Ethical Considerations for HIV Cure Research

CUREiculum

This research training curriculum is a collaborative project aimed at making the science of HIV cure-related research accessible to the community and the HIV research field.

Glossary of Key Terms

Ethics

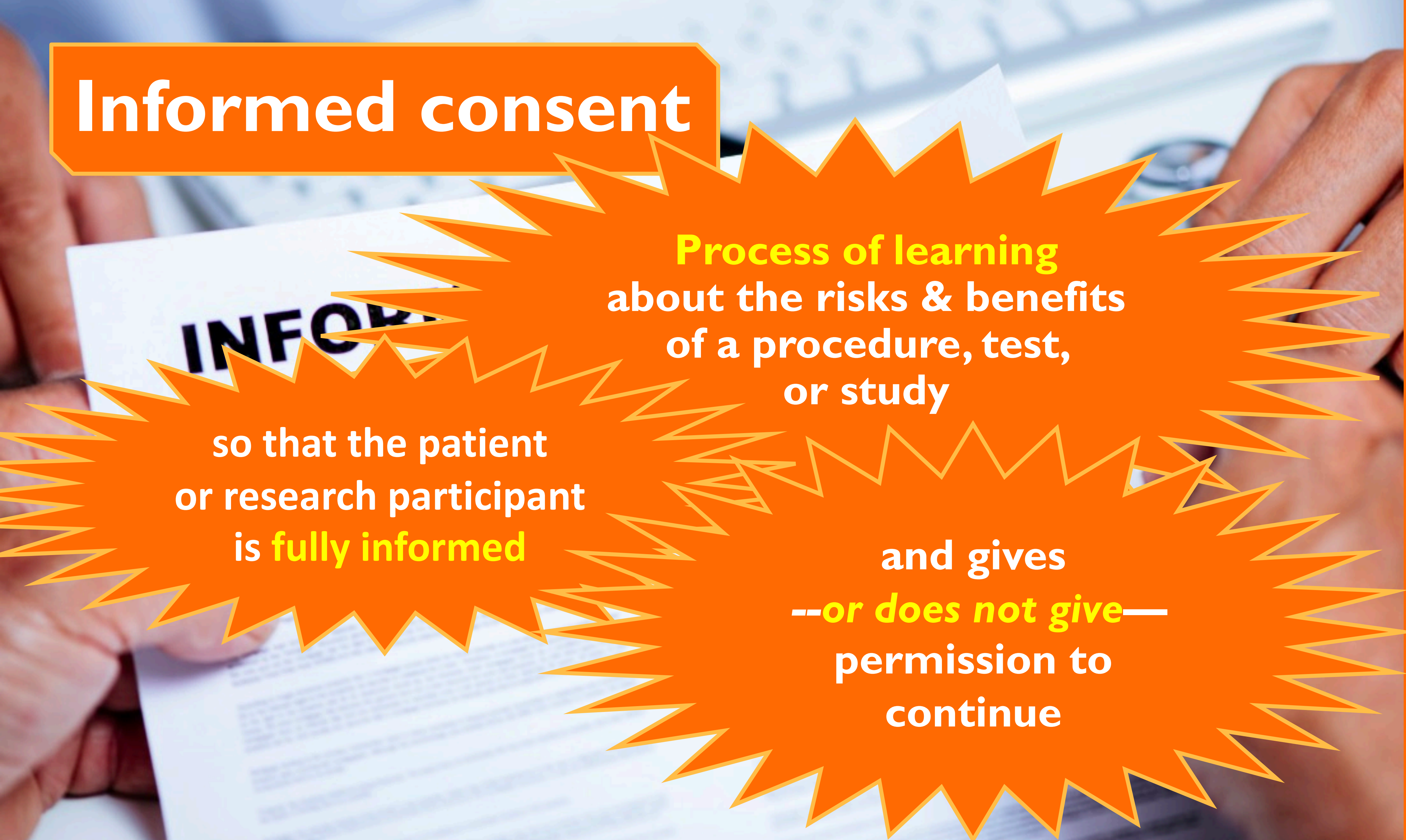
ethical considerations

Ethics

Bioethics is the application of this reasoning to health, healthcare, and research.

ethical considerations

Informed consent



Process of learning
about the risks & benefits
of a procedure, test,
or study

so that the patient
or research participant
is **fully informed**

and gives
--*or does not give*—
permission to
continue

ethical considerations

Regulations

Rules that govern
how new therapies
are approved
by authorities

ethical considerations

Importance of community in contemporary HIV Cure-Related Research

Good participatory practice
guidelines for biomedical HIV
prevention trials

UNAIDS

tagline Vol. 26, No. 1, May 2019

SCIENTIFIC COMPLEXITY AND ETHICAL UNCERTAINTIES: THE IMPORTANCE OF COMMUNITY ENGAGEMENT IN HIV CURE RESEARCH

By Richard Jefferys

AVAC

An incredible history of community participation in HIV research

Gaining knowledge about research ethics is an important step for being able to add your voice to shaping what comes next

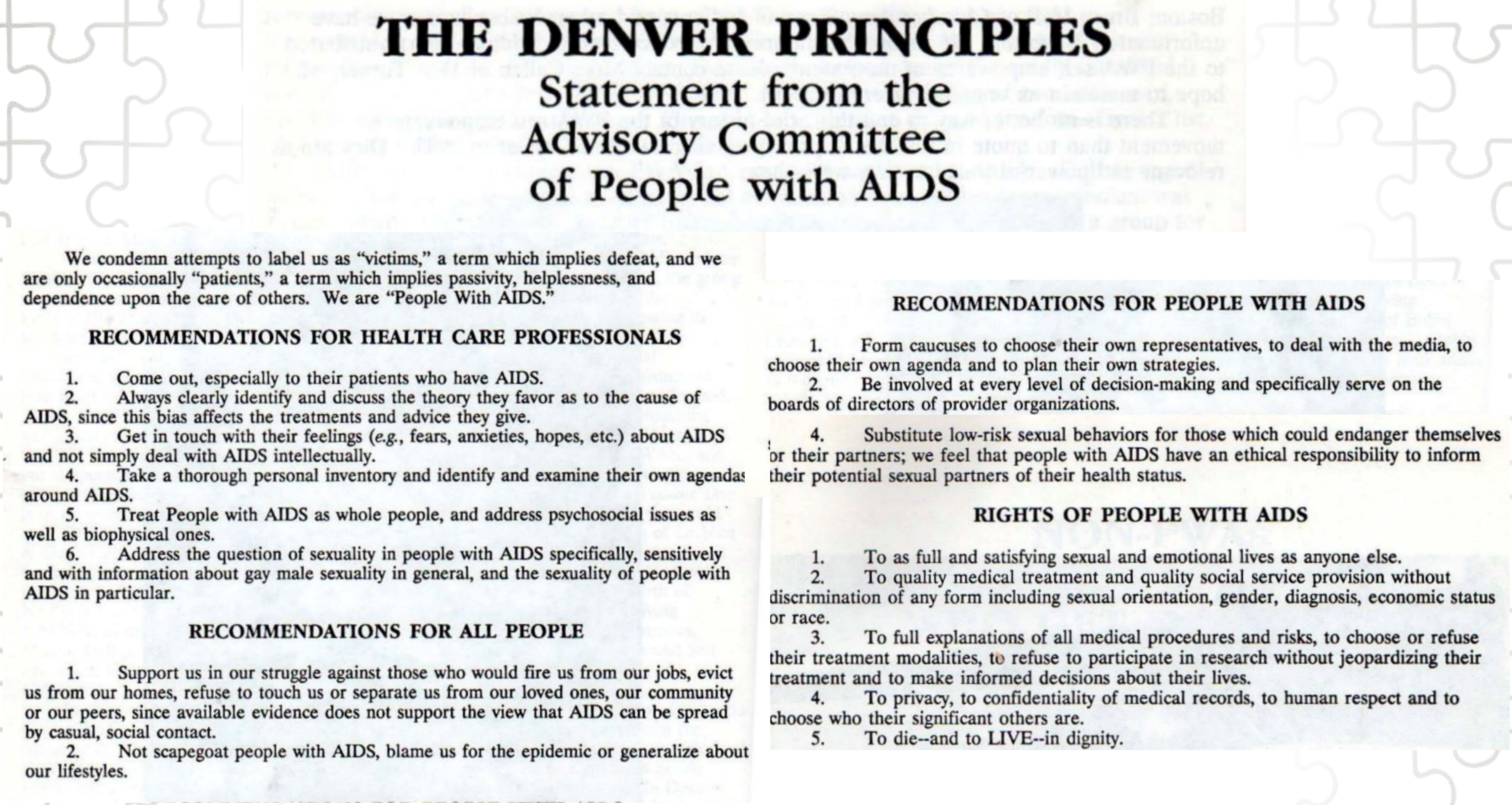
ethical considerations

Denver Principles

Community involvement in HIV/AIDS research began with the Denver Principles in 1983

when people living with AIDS demanded a place at the table

ethical considerations



THE DENVER PRINCIPLES

Statement from the Advisory Committee of People with AIDS

We condemn attempts to label us as "victims," a term which implies defeat, and we are only occasionally "patients," a term which implies passivity, helplessness, and dependence upon the care of others. We are "People With AIDS."

RECOMMENDATIONS FOR HEALTH CARE PROFESSIONALS

1. Come out, especially to their patients who have AIDS.
2. Always clearly identify and discuss the theory they favor as to the cause of AIDS, since this bias affects the treatments and advice they give.
3. Get in touch with their feelings (*e.g.*, fears, anxieties, hopes, etc.) about AIDS and not simply deal with AIDS intellectually.
4. Take a thorough personal inventory and identify and examine their own agendas around AIDS.
5. Treat People with AIDS as whole people, and address psychosocial issues as well as biophysical ones.
6. Address the question of sexuality in people with AIDS specifically, sensitively and with information about gay male sexuality in general, and the sexuality of people with AIDS in particular.

