MANCHESTER 1824
The University of Manchester

Consent

Nalin Thakker

Consent

- What is consent for?
- How ‘informed’ is ‘informed consent’?
- Consent & incidental findings

What is consent for?

Clinical vs. Research Consent

- Clinical
  - For care & treatment of the patient
  - Anticipated direct personal benefit
  - Acceptance of risks
  - Fiduciary relationship

- Research
  - Focus on generating new knowledge or understanding
  - May have no anticipated personal benefit
  - Risks and potential benefits may not be well defined
  - No legal/fiduciary obligation for provision of care

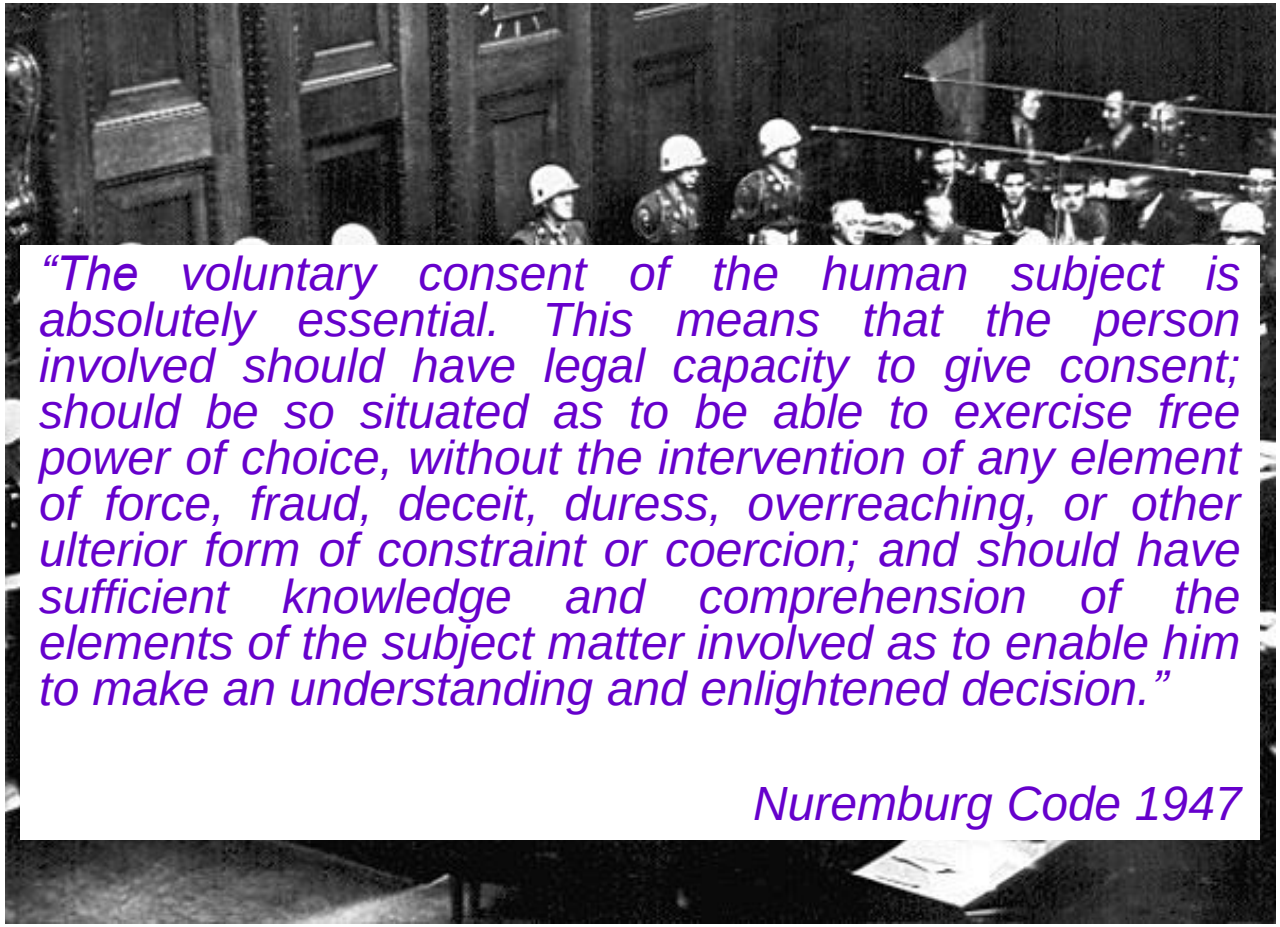
