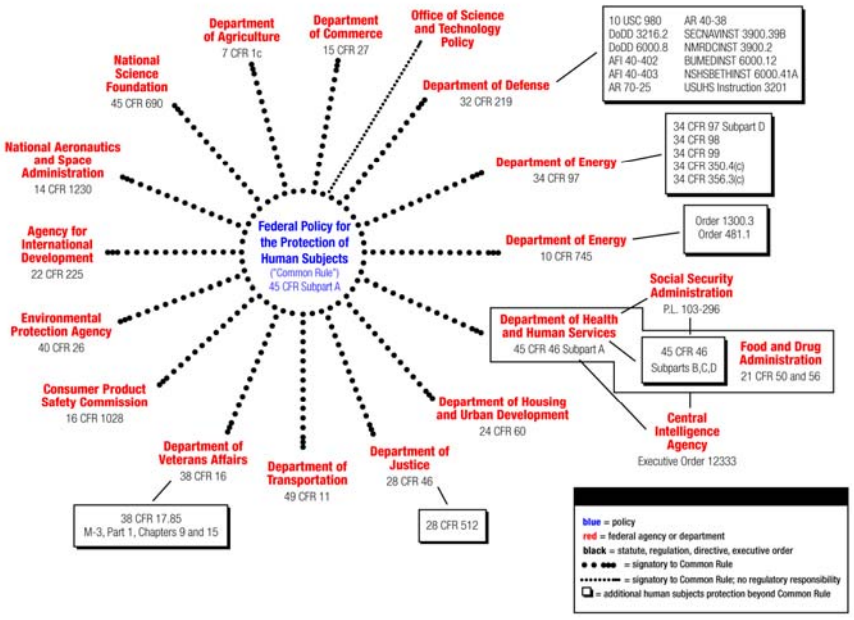
"As science speeds ahead, it often pushes the edges of society's readiness to cope with its consequences. Increasingly, **research creates possibilities before the accompanying ethical…ramifications have been resolved**."

Editor
"Science on the Ethical Frontier" series
Washington (DC, USA) Post, 1998 – 1999

Briefly

- Why do IRB's behave in a hyper-reactive manner today?
- How did we get here?
- Do we need to impose additional barriers to conducting research that are good and worthwhile for society?

Current Federal Regulatory Structure



What is the regulatory "scope" of the IRB?

- **§56.101 Scope.**

  (a) This part contains the general standards for the composition, operation, and responsibility of an Institutional Review Board (IRB) that reviews clinical investigations regulated by the Food and Drug Administration under sections 505(i) and 520(g) of the act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration, including foods, including dietary supplements, that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. Compliance with this part is intended to protect the rights and welfare of human subjects involved in such investigations.

How do we define "research?"

- 45 CFR 46.102(d) *Research* means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

Criteria for IRB Approval

(56) 46.111 -

- "risks to subject are minimized"
- "risks to subject are reasonable in relation to anticipated benefits, if any, to subject…"
- "selection of subjects is equitable"
- "IC will be sought for each prospective subject or legal representative"
- "IC will be appropriately documented"
- "…research plan makes adequate provisions for monitoring"
- "…there are adequate provisions to protect the privacy of subject and to maintain the confidentiality of data"
- "when some or all subjects, are likely to be vulnerable to coercion or undue influence additional safeguards have been included in the study…"

IRB Mission Statement

…to review, to approve…to conduct periodic review of, biomedical research involving human subjects…primary purpose of such review is to assure the protection of the rights and welfare of human subjects…

21 CFR 56.102g
E-6 ICH 1.31
45 CFR 46

IRB Mission Statement (cont)

An IRB shall conduct continuing review of research covered by these regulations at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research.

21 CFR 56.109 (f)
E-6 ICH 3.1.4
45 CFR 46.109 (e)

Belmont Report
April 18, 1979

Basic Ethical Principles

- **Respect for Persons → Consent**
- **Beneficence → Risk:Benefit**
- **Justice → Subject Selection**

www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm

Clinical "Practice"

The term "practice" refers to interventions that are designed solely to enhance the well being of an individual patient or client to have a reasonable expectation of success.

The purpose of medical and behavioral practice is to provide diagnosis, preventative treatment or therapy to particular individuals.

The Belmont Report

Clinical "Research"

The term "research" designates an activity designed to test a hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles and statements of relationships).

Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.

The Belmont Report

Historical Perspective: On the Way to Belmont

- 1900 Walter Reed
- 1902 "The Jungle" Upton Sinclair
- 1906 Pure Food and Drug Act (misbranding)
- 1934 FDA Set up as separate Agency
- 1937 Elixir Sulfanilamide
- 1938 Federal Food, Drug and Cosmetic Act
- **1946 Nuremberg Trial ('47 Code)**
- 1953 Wichita Jury Study
- 1960 Thalidomide
- 1962 K-H Amendment to 1938 FDC Act
- 1962 FDA Informed Consent

Historical Perspective: On the Way to Belmont (cont)

- 1963 Sloan Kettering/Jewish Chronic Disease Hospital
- 1964 Director of NIH Memo to Study Issues
- 1963 CGMP Part 211
- 1963 Yale study "…obedience & disobedience to authority"
- **1964 Declaration of Helsinki**
- **1966 Henry Beecher/NEJM Article**
- 1966 All PHS Funded Studies Must Be Reviewed
- **1972 Publicity of Tuskegee Experiment**
- National Research Act of 1974 Established IRBs
- **1979 Belmont Report**

Those who cannot remember the past

are condemned to repeat it.