RECOMMENDATIONS FOR ALL PEOPLE

1. Support us in our struggle against those who would fire us from our jobs, evict us from our homes, refuse to touch us or separate us from our loved ones, our community or our peers, since available evidence does not support the view that AIDS can be spread by casual, social contact.
2. Not scapegoat people with AIDS, blame us for the epidemic or generalize about our lifestyles.

RECOMMENDATIONS FOR PEOPLE WITH AIDS

1. Form caucuses to choose their own representatives, to deal with the media, to choose their own agenda and to plan their own strategies.
2. Be involved at every level of decision-making and specifically serve on the boards of directors of provider organizations.

4. Substitute low-risk sexual behaviors for those which could endanger themselves or their partners; we feel that people with AIDS have an ethical responsibility to inform their potential sexual partners of their health status.

RIGHTS OF PEOPLE WITH AIDS

1. To as full and satisfying sexual and emotional lives as anyone else.
2. To quality medical treatment and quality social service provision without discrimination of any form including sexual orientation, gender, diagnosis, economic status or race.
3. To full explanations of all medical procedures and risks, to choose or refuse their treatment modalities, to refuse to participate in research without jeopardizing their treatment and to make informed decisions about their lives.
4. To privacy, to confidentiality of medical records, to human respect and to choose who their significant others are.
5. To die--and to LIVE--in dignity.

a deeper dive:

How 'The Denver Principles' Changed Healthcare Forever - POZ

Let's dive in!

Outline of Module

- **What is Bioethics?**
  - What is it *not*?
  - A primer on the principles and theories of bioethics
  - The birth of bioethics
- **Research Ethics**
  - Focus on informed consent
  - Regulatory agencies
- **Ethics of HIV cure-related research**
- **Conclusions & Take-Aways**

ethical considerations

Part 1:
What is Bioethics?

What is Bioethics?

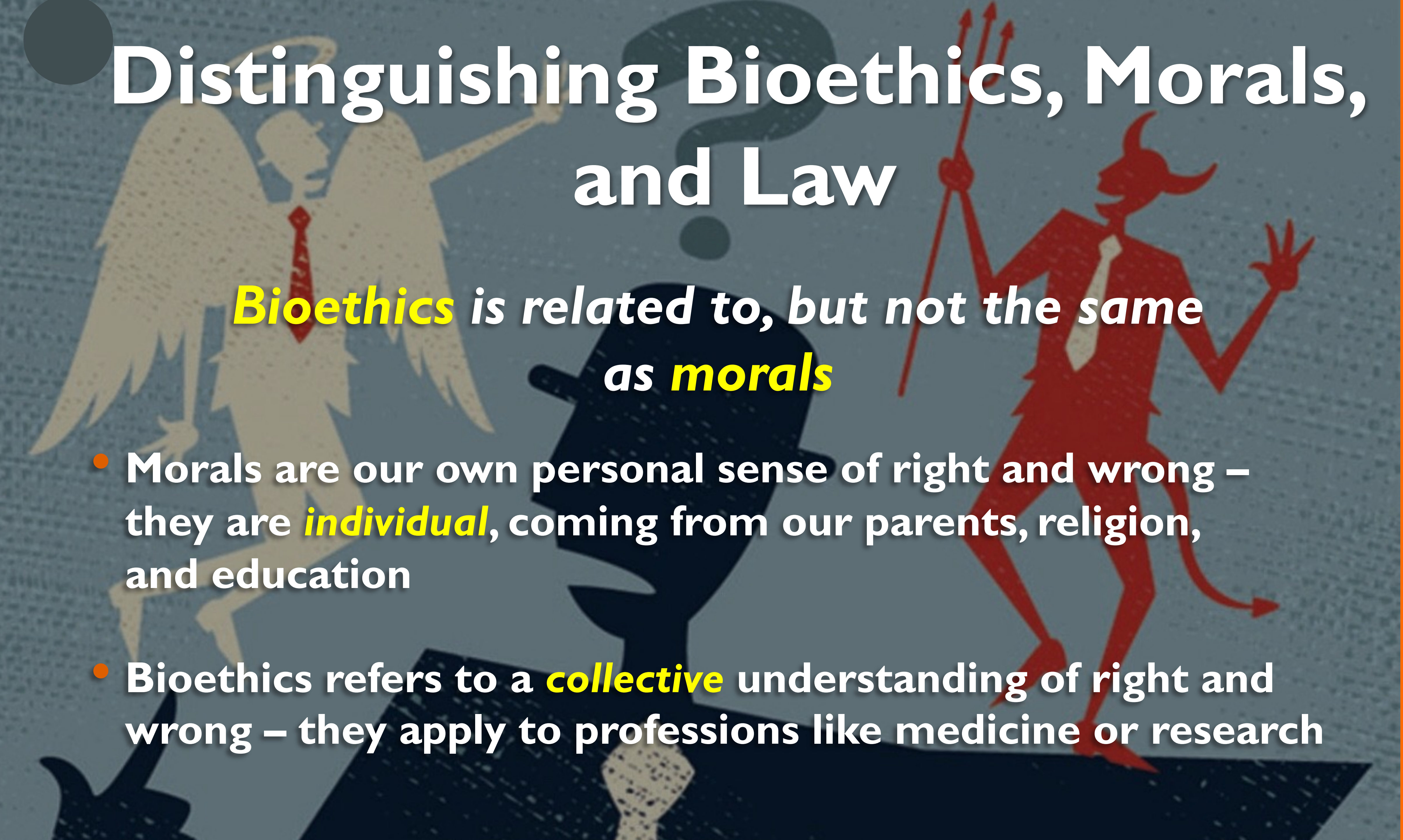
Ethics is a field of study that helps us answer questions like:

- What must we* do?
- What must we* not do?
- What is permissible to do?
- How may we (not) do what we do?

"we" = doctors, scientists, researchers, ourselves

Bioethics asks these questions in places where health, medicine, disease, research, healthcare, science, and society intersect

Distinguishing Bioethics, Morals, and Law



Bioethics* is related to, but not the same as *morals

- **Morals are our own personal sense of right and wrong – they are *individual*, coming from our parents, religion, and education**
- **Bioethics refers to a *collective* understanding of right and wrong – they apply to professions like medicine or research**

ethical considerations

Distinguishing Bioethics, Morals, and Law

Bioethics* is related to, but not the same as *the law

- **Laws and regulations come from ethical reasoning, but the law changes over time and place, and at times, something can be legal (or at least not illegal) but deemed not to be ethical**

- **US laws have established offices – like Institutional Review Boards – to help make sure that research is ethical**

Bioethics as guideposts and a toolbox

You can think of bioethics as both a set of guideposts, indicating right and wrong action…

…AND

a toolbox to help us make those decisions

The Bioethics Toolbox

what matters
to each stakeholder

guides for making
a decision about
a course of action

A Bioethics Toolbox – Principles

What matters to each person involved

Autonomy

The right to determine what happens to one's own body

Beneficence

This principle highlights 'doing good' for others – for research participants, patients, each other

Non-maleficence

This principle highlights the need to actively avoid doing harm to others

Justice

Justice is the principle that says we must allocate resources in a fair and just manner

A Bioethics Toolbox – Principles

What matters to each person involved

Equity and Community-based Principles

Agency

Agency refers to someone's ability to make and carry out a choice. We all have limits on our agency, and ignoring that fact is like being 'color blind' – racism, sexism, and homophobia

Social Justice

Social justice asks us to consider the fact that 'equal' is not always 'equitable'. We should be conscious of how social and structural forces can be discriminatory and actively work to counter them

A deeper dive: A short primer on Urban Bioethics

The Bioethics Toolbox - Theories

Sometimes there is more than one *right and ethical principle*. Theories help us make a decision when there is more than one *right* principle to follow

For example:

- *A patient may want to stop treatment for advanced cancer, choosing instead to receive comfort care. This is their right – they have autonomy*
- *Their doctor may may have medical knowledge of another treatment that may give the patient more years of life (beneficence)*

There is a conflict here between autonomy and beneficence – both are *ethically right,* but they are in conflict

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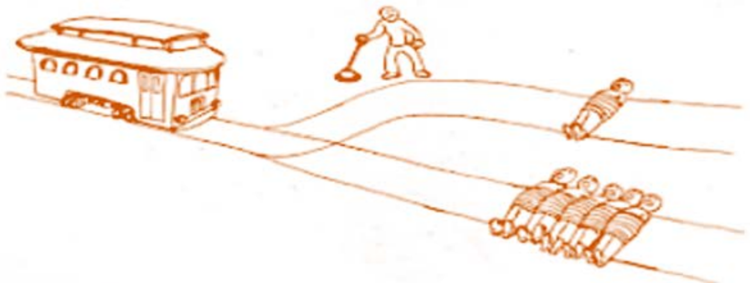
A Bioethics Toolbox – Theories



- Most ethical action is the one that leads to the **most ‘best’ outcomes** (*pull the lever, kill one person, and save 5*)

vs.

- Most ethical action is the one that most **follows our duties** *(don’t pull the lever because actively killing is wrong; doesn’t matter that 4 more folks die)*

‘best’ outcome

following duty

The **Birth** of Bioethics

- Bioethics was born as a field after the public learned that researchers and doctors **did not always** act *ethically* – they took advantage of vulnerable people for their own ends.

- History is unfortunately full of examples of scientists abusing their power in the name of science.

