1. Education
2. Biobanks
3. Community engagement
4. Consults
5. Collaboration
6. IRB Quality
Human subjects research

✓ Most not complicated
  ‣ Minimum risk (80-90% at Michigan)

✓ Some poses real dilemmas (no best answer)
  ‣ Example, re-use of cardiac pacemakers

✓ Some areas need more study
  ‣ Informed consent
Why informed consent?

✓ Nuremberg Code
  ‣ The voluntary consent of the human subject is absolutely essential
  ‣ Consent must be informed

✓ Primary goal/mission of ethics committees

✓ Significant shortcomings in current process
  ‣ Focus has been primarily on specific cases
  ‣ This presentation will focus on systemic problems
Informed consent dilemma

- As research becomes more complex
  - Longer IC forms
  - More complex IC forms
  - Less understanding

- Research has shown
  - IC forms not written at understandable levels
  - Longer IC forms $\rightarrow$ less understanding

- Dilemma: The need to document understanding in IC forms has reduced subject understanding of the research
MICHR Genomic DNA BioLibrary Project

Two goals:
1. RESOURCE for translational research
2. RESEARCH LABORATORY for study of ethical and policy issues
Primary Goal: Service

- Collect, store and share biological materials & health information

Specific goals:
- Initially genomic DNA; may broaden later
- Serve MICHR researchers and through them broader collaborations
- Large collection – 100,000 samples
- Safely stored
- ...and shared
Secondary goal: Research

✓ Hypothesis: can establish and maintain a scientifically useful and ethically responsible Genomic DNA BioLibrary

✓ Aims:

- Establish and validate a process/system to collect, isolate, annotate, store and retrieve samples of genomic DNA
- Establish and validate a process/system to distribute and share samples of genomic DNA
- Determine the scientific and societal value of the BioLibrary at both an institutional and national level
Why BioLibrary?

✓ Set tone for project, considered:
  ▶ (BIO) Repository: a place for storing things
  ▶ (Bio) Bank: brings in concept of security
  ▶ (Bio) Trust: Sense of collaboration/trust between two parties

✓ Library
  ▶ Talk in terms of donating “books”
  ▶ Books contain useful information
  ▶ Information in books is regularly shared
  ▶ Libraries are a community resource

✓ Emphasize community (social) over individual
Organizational Model

Recruitment Layer
- Neonates
- Wellness
- Aged
- Fatal Illness
- Participant Portal
- UM ClinicalStudies.org

Informed Consent Layer
- Informed Consent Process/Forms
- Center for Health Communication Research
- Genomic DNA + EHR/PHI
- No Restrictions
- Disease Only
- Re-consent

Permission Layer
- Genomic DNA + EHR/PHI
- DNA Samples
- caTISSUE Database
- EHR/PHI Data

Asset Layer
- DNA Samples
- Research Data Warehouse
- i2b2/SHRINE Data Sharing

Biomedical Informatics Layer
- DNA Sequencing Core & Data
- EMERGE Broker
- PI Portal
- PI-Driven Informatics Analysis (BIC)
- Design & Enable Specific Protocols (BERD)
- IRB review & approval
- Access DNA Samples (De-ID or Re-ID)

MICHR Stewardship
- DNA Sequencing Core & Data
- EMERGE Broker
- PI Portal
- PI-Driven Informatics Analysis (BIC)
- Design & Enable Specific Protocols (BERD)
- IRB review & approval
- Access DNA Samples (De-ID or Re-ID)

Data Organization, Analyses, Integration & Sharing
- Sequence DNA Samples
- Sequence DNA
- De-ID Data
- Sequence Data
- i2b2/SHRINE Data Sharing
- DNA Sequencing Core & Data
- EMERGE Broker
- PI Portal
- PI-Driven Informatics Analysis (BIC)
- Design & Enable Specific Protocols (BERD)
- IRB review & approval
- Access DNA Samples (De-ID or Re-ID)

Informed Consent Process/Forms
- Genomic DNA + EHR/PHI
- No Restrictions
- Disease Only
- Re-consent

I2b2/SHRINE
- Data Sharing
- DNA Samples
- Research Data Warehouse
- i2b2/SHRINE Data Sharing
- DNA Sequencing Core & Data
- EMERGE Broker
- PI Portal
- PI-Driven Informatics Analysis (BIC)
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De-ID Sequence DNA
- Sequence Data
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Project 1: Informed consent

✓ Major challenge: enrolling 100,000 subjects
✓ Options:
  ‣ Opt-out without REC (IRB) approval
  ‣ Opt-out with REC (IRB) approval
  ‣ Opt-in with REC (IRB) approval
✓ Goal: greatest efficiency without compromising ethics
✓ Poll: which option?
Opt-out without RE approval

✓ Use excess materials from routine visits
✓ De-identify, which exempts from US regs.
✓ Use “honest broker” to link with health record
✓ Provide opt-out option during admission
✓ Objections:
  ‣ Participants want information and choice
  ‣ No evidence that participants understand their choice
Opt-out with approval

✓ Bring to REC for approval
✓ Provide participants full information, validated for effectiveness
✓ Present choice as an opt-out option
✓ Objections:
  ‣ Choice based on presumed higher enrollments
  ‣ Enrolling subjects who might do so if asked to opt-in
  ‣ Not setting highest ethical standard
Opt-in with REC approval

✓ Slow, expensive, slows research
✓ Solution: improve informed consent process
✓ Approach:
  › Separate “informing” from “consenting”
  › Validate informing process
  › Integrate into clinical workflow
✓ Goal: validated consent as part of normal clinical workflow
BioLibrary Pamphlet

- Include essential information about trial
- Designed to convey understanding
- Validate prior to use

Current IC Forms

- Include essential information about trial
- Often long & complex
- Studies show do not convey understanding

✓ BioLibrary IC Forms

- Essential regulator information
- Signatures
- Record
BioLibrary:
Stores medical information and blood samples like a library stores books.
Depending on volunteers, like you, to give permission to collect and use their books.