Clinical vs. Research Consent

- Clinician looking after the patient is also the researcher
  - Dependent relationship
  - Competing interests
  - Feedback of findings
- Research intervention is also treatment
  - Perceived therapeutic benefit

Ethical Necessity For Consent

- Stems from
  - respect for autonomy of individuals
  - right to protection when autonomy is diminished
- Serves to protect from unequal power relationship
  - Voluntary participation
  - Right to withdraw

Historical Perspective

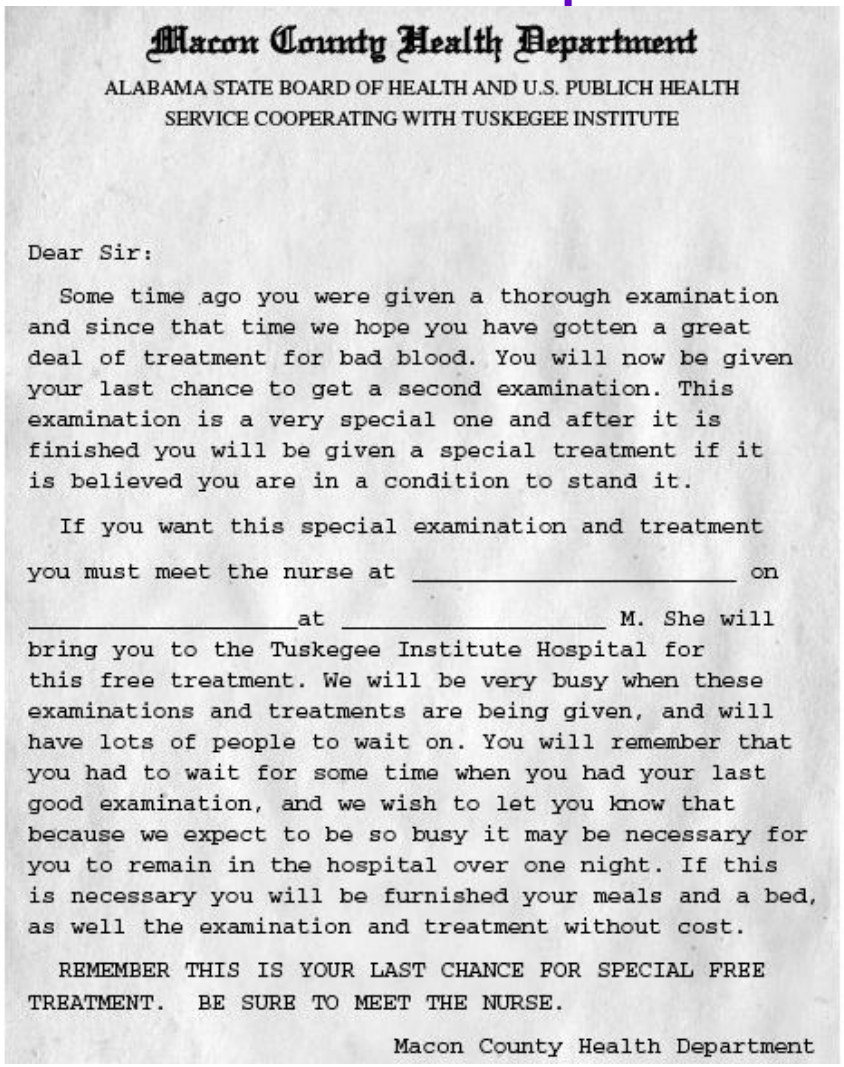


"The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision."