There are 2 specific examples that have led to modern *research ethics….*

#1

Nazi Medical Experiments in WWII

A deeper dive:

https://www.pbs.org/wgbh/nova/holocaust/experiside.html

https://encyclopedia.ushmm.org/content/en/article/nazi-medical-experiments

ethical considerations

ethical considerations

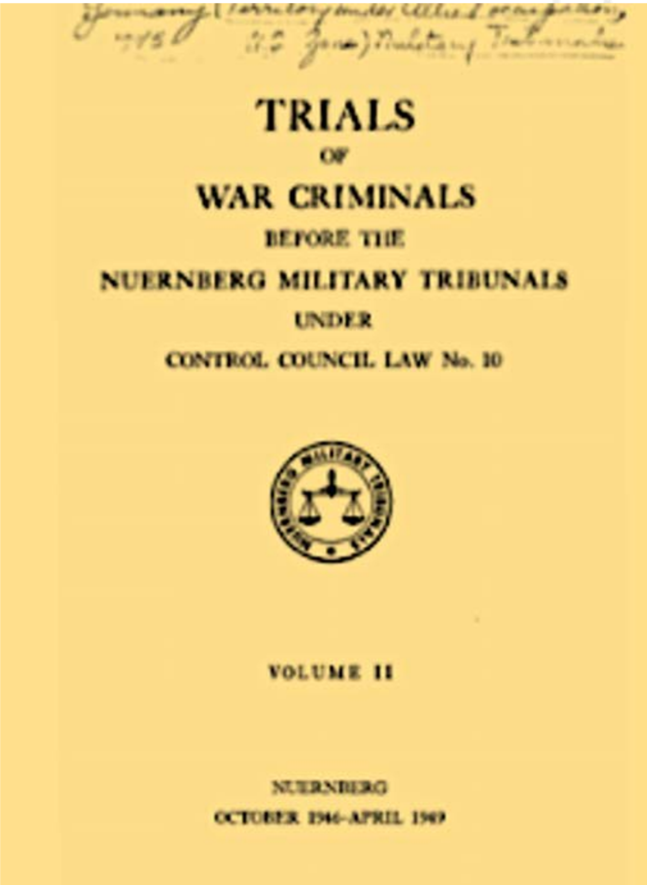
Case No. 1 of the Nuremberg Military Tribunal

U.S.A. vs. Karl Brandt et al.

Dec. 9, 1946 – Aug. 20, 1947

Nuremberg Code of 1947

- Voluntary informed consent essential
- Research should yield useful results
- Base research on prior work
- Avoid physical and mental suffering
- No expectation of death or disabling injury
- Risk must be outweighed by importance
- Participants must be protected from injury
- Qualified scientists, adequate facilities
- Participant free to stop at any time
- Investigator must be ready to withdraw participant



Germany (Territory under Allied occupation,
1945 U.S. Zone) Military Tribunals

TRIALS
OF
WAR CRIMINALS
BEFORE THE
NUERNBERG MILITARY TRIBUNALS
UNDER
CONTROL COUNCIL LAW No. 10

VOLUME II

NUERNBERG
OCTOBER 1946-APRIL 1949

A deeper dive: https://cioms.ch/

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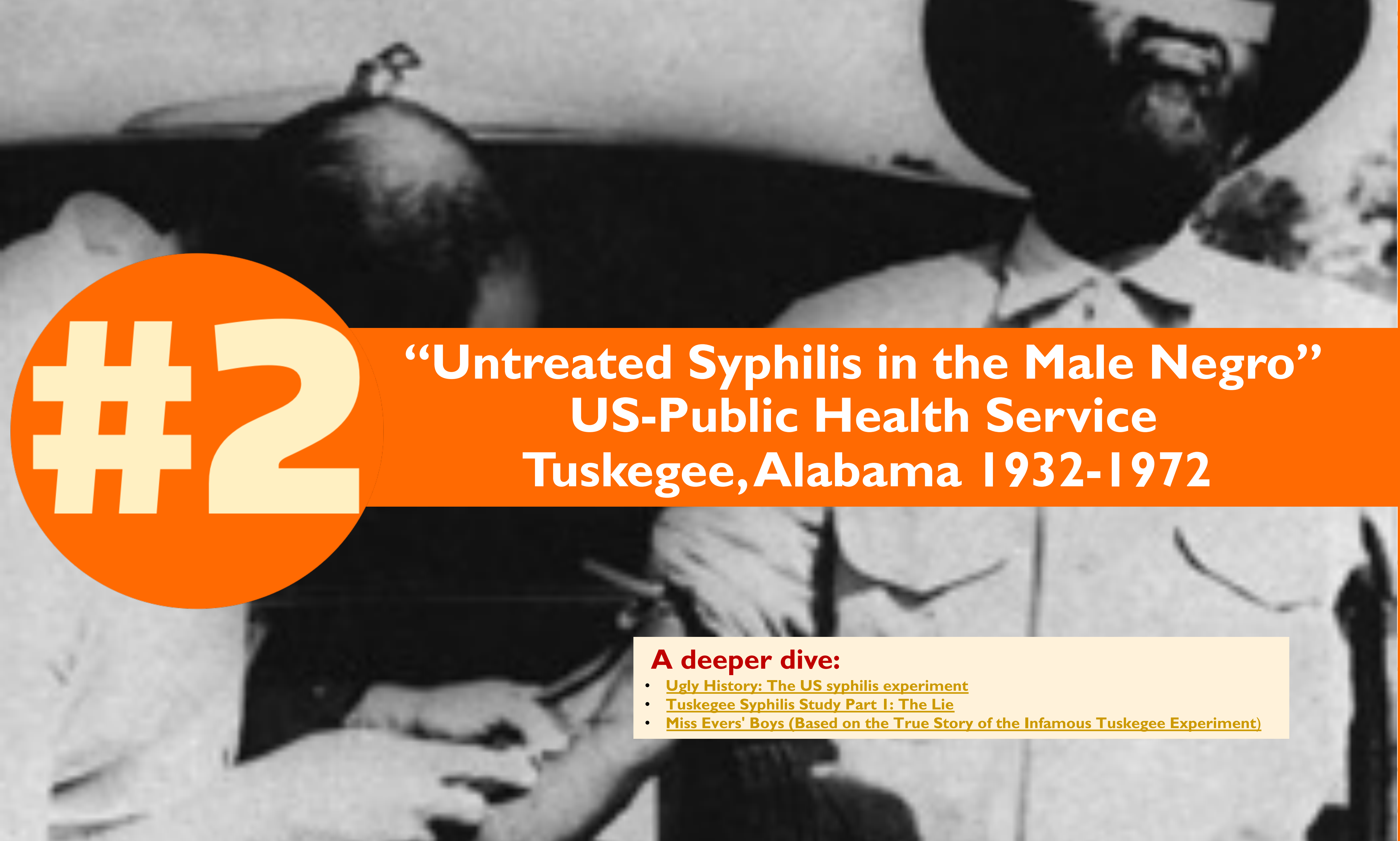


#2

“Untreated Syphilis in the Male Negro”
US-Public Health Service
Tuskegee, Alabama 1932-1972

A deeper dive:

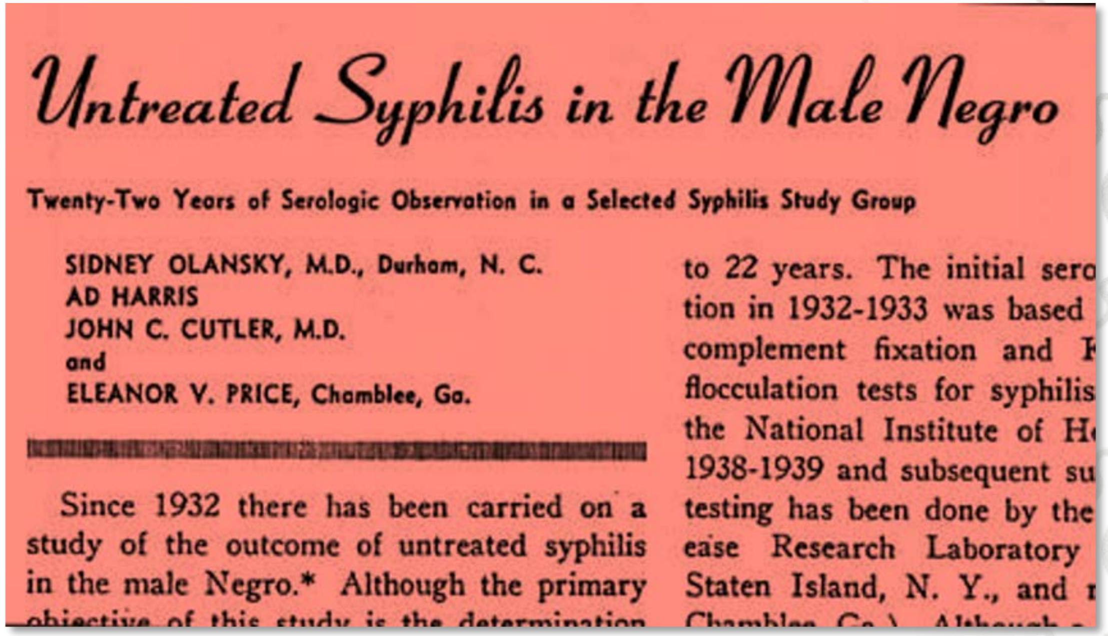
- Ugly History: The US syphilis experiment
- Tuskegee Syphilis Study Part 1: The Lie
- Miss Evers' Boys (Based on the True Story of the Infamous Tuskegee Experiment)

ethical considerations

This study wasn't hidden…

1956

Journal of Chronic Diseases



Untreated Syphilis in the Male Negro

Twenty-Two Years of Serologic Observation in a Selected Syphilis Study Group

SIDNEY OLANSKY, M.D., Durham, N. C.
AD HARRIS
JOHN C. CUTLER, M.D.
and
ELEANOR V. PRICE, Chamblee, Ga.

Since 1932 there has been carried on a study of the outcome of untreated syphilis in the male Negro.* Although the primary objective of this study is the determination

to 22 years. The initial sero tion in 1932-1933 was based complement fixation and K flocculation tests for syphilis the National Institute of H 1938-1939 and subsequent su testing has been done by the ease Research Laboratory Staten Island, N. Y., and Chamblee, Ga.). Although

It wasn't addressed because of **racism** and the power of the **United States Public Health Service.**

It was only after a **1972 New York Times** article 'broke the story' that it was stopped.