“Book”
A book has two parts that are linked together:
- DNA that is taken out of a sample of your blood. Your DNA:
  - Is like your fingerprints. Nobody has the same DNA.
  - Has information about what makes you the way you are, such as your hair color or how easy it is for you to get sick.
  - Will be frozen and stored at the University of Michigan Center for Translational Pathology.
  - Does not have any information about who you are on its own.
- Medical record information, such as:
  - Parts of your doctor and hospital visits records.
  - Results from x-rays, blood tests or urine tests that you’ve had.
  - Your health history, including any mental health treatment.

Contact Information
Please let us know if you would like more information or if you have any questions about the BioLibrary.

MICHR:
www.michr.umich.edu/ or 734-998-7474

MICHR Genomic DNA BioLibrary:
www.michr.umich.edu/services/biorepository

Michigan Clinical Research Unit (MCRU):
www.michr.umich.edu/services/mcru

HIPAA:
www.med.umich.edu/hipaa/npp.htm.

IRBMed:
www.med.umich.edu/irbmed/

UMHS links:
www.med.umich.edu/
Consent

A. IRB approved
B. Elements of Consent
C. HIPAA
D. Options
E. Record

Laws about human research at the University of Michigan can be hard to understand. There are three key points you need to know before you join this study:

1. Institutional Review Board Approval. An Institutional Review Board, or IRB, must approve or certify research done with humans. The MICH (Michigan Institute for Clinical and Health Research) Genomic DNA BioLibrary has IRB approval. You can see a copy of the IRB approval on the top of this page.

2. Elements of Consent. You must be informed about the project and agree on your own to join. This is called “informed consent.” The BioLibrary pamphlet has the details that you need to know. In general, you need to understand that:
   - Your blood sample and health records are called your “book.” They will be used for research as the BioLibrary exists. Your “book” will stop being used for new research if you ask it to be removed.
   - Your “book” will be stored and safe. Only approved researchers can look at it. However, sometimes someone who is not approved might look at your “book.” You can read more about who can see “book” in section C of the pamphlet.
   - There are a few risks related to giving a blood sample and sharing your health records. This is your “book.” You will not benefit directly from the research that your “book” is used for. You will get paid for traveling to and parking at the clinic.
   - You might help health research more by enrolling in other studies.
   - It’s up to you whether or not you join the BioLibrary. Your choice will not affect the health care you get from UMHS. You can withdraw from the study at any time without any harm to you.

3. HIPAA Privacy Rule. The use of your health information is watched and kept safe by the Insurance Portability and Accountability Act of 1996 (HIPAA, Public Law 104-191). You can read more about this on the second page.

(Initial here if you understand and accept the HIPPA Privacy Rule)

Consent:
1. I was given a pamphlet that describes this project in detail. I give permission to the MICH Genomic DNA BioLibrary to collect and use my blood sample and UMHS health records. (Initial which blank you agree to the following:)
   - ______ without any limits
   - ______ only for studies related to my illnesses
   - ______ only for use by researchers at or associated with the University of Michigan
   - ______ other limits (please give details):

2. I also agree to be interviewed to assess my informed consent. The answers will be used to improve future research. My informed consent is described to volunteers in this study.

(Participant Name Printed)  (Participant Signature)  (Date)
Validation process

✓ Recruiting through UMclinicalstudies.org
✓ Email pamphlet, ask if interested
✓ If yes, schedule visit
  ‣ Consent (one page, BioLibrary and HIPAA)
  ‣ Understanding assessment
  ‣ Further explanation of misunderstandings
  ‣ Opportunity to withdraw
  ‣ Provide blood sample
Results of validation process

✓ Participation / 100 potential subjects contacted
  ‣ 45% respond, agree to participate, schedule appointment
  ‣ 99% of those who visit clinic provide a sample
  ‣ Pamphlet provides essential information, few misunderstandings

✓ Limitations:
  ‣ Study population has already agreed to participate in research
  ‣ Literate, university-oriented population (selected by zip codes)

✓ Next step to broaden to other populations
  ‣ First University clinics, then community settings
Clinical workflow study:

✓ Challenges:
  ‣ Recruiting ~ how and when to introduce the study
  ‣ Space/time ~ can’t slow patient flow, occupy valuable space
  ‣ Expertise ~ training clinical staff to respond to questions

✓ Ethical issues ~ coercion and distraction
  ‣ Increasing pressure to recruit during clinical visits
  ‣ Physician has authority and can have conflicts of interest
  ‣ Participant’s first concern is person health, not research

✓ Launching workflow study in 3 clinical settings
Cost-benefit study

✓ Nuremberg

- The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, ...

✓ Two questions:

1. Do “BioLibraries” yield fruitful results, unprocurable by...”?
2. Is “opt-in” too expensive to justify taking moral high road?

✓ Cost-benefit of biobanks not carefully studied

- Opt-in may add as little as $8.00/sample
ICs are complex documents
Information in ICs is largely not shareable
- At Michigan, scanned and put is patient/participant file
- Image file, not possible to access content

Why is this important?
- Vital to sharing samples and information (biobanks)
- Essential for regulatory oversight

Goal: to create a framework for collecting, storing and sharing IC information
IC = Authorized Informed Permission to conduct Research on research Subject.
Two purposes: Organize & Guide

Patient Record

Institutional Record

Protocol

REC

Informed Consent Form

Subject

Authority

Research

Permission

Inform

IC

20%

20%

20%

20%
Challenges

1. Developing a comprehensive ontology
2. Connecting the ontology with research, patient, and institutional records
Questions