Nuremburg Code 1947

"The whole discipline of biomedical ethics rises from the ashes of the Holocaust"
Arthur Caplan

Historical Perspective



Macon County Health Department

ALABAMA STATE BOARD OF HEALTH AND U.S. PUBLICH HEALTH SERVICE COOPERATING WITH TUSKEGEE INSTITUTE

Dear Sir:

Some time ago you were given a thorough examination and since that time we hope you have gotten a great deal of treatment for bad blood. You will now be given your last chance to get a second examination. This examination is a very special one and after it is finished you will be given a special treatment if it is believed you are in a condition to stand it.

If you want this special examination and treatment you must meet the nurse at _____ on _____at _____ M. She will bring you to the Tuskegee Institute Hospital for this free treatment. We will be very busy when these examinations and treatments are being given, and will have lots of people to wait on. You will remember that you had to wait for some time when you had your last good examination, and we wish to let you know that because we expect to be so busy it may be necessary for you to remain in the hospital over one night. If this is necessary you will be furnished your meals and a bed, as well the examination and treatment without cost.

REMEMBER THIS IS YOUR LAST CHANCE FOR SPECIAL FREE TREATMENT. BE SURE TO MEET THE NURSE.

Macon County Health Department

Tuskegee Syphilis Experiments 1932- 1972

Historical Perspective

Guatemala 1946-1948 STD Experiments

Declaration of Helsinki 1964

- Basis of all informed consent in medical research
- Voluntary participation
- Adequate information of nature of study
- Need to ensure it is understood
- Right to withdrawal

Ethical Necessity For Consent

- Data
  - Privacy & confidentiality
- Tissues
  - Ownership rights
  - Bodily integrity

Legal Necessity for Consent

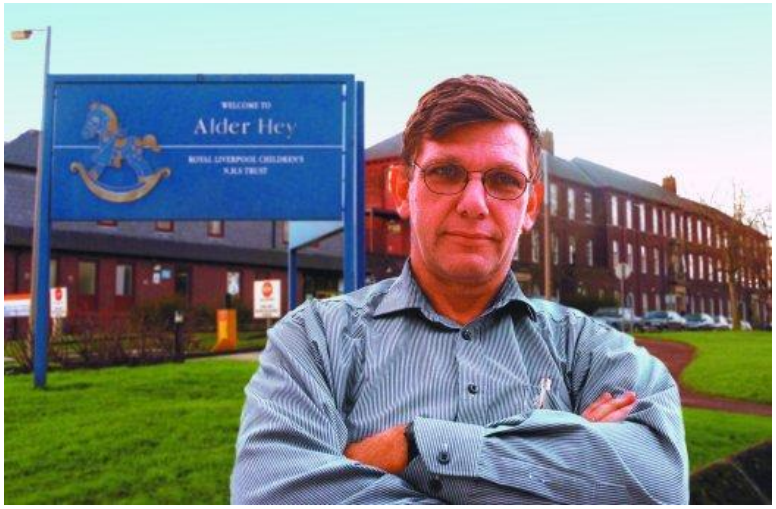
- Overall
  - ?Human Rights legislation
- Physical intervention
  - common law
- Data
  - Data Protection Act1998
- Tissues & DNA
  - Human Tissue Act 2004
- Mental Capacity
  - Mental Capacity Act 2005
- Clinical Trials
  - EU Clinical Trials Directive 2006

Regulatory Necessity for Consent

- NHS Research Governance Framework and Governance Arrangements for Research Ethics Committees (GAfREC)

- Indirectly through requirement for ethics review

Human Tissue Act 2004



'CONSENT a fundamental principle underpinning removal, use ("scheduled purposes") and storage of tissues'

Objectives - 1

Provides safeguards and penalties to prevent a recurrence of the distress caused by retention of tissue and organs without proper consent

Objectives - 2

Will help improve public confidence so that people will be more willing to agree to valuable uses of tissue and organs

Objectives - 3

Will improve professional confidence so that properly authorised supplies of tissue for research, education and transplantation can be maintained or improved

HT Act 2004 – Consent For Tissues

- From deceased
  - Required for lawful removal, retention & use
- From living
  - Required for lawful retention & use
  - Removal regulated by common law
- Applies to
  - Relevant material only for tissues
  - Bodily material for DNA (& RNA)