A deeper dive:
Bill Jenkins, Who Tried to Halt Tuskegee Syphilis Study, Dies at 73

THE BELMONT REPORT

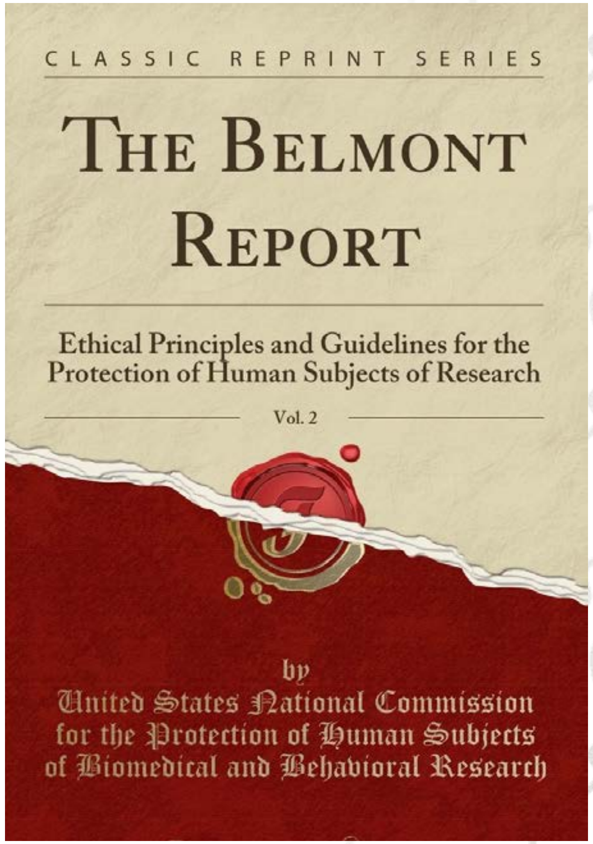
Ethical Principles and Guidelines for the Protection of Human Subjects of Research

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979

Respect for persons: *protecting autonomy, Informed Consent with truthfulness and without deception*

Beneficence: *doing no harm to the participant while maximizing the project's benefits*

Justice: *distributing costs and benefits fairly and equally among participants and potential participants*



CLASSIC REPRINT SERIES

THE BELMONT REPORT

Ethical Principles and Guidelines for the Protection of Human Subjects of Research

Vol. 2

by

United States National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

ethical considerations

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National Research Act, July 1974

Responding to Tuskegee Syphilis Experiment

- Established *National Commission for Protection of Human Subjects*
- Led to 1981 Code of Federal Regulations:

    Institutional Review Boards (IRBs)

    Informed consent
- And the Common Rule harmonizing regulations across all US federal bodies, 1991

Public Law 93-348

Importance of an ethical toolbox for everyone!

Ethical research requires:

- Transparency
- Accountability
- An engaged public that understands and can demand ethical research

ethical considerations

Part 2:
Research Ethics

Contemporary Research Ethics

- Beyond the Belmont Report
- Informed consent

What Makes Research Ethical?

- **Scientific Validity**
  - *Is the research designed well enough to answer the research question?*
- **Social Value**
  - *Is the research likely to foster scientific progress and provide an important benefit to society?*
- **Scalability**
  - *Can the end products of the research eventually be implemented on a large scale to those who need it?*
- **Fair Participant Selection**
  - *Are benefits and burdens equitably distributed between selected research participants and potential research beneficiaries?*
- **Favorable Risk/Benefit Ratio**
  - *Are risks to participants minimized and acceptable in view of personal or social benefits?*

Adapted from Lo and Grady, *Curr Opin HIV AIDS* 2013

What Makes Research Ethical?

- **Informed Consent, Confidentiality, Privacy**
  - *Do participants understand enough to consent? Is what they disclose during research protected?*
- **Community Engagement**
  - *Are communities impacted by the research meaningfully involved at all stages of the research?*
- **Independent Review**
  - *Will the research be subject to scientific and ethical evaluation by legitimate third parties?*
- **Justice, solidary, & public health ethics – an increasingly recognized value!**
  - *Public health values include the advancement of research justice and the recruitment/involvement of under-represented communities into the research process*

ethical considerations

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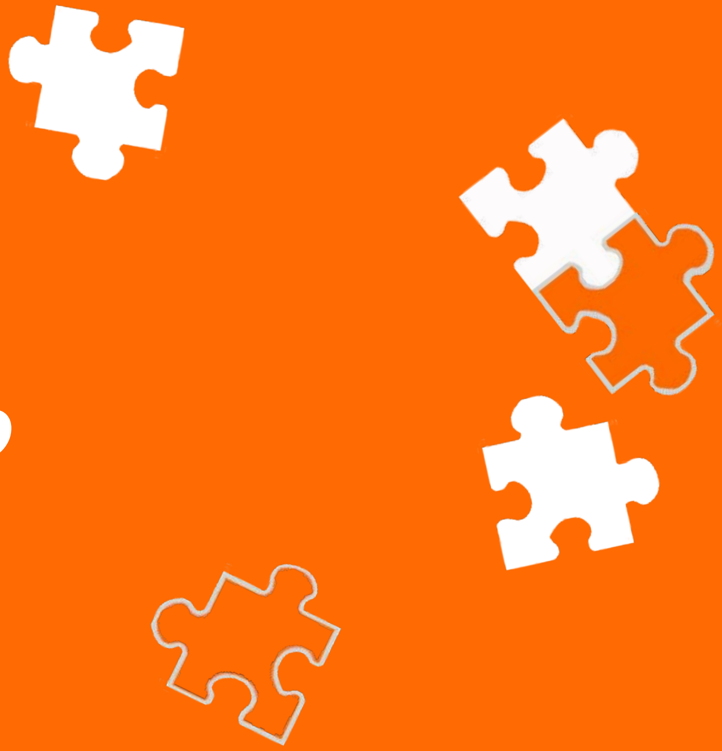
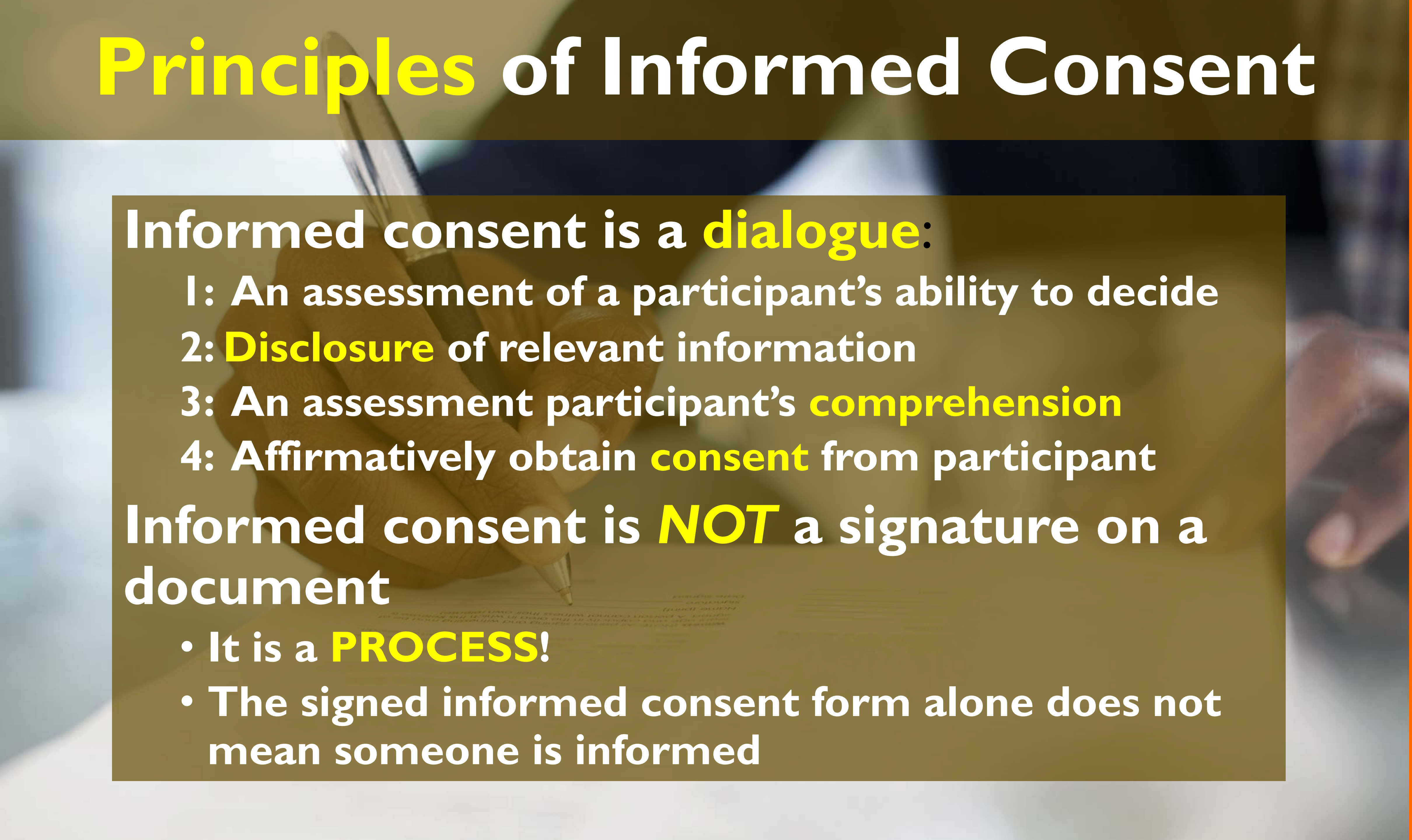
Adapted from Lo and Grady, *Curr Opin HIV AIDS* 2013

A deep dive into ‘Informed Consent’



Principles of Informed Consent



Informed consent is a dialogue:

1: An assessment of a participant’s ability to decide
2: Disclosure of relevant information
3: An assessment participant’s comprehension
4: Affirmatively obtain consent from participant

Informed consent is *NOT* a signature on a document

- It is a PROCESS!
- The signed informed consent form alone does not mean someone is informed

ethical considerations

The ethics underlying Informed Consent in research

Autonomy

- Participants have the right to be fully informed of the procedures, tests, interventions
- Participants have the right to have their questions answered and concerns addressed
- Participants have the right to **decide for themselves**

Beneficence

- Obligation to maximize potential benefit to the participants
- Obligation to minimize harm to the participants

Non-maleficence

- Doctrine of *primum non nocere* (first do no harm)

Justice

- People should be treated equally
- Research cannot selectively burden certain populations

Agency + Social Justice

- Informed consent forms and conversations must be presented in a way that the potential participant can understand – attention to health literacy

Required Elements of Informed Consent

1. The study involves research; explanation of study purpose, procedures and duration
2. Reasonably foreseeable risks/discomforts
3. Benefits to participants/others; lack of direct benefit should be stated; inclusion of potential societal benefits
4. Alternative possibly advantageous procedures and treatments
5. Confidentiality of records identifying the participant
6. Explanation of compensation and/or treatments if injury occurs when risk is greater than minimal
7. Whom to contact for answers to questions
8. Participation is voluntary; refusal will involve no penalty/loss of entitled benefits; discontinue participation at any time

Possible Challenge to Informed Consent

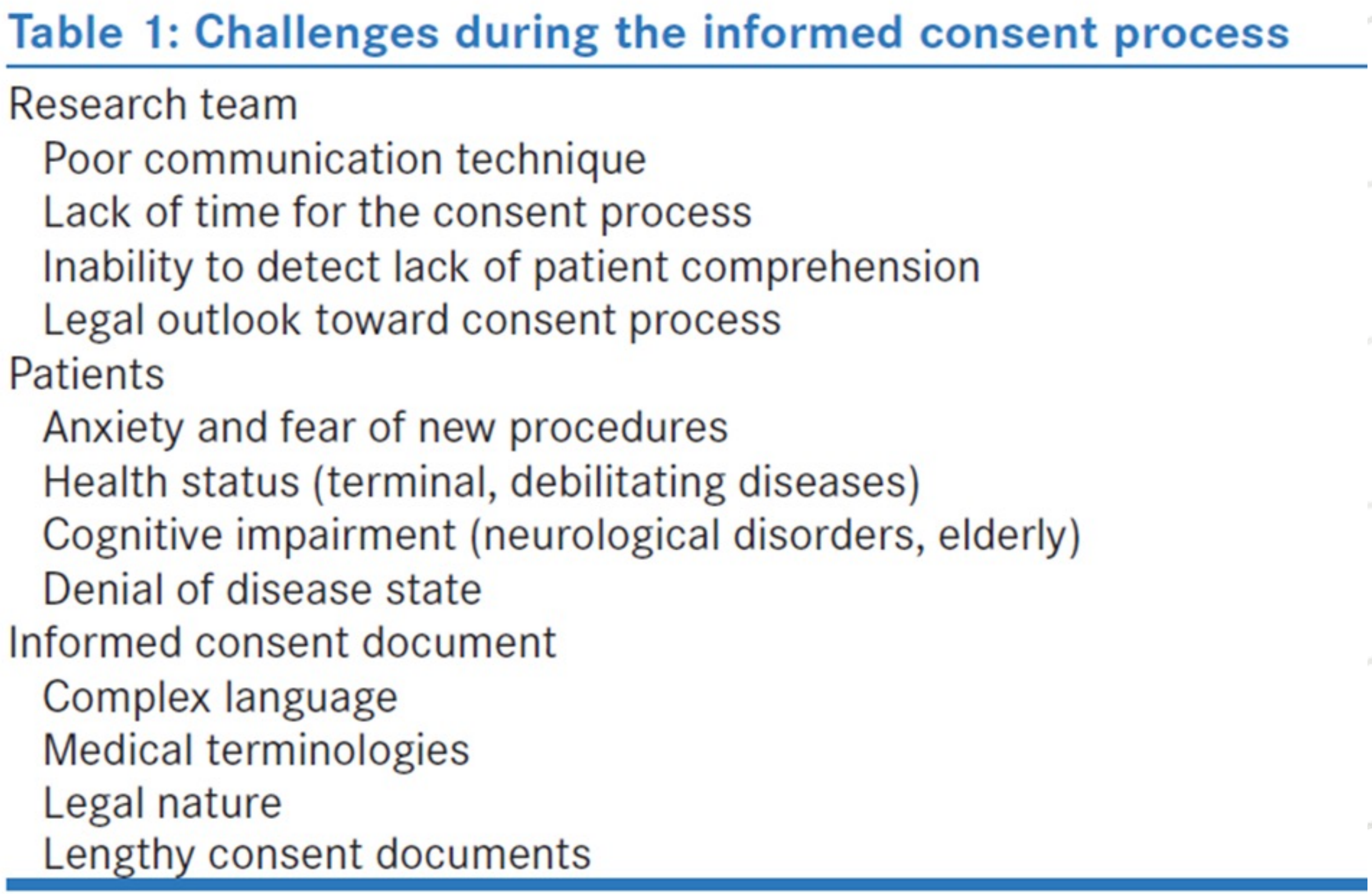


Table 1: Challenges during the informed consent process

- Research team
  - Poor communication technique
  - Lack of time for the consent process
  - Inability to detect lack of patient comprehension
  - Legal outlook toward consent process
- Patients
  - Anxiety and fear of new procedures
  - Health status (terminal, debilitating diseases)
  - Cognitive impairment (neurological disorders, elderly)
  - Denial of disease state
- Informed consent document
  - Complex language
  - Medical terminologies
  - Legal nature
  - Lengthy consent documents

Kadam RA. Informed Consent Process: A Step Further Towards Making It Meaningful!
Perspectives in Clinical Research 2017; 107 – 12.

Making Informed Consent Meaningful

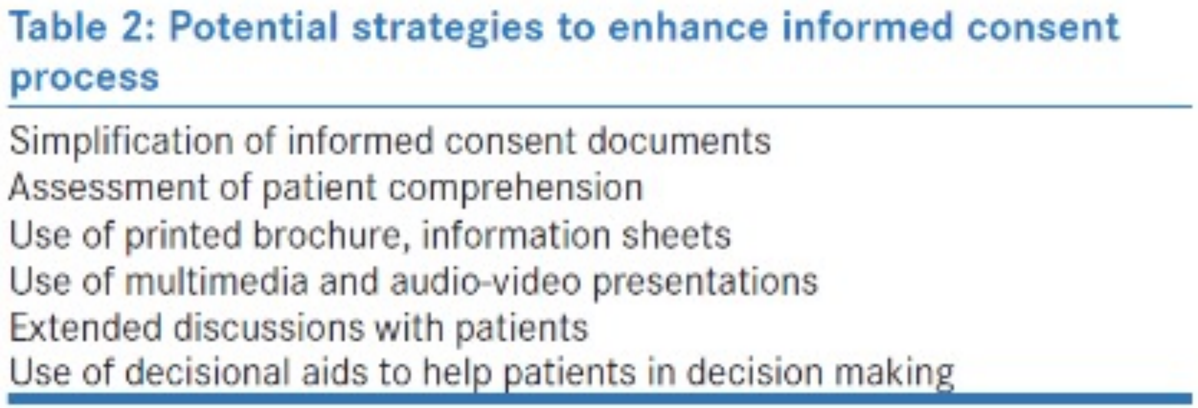


Table 2: Potential strategies to enhance informed consent process

Simplification of informed consent documents
Assessment of patient comprehension
Use of printed brochure, information sheets
Use of multimedia and audio-video presentations
Extended discussions with patients
Use of decisional aids to help patients in decision making

Continuous, dynamic process rather than one-time, isolated event

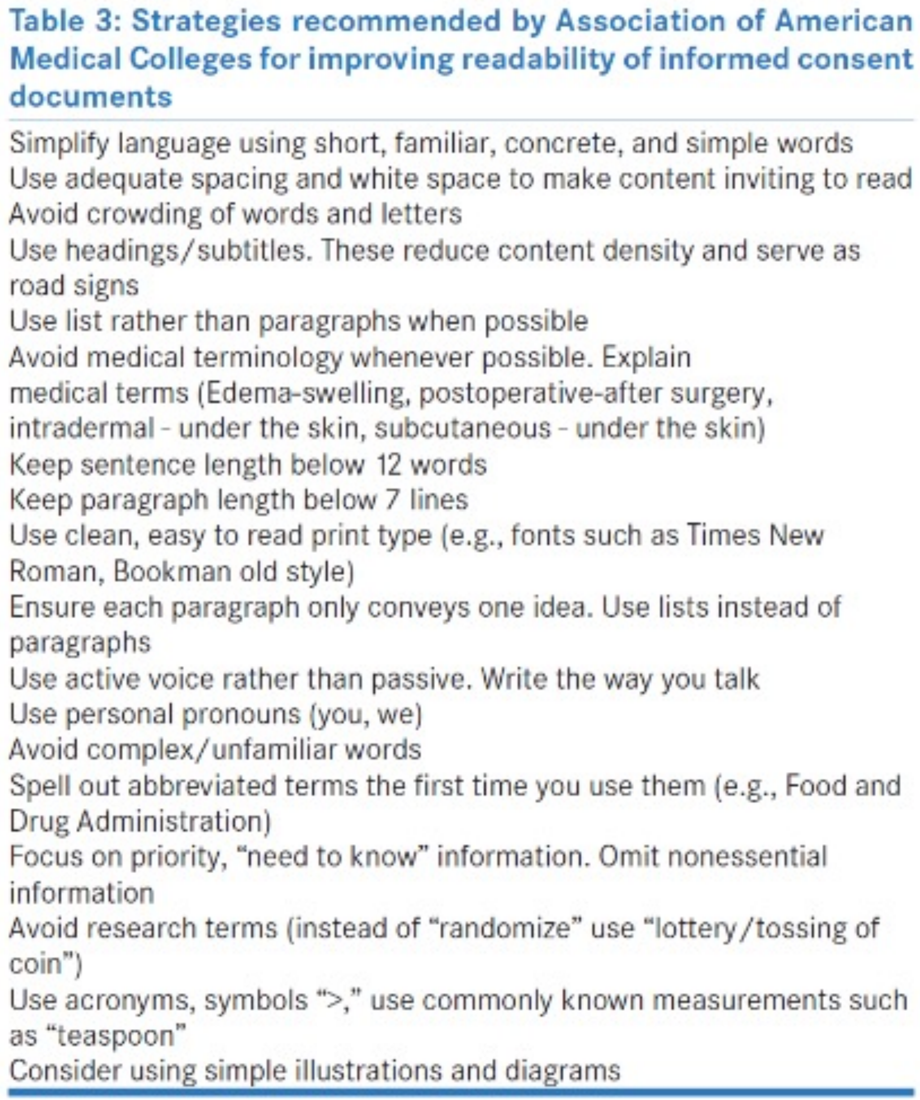


Table 3: Strategies recommended by Association of American Medical Colleges for improving readability of informed consent documents

Simplify language using short, familiar, concrete, and simple words
Use adequate spacing and white space to make content inviting to read
Avoid crowding of words and letters
Use headings/subtitles. These reduce content density and serve as road signs
Use list rather than paragraphs when possible
Avoid medical terminology whenever possible. Explain medical terms (Edema-swelling, postoperative-after surgery, intradermal - under the skin, subcutaneous - under the skin)
Keep sentence length below 12 words
Keep paragraph length below 7 lines
Use clean, easy to read print type (e.g., fonts such as Times New Roman, Bookman old style)
Ensure each paragraph only conveys one idea. Use lists instead of paragraphs
Use active voice rather than passive. Write the way you talk
Use personal pronouns (you, we)
Avoid complex/unfamiliar words
Spell out abbreviated terms the first time you use them (e.g., Food and Drug Administration)
Focus on priority, "need to know" information. Omit nonessential information
Avoid research terms (instead of "randomize" use "lottery/tossing of coin")
Use acronyms, symbols ">," use commonly known measurements such as "teaspoon"
Consider using simple illustrations and diagrams

Kadam RA. Informed Consent Process: A Step Further Towards Making It Meaningful! *Perspectives in Clinical Research* 2017; 107 – 12.

Who ensures the Informed Consent process is ethical?

Institutional Review Boards *(IRBs for short)*

- Because of the Belmont Report, **all institutions receiving federal money to conduct research** must have an IRB.
- The IRB must have researchers AND community representation.
- One important job of the IRB is to make sure the recruitment process **is fair and just** and that the informed consent process and documents are **clear and truthful**.

Other Regulatory Bodies

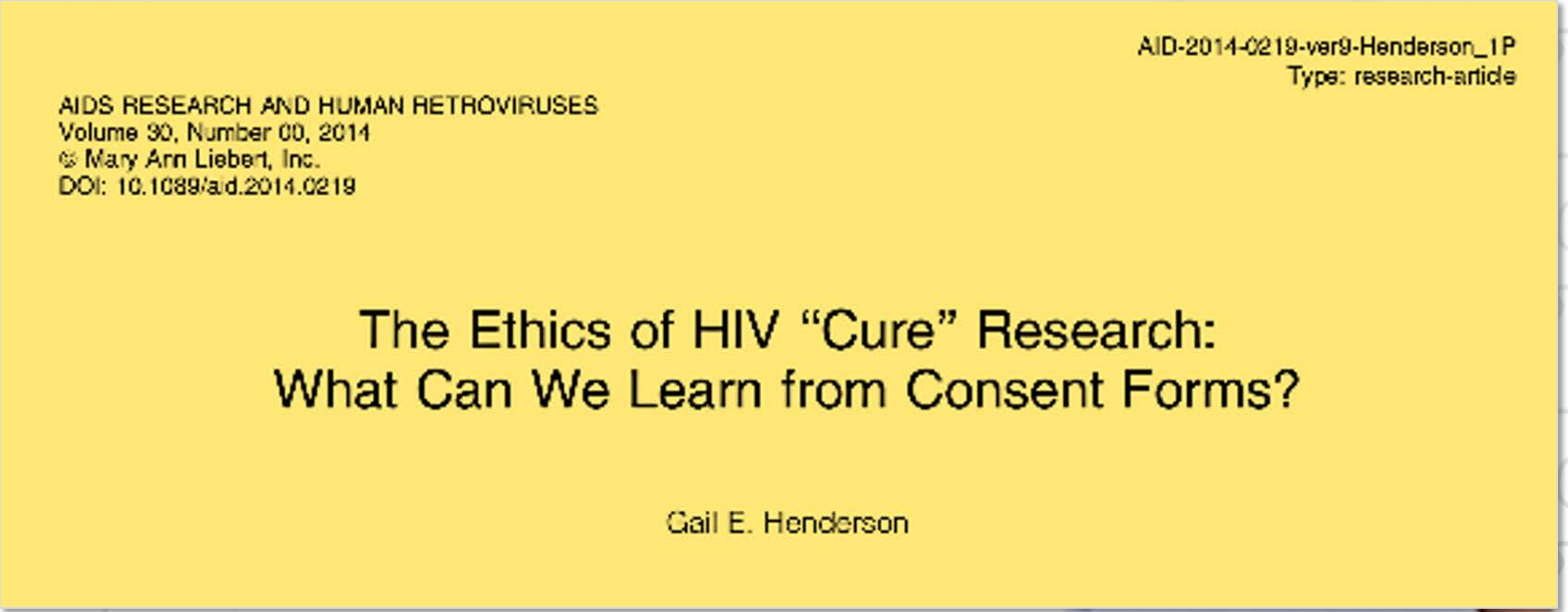
1. Scientific Review Committees

Committees within institutions that review investigator's study plans to make sure that they are scientifically sound – does the plan for the study actually provide information that answers the question.

2. DSMB (Data and Safety Monitory Board)

Sometimes a DSMB will be asked to monitor the data that a study is finding to make sure that the study continues to maximize benefit while minimizing harm

A Question:



AID-2014-0219-ver9-Henderson_1P
Type: research-article

AIDS RESEARCH AND HUMAN RETROVIRUSES
Volume 30, Number 00, 2014
© Mary Ann Liebert, Inc.
DOI: 10.1089/aid.2014.0219

The Ethics of HIV "Cure" Research: What Can We Learn from Consent Forms?

Gail E. Henderson

Part 3:
Ethics of HIV Cure-Related Research

Informed Consent in HIV Cure-Related Research

In addition to everything discussed so far, HIV-cure directed research is particularly susceptible to:

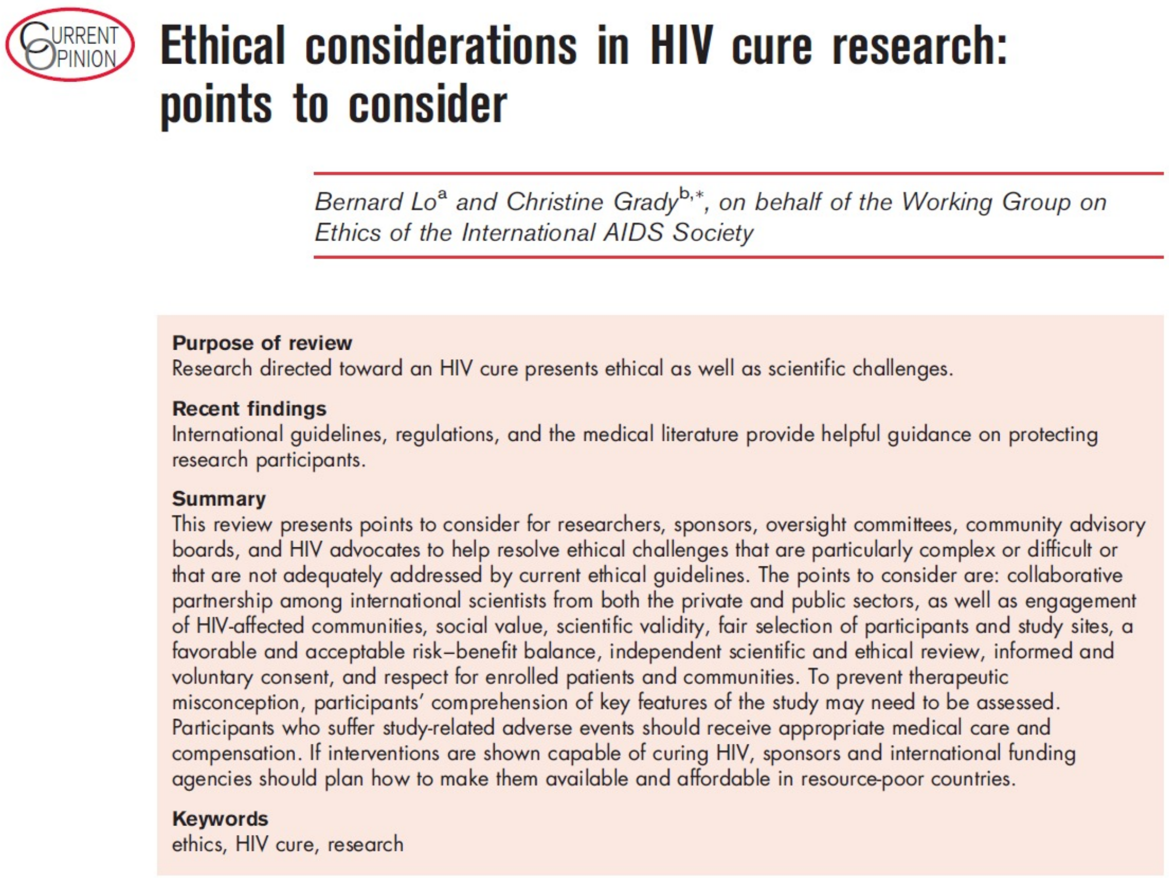
- **Therapeutic Misconception**
  - *False belief that the purpose of the research is personal health benefit for participants*
- **Curative Misconception**
  - *False belief that HIV cure research will provide a cure for research participants*

Informed Consent in HIV Cure-Related Research

HIV cure-related research is scientifically and socially complex. There is a need for **mutual literacy** between communities and researchers

- **Scientific Literacy**
  - Initiatives to translate research terms in to lay language for broader audiences
- **Community Literacy**
  - Initiatives to improve awareness of how cure research engages with the lives of community members and research participants' lives and concerns

General Ethical Considerations HIV Cure Research



Ethical considerations in HIV cure research: points to consider

Bernard Lo[a] and Christine Grady[b,], on behalf of the Working Group on Ethics of the International AIDS Society*

Purpose of review
Research directed toward an HIV cure presents ethical as well as scientific challenges.