George Santayana

Today after Belmont

- 1989 ASU Research with Havasupai
- 2006 Theft of VA laptop with identifiable information
- 2010 revelation of (1946) syphilis, gonorrhea, and chancroid research in Guatemala

What can we do today to accommodate CER?

- Does CER qualify as human subjects research?
- Is CER research a “clinical investigation?”
- Can we accommodate CER under an “exempt” criteria?

WITTIE, LETSCHE & WALDO LLP

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Do We Need A New Privacy Framework For Information-Based Research?

- Comparative Effectiveness Research has huge potential to advance medical breakthroughs, increase efficiency, and help patients
- BUT … serious privacy impediments exist
  - Existing barriers
  - Possible new barriers
- *Could we create a new privacy framework with:*
  - Ill-advised burdens eliminated
  - Meaningful and cost-effective protections for data
  - A clear and enduring regulatory Safe Harbor that encourages research

The HITECH (Post-HIPAA) Environment

- Heightened enforcement
- Punitive, judgmental atmosphere – regulators, patients, plaintiffs' lawyers
- Data breach liability and costs
- De-identification scrutiny
- Ban on sale of Protected Health Information (PHI)
  - Very narrow research exception

Type of Data	HIPAA Requirements for Research Use
De-identified (per HIPAA definition)	None
PHI - Limited Data Set (LDS)	Data Use Agreement (DUA); use limited to research or public health
PHI - Identifiable (*i.e.*, more identifiable than LDS)	Patient authorization (or waiver)

Type of Data	HIPAA Requirements for Research Use	New HITECH Requirements
De-identified	None	
PHI - Limited Data Set (LDS)	Data Use Agreement (DUA)	**Breach Reporting** **Ban on Sale of PHI**
PHI - Identifiable	Patient authorization (or waiver)	**Breach Reporting** **Ban on Sale of PHI**

Ban on Sale of PHI

- **HITECH bans sale of PHI by a Covered Entity or Business Associate without an authorization, unless an exception applies**
- **Sale = direct or indirect remuneration**
- **Research exception is very narrow**
  - Price can reflect only "the costs of preparation and transmittal of the data"
  - Expect legal uncertainty and wrangling over interpretations of cost
  - Unrealistic to think data will be shared if the only incentive is to cover marginal costs
  - **Bottom line – the ban will be a serious deterrent to sharing data, even Limited Data Sets, for research**

Possible New Barriers To Information-Based Research

- De-identification changes? – HHS Guidance coming
- Potential new restrictions on de-identified data under discussion
  - Ban on attempted re-identification
  - Security safeguards
  - Contractual controls
- Misconceptions and exaggerations about risk of re-identifying de-identified data
  - Gov. Weld case and other pre-HIPAA cases
  - Netflix, AOL
- Perceptions among policymakers
  - FTC: "the blurring of the distinction between personally identifiable information and supposedly anonymous or de-identified information"

Possible New Barriers to Database Research

- Comprehensive privacy bills (Sen. Kerry, etc.) – if definitions are sloppy and/or if carve-outs are inadequate, legislation could sweep HIPAA de-identified data into scope, imposing new regulators and requirements re:
  - Notice
  - Consent
  - Access and correction rights
  - Security
- Data segmentation – PHI and "sensitive PHI"?
- New consent requirements?
  - Watch policy discussions about consent in various contexts – HIEs, ACOs, President's Council of Advisors on Science and Technology, health care operations (e.g., clinical registries)

Type of Data	HIPAA Requirements for Research Use	New HITECH Requirements	[Disastrous] Hypothetical New Burdens on Research
De-identified	None		New de-ID'n standard reduces data utility; New operational burdens; New federal and state regulators; New duties – notice, consent, access, correction
Limited Data Set (LDS)	Data Use Agreement (DUA)	Ban on Sale of PHI Breach Reporting	Same as above?
Identifiable	Patient authorization (or waiver)	Ban on Sale of PHI Breach Reporting	Special consents for "sensitive PHI"?

A New Privacy Framework For Research?

Guiding principles for a framework

- **Avoid requirements that are:**
  - **Expensive to comply with**
  - **Confusing**
  - **Subject to endless dispute**
  - **Inefficient at achieving desired goals**
  - **Formalistic**
  - **Inconsistently applied**
  - **Enforced by multiple regulators**
  - **Relished by plaintiffs' lawyers**
- **Be rational about risks, especially privacy risks**
- **Balance risks – we want privacy and biomedical progress**

A New Privacy Framework For Research?

1. **Comprehensive privacy legislation must have a well-written HIPAA carve-out that includes HIPAA de-identified data**
2. **Expand research exception to Ban on Sale of PHI – be realistic about compensation needed to incentive data fluidity**
3. **Consider a new Safe Harbor with streamlined regulatory burdens as quid pro quo for meaningful, verifiable data safeguards**

Potential Safe Harbor Duties	Potential Safe Harbor Benefits
- *Specific controls beyond HIPAA Security Rule* - *Third party security assessments* - *Executive attestation of compliance (like SOX)*	- *No new consents* - *Exemption from PHI sale ban* - *No IRB review for privacy* - *Draw data from EHRs and HIEs, regardless of divergent state laws*

Conclusion

- Acceleration of CER and information-based research is needed
- Existing privacy regimen poses heavy burdens, especially as exacerbated by HITECH
- Certain policy proposals pose incalculable threats to information-based research
- Research Safe Harbor Framework concept is a starting point – goal is a balanced, rational, and efficient regulatory system that protects privacy and advances biomedical breakthroughs

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