HT Act 2004 – Consent Exemptions For Tissues

- Both living and deceased
  - Existing collections at 1st September 2006
  - Imported tissues
  - By authority of Minister of State
- Deceased
  - 100 years rule
- Living
  - Residual tissue

    (only if anonymised and with NHS ethics approval)
  - Audit, education, quality assurance, performance assessment
  - Adults lacking capacity to consent

    (subject to Clinical Trials Regulations 2004 or Mental Capacity Act 2005)

Main Categories of Tissues & Consent

Research project (RP)	**Project specific consent** **Consent for storage and future use (generic and enduring consent)**
Research tissue bank (RTB)	**Consent for use in specified programme of research** **Consent for storage and future use (generic and enduring consent)**
Diagnosis/treatment & RP	**Clinical consent** **Project specific consent** **Consent for storage and future use (generic and enduring consent)**
Diagnosis/treatment & RTB	**Clinical consent** **Consent for storage and future use (generic and enduring consent)**
Existing clinical archival tissues Pre-1/9/2006 - all Post-1/9/2006 – from living only	**Consent exemption**

HT Act 2004 – DNA Analyses

- Applies to any bodily material
- No specific provision for DNA analyses
  - Consent for research permits DNA analyses as part of that research
- Consent exemptions apply as for tissue

What Do RECs Consider in Permitting Consent Exemption?

- Balanced view of risks and benefits
  - Risks to privacy and wellbeing of the donors
  - Benefit of the research
- Difficulty or intrusiveness of obtaining consent
- Possibility of anonymising the tissue
- Nature of the research tests and findings
- Possibility of commercial exploitation

How Do You Demonstrate Consent?

- No specific requirement
- A signed consent form only means that the consent form was signed.
- Highest forms of evidence
  - Copies of signed consent forms
  - View consent forms and document it
- Acceptable forms of evidence
  - Due diligence & assurance from supplier
  - REC approval
  - MTA, SLA

How 'Informed' is 'Informed Consent'?

How Informed is Informed Consent?

	Understanding and Satisfaction (%)		
Clinical Trial	Adequate	Moderate	Inadequate
Amount			
Aim			
Randomisation			
Volunteerism			
Withdrawal			
Risks			
Benefits			
Therapeutic Misconception			
Alternatives			

Falagas et al., The American Journal of Surgery (2009) 198, 420–435

‘Fully Informed’ Consent

- Unrealistic and limited in most cases
- Consent can be given for a course of action only as described and understood in a specific way
- Description cannot be exhaustive and/or understanding may be limited
- Thus consent is almost always for an incompletely described or understood action

Main Categories of Tissues & Consent

Research project (RP)	**Project specific consent** **Consent for storage a… …generic and enduring …**
Research tissue bank (RTB)	**Consent for … programme of rese…** **Co… …e and future use (generic …ng consent)**
Diagnosis/treatment & RP	**…al consent** **…roject specific consent** **Consent for storage and future use (generic and enduring consent)**
Diagnosi… …TB	**Clinical consent** **Consent for storage and future use (generic and enduring consent)**
…linical archival tissues …1/9/2006 - all Post-1/9/2006 – from living only	**Consent exemption**

How ‘Informed’ is ‘Informed Consent’?

Consent and Biobanking - Concerns

- Storage of tissue (and personal information) for future unspecified use.
- Donors cannot make real judgements about how their samples are used.
- Any ethics review cannot possibly know about potential future benefits.
- Concern about misuse of personal information.

Declaration of Helsinki 1964

- Basis of all informed consent in medical research
- Voluntary participation
- Adequate information of nature of study
- Need to ensure it is understood
- Right to withdrawal

Consent and Biobanking - Response

- Cannot realistically seek permission for each and every project on prospective basis
- Need to weigh up potential benefit against any harm
- Consent is not about ownership
- Research shows:
  - Research details are poorly understood generally by donors
  - Consent is given on the basis of trust in the researchers, processes and institutions and altruism
  - Very few donors refuse to give consent for unspecified future use

‘Generic’ Consent

Consent to permit use of the tissue

- with knowledge of any planned future research use
- with knowledge that one cannot be fully informed about all
  - possible future uses of the tissues
  - possible outcomes (including commercial exploitation)
- with appropriate checks and balances
  - research ethics review
  - sponsor governance oversight
  - compliance with an HTA licence

Generic Consent Can Be More Informed than ‘Informed Consent’!