Recent findings
International guidelines, regulations, and the medical literature provide helpful guidance on protecting research participants.

Summary
This review presents points to consider for researchers, sponsors, oversight committees, community advisory boards, and HIV advocates to help resolve ethical challenges that are particularly complex or difficult or that are not adequately addressed by current ethical guidelines. The points to consider are: collaborative partnership among international scientists from both the private and public sectors, as well as engagement of HIV-affected communities, social value, scientific validity, fair selection of participants and study sites, a favorable and acceptable risk–benefit balance, independent scientific and ethical review, informed and voluntary consent, and respect for enrolled patients and communities. To prevent therapeutic misconception, participants' comprehension of key features of the study may need to be assessed. Participants who suffer study-related adverse events should receive appropriate medical care and compensation. If interventions are shown capable of curing HIV, sponsors and international funding agencies should plan how to make them available and affordable in resource-poor countries.

Keywords
ethics, HIV cure, research

Ideas and Opinions | 1 October 2013

HIV Cure Research: Expanding the Ethical Considerations

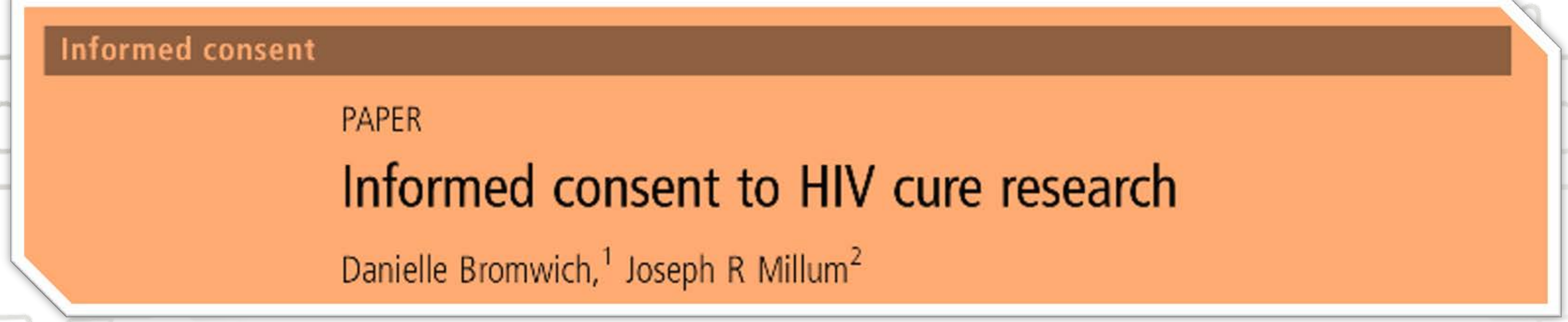
Jeremy Sugarman, MD, MPH, MA

Author, Article and Disclosure Information

https://doi-org.proxy.library.cornell.edu/10.7326/0003-4819-159-7-201310010-00694

Mounting evidence is fueling excitement over the possibility of curing HIV infection. Two "Boston patients" who had bone marrow transplantations (1) and a "Mississippi baby" who was given aggressive antiretroviral therapy (2) soon after birth seem to be free of HIV infection. These accounts add to earlier reports of the "Berlin patient" who lacks evidence of HIV infection after transplantation with cells conferring HIV resistance (3) and members of the Visconti cohort who appear to be free of HIV infection after stopping antiretroviral therapy (4). In aggregate, these findings support the plausibility of "HIV cure research" aimed at eliminating the …

Lo B and Grady C. Ethical Considerations in HIV Cure Research: Points to Consider. *Curr Opin HIV AIDS* 2013, 8: 243 – 9.
Sugarman J. HIV Cure Research. Expanding the Ethical Considerations. *Annals of Internal Medicine* 2013: 159



Informed consent

PAPER

Informed consent to HIV cure research

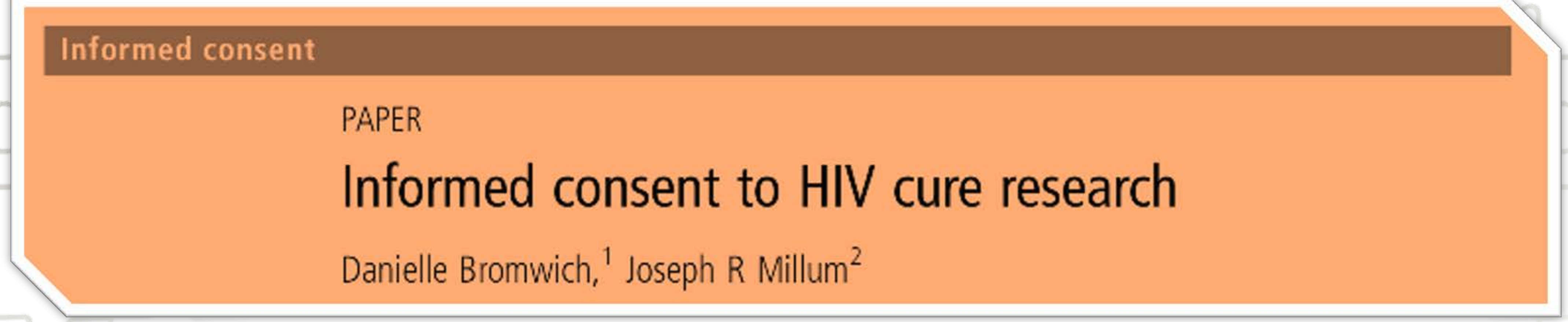
Danielle Bromwich,[1] Joseph R Millum[2]

Research programs that are the first of their kind – like HIV cure-related research – often carry more risk than potential benefit and raise questions about the quality of the consent of research participants

Three concerns:

1. How information is communicated to potential participants
2. Participants' motivations for enrolling in potentially high-risk research with no prospect of direct benefit
3. Participants' understanding of the details of the trials in which they enroll

Bromwich D and Millum JR. Informed Consent for HIV Cure Research.
Journal of Medical Ethics 2017; 43(2): 108 – 12.



Informed consent

PAPER

Informed consent to HIV cure research

Danielle Bromwich,[1] Joseph R Millum[2]

- The research is increasingly focused on achieving **sustained viral remission** – need to use careful language to describe the research

- Participants in early-phase trials tend to **overestimate the benefits** of study participation

Bromwich D and Millum JR. Informed Consent for HIV Cure Research. *Journal of Medical Ethics* 2017; 43(2): 108 – 12.

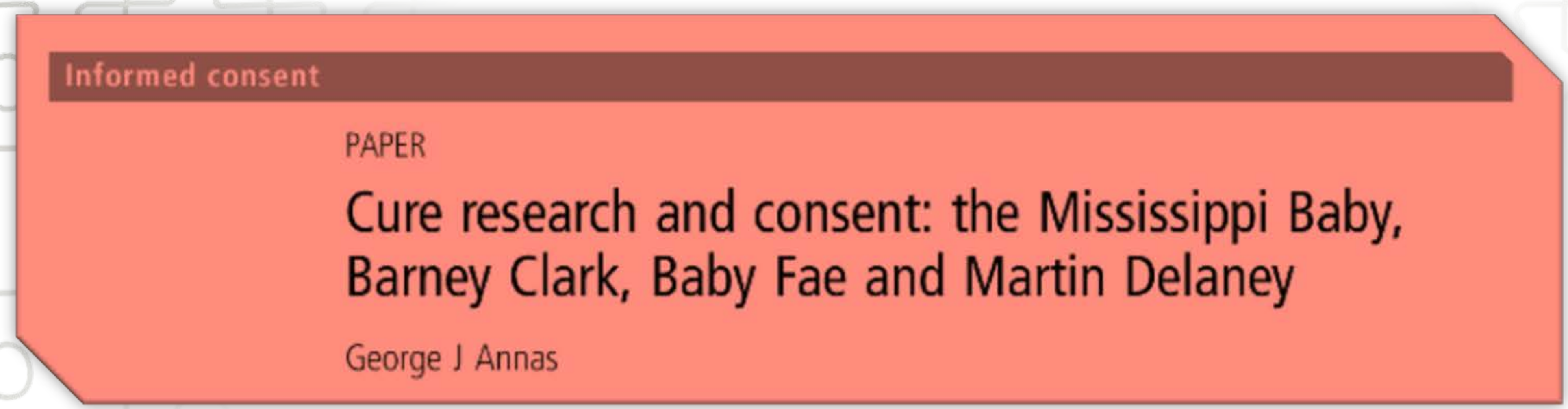
ethical considerations

In other words…

- Many early HIV cure studies will **NOT** have individual medical benefits for participants
- There may be health-related **'side-benefits'** from participation

Side-benefits are positive outcomes related to participation (e.g., better medical care or increased self-esteem) that are not the focus of the study

ethical considerations



Informed consent

PAPER

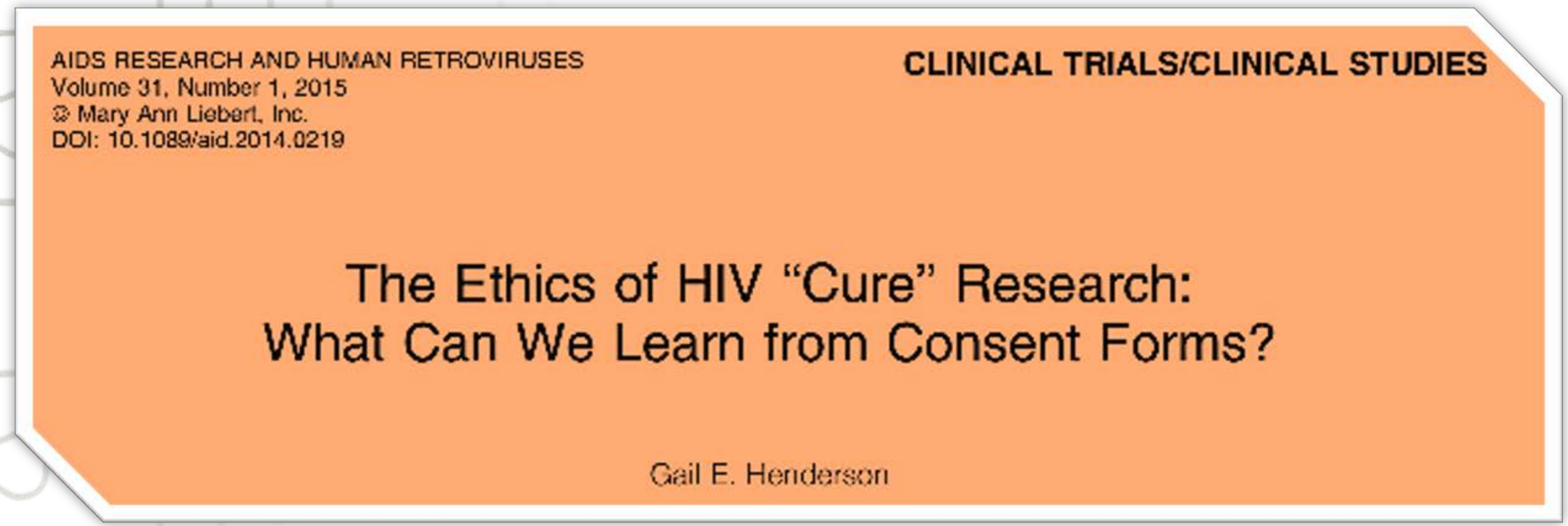
Cure research and consent: the Mississippi Baby, Barney Clark, Baby Fae and Martin Delaney

George J Annas

- Word "cure" should **not** be used in obtaining consent for 'HIV cure' trials
  - *The language we recommend include terms such as …*
- Names of people in past experiments should be avoided in the informed consent process
- These two modest proposals should reduce the risks of the therapeutic misconception in 'cure research'

ethical considerations

Annas GJ. Cure Research and Consent: The Mississippi Baby, Barney Clark, Baby Fae and Martin Delaney. *Journal of Medical Ethics* 2017; 43: 104 – 7.



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CLINICAL TRIALS/CLINICAL STUDIES

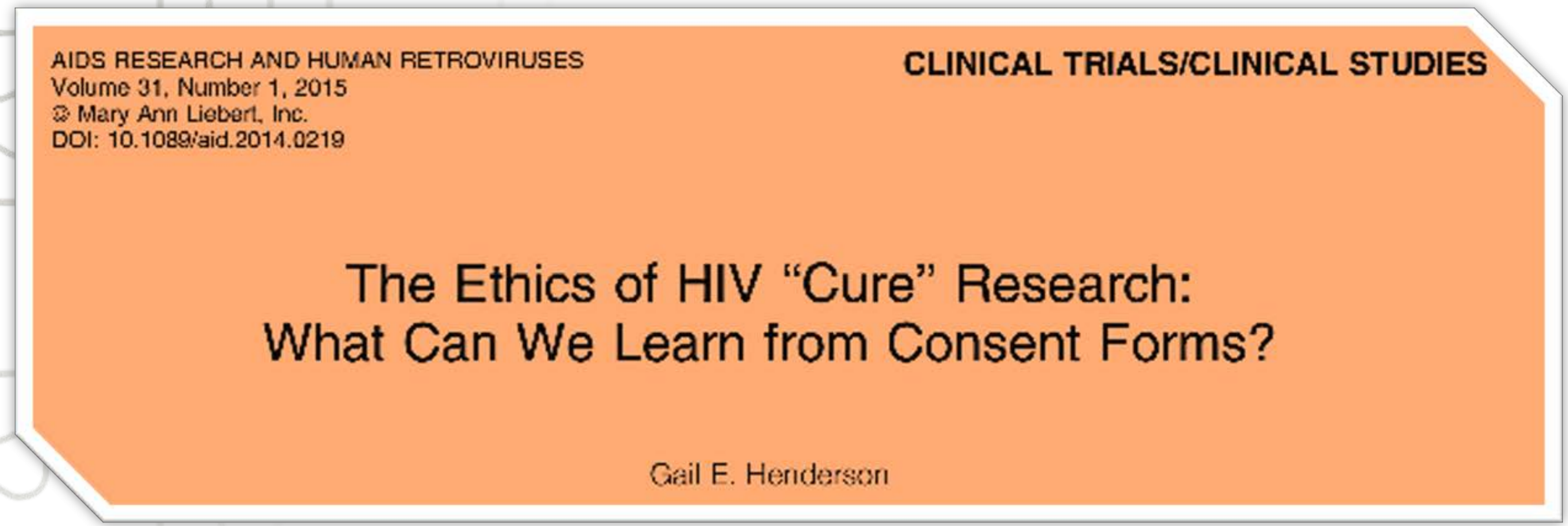
The Ethics of HIV "Cure" Research:
What Can We Learn from Consent Forms?

Gail E. Henderson

- Benefits may potentially be **over-emphasized or over-estimated,** while risks may be less talked about
- Because HIV-cure directed research is so new, there is **less consistency** across studies
- It is ethically important that there be **more consistency** and **clear, specific language** when describing study aims, risks, benefits, and possible return of results

ethical considerations

Henderson G. The Ethics of HIV "Cure" Research: What Can We Learn from Consent Forms?
AIDS Res Hum Retrov 2015; 31(1): 56 – 63.



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CLINICAL TRIALS/CLINICAL STUDIES

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- When recruiting relatively healthy participants into **treatment interruption trials**, treatment interruption is necessary to observe the effectiveness of early interventions
- but they need to be extra ethically careful when asking participants to stop doing something that has been keeping them healthy

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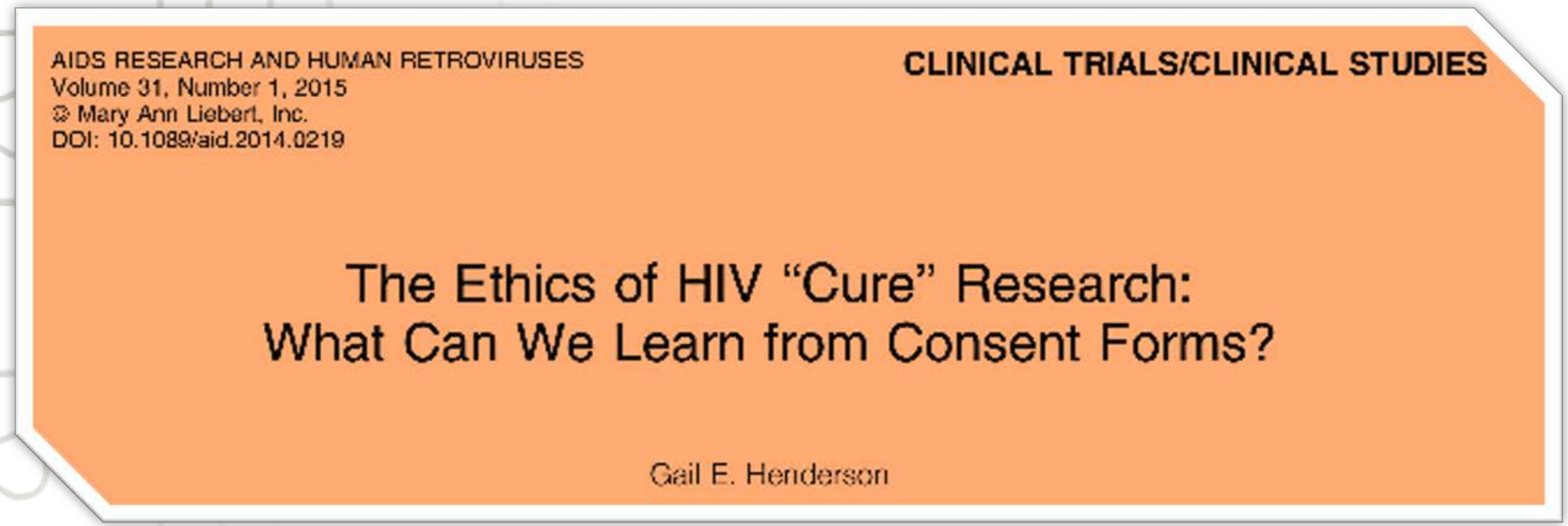

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CLINICAL TRIALS/CLINICAL STUDIES

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- Researchers need to recognize that what they know to be the endpoint of the study – what information they are looking for – is often **not what a participant understands** as an endpoint
- It makes sense that participants without scientific training may not understand the importance of small changes in lab values that don't translate to any changes in how they feel

ethical considerations

CUREiculum

Henderson G. The Ethics of HIV "Cure" Research: What Can We Learn from Consent Forms?
AIDS Res Hum Retrov 2015; 31(1): 56 – 63.

Ethical Highlight:
Language Matters

Shaping Attitudes through Person-First Language

STAMP OUT STIGMA

- puts a person before a diagnosis
- what a person "has" rather than what a person "is”
- avoids marginalization or dehumanization when discussing people with a chronic illness or disability

people with HIV
not HIV-infected people

participants
not subjects
not volunteers

> **"show that language is not merely an instrument for voicing ideas but that it also plays a role in *shaping* ideas"**
> **- beatrice wright**

ethical considerations

Ethical Highlight:

Analytical Treatment Interruption

See separate ATI module for further details

- Analytic treatment interruptions (ATI) are currently an important part of many cure-related studies.
- ATI studies **ask participants to pause ART**. Viral loads and health status are very closely monitored in ATI studies. They have a stopping point if viral loads get too high.
- ATIs may have notable risks, but there's much uncertainty. Examples include:
    - If or when