Consent and Incidental Findings

'Anticipate and Communicate'

Feedback of Study Results

- Pertinent Findings
  - You know *a priori* the significance of a positive finding
  - Individual results usually fed back
- Incidental Findings
  - Variable and unknown significance of the results
  - Feedback strategy more difficult

Hay

Other needles

Pink needle

Incidental findings

Pertinent finding

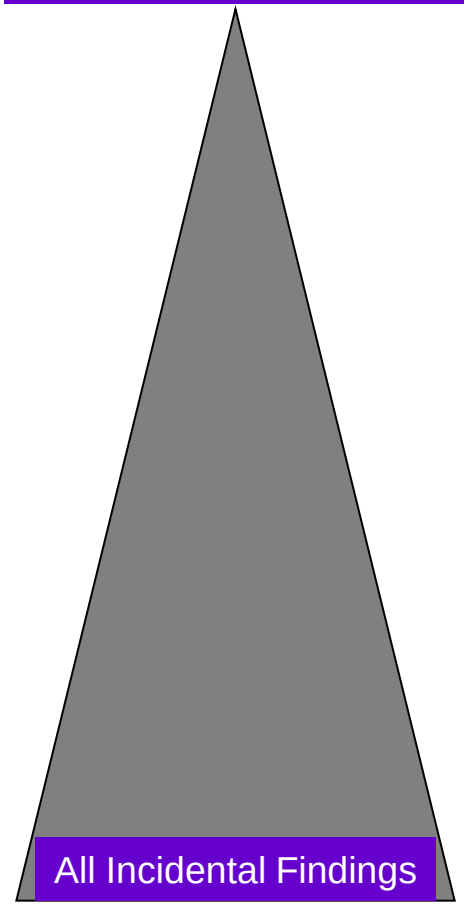
Specific

Method used to find the needle

Less specific

Even less specific

Clinical Significance of Incidental Findings From Genomic Analysis



0-5

Variants With
Known Clinical Value
and/or Utility

10-50

Potential Pathological Variants

100s

Known Variants in Genes
Associated With
Disease Phenotype

~3,500,000

All Variants

Global Analysis In Genetic Research

- Increasingly common
- High potential for incidental findings
- Need to
  - anticipate
  - plan how to deal with information
  - communicate with donors, manage expectations
  - seek consent
  - respect autonomy

Feedback of Incidental Findings in Research

- Fiduciary obligation for clinical care
- Expertise
- Numbers and costs/benefits
- Analytic validity
- Consent
- Feedback pathway

WT/MRC – Draft Guidance

'We consider that it is appropriate for researchers to feed back health related findings where the benefits of feedback to an individual clearly outweigh the harms.

However, at this time, we do not consider it appropriate to advocate a single approach to the feedback of health related findings because further empirical evidence is needed on the risks and benefits associated with feedback; research contexts vary widely; and the balance, including between public and individual benefit, must be assessed in each case.'

‘There are no right or wrong answers…only appropriate answers’

Summary - Consent

- What is consent for?
  - Ethical, legal, regulatory necessity
  - Demonstrating consent to regulators
- How ‘informed’ is ‘informed consent’?
  - Not very!
  - Generic consent is ethical
  - Generic consent is acceptable to donors
- Consent & incidental findings
  - Decide what is important
  - Anticipate and communicate
  - Different considerations apply to research compared to clinical practice

Final Thoughts…..

Do we need consent in all cases?

The Case for A Rethink on Consent

- Informed consent is not very informed
- Researchers do many things without consent
- Real harm from restrictive requirements
- Need to consider society as well as an individual
- We have developed a culture of legal/regulatory compliance rather than ethical or professional standards
- Regulatory and governance framework much better now than in the past – can we not relax some requirements for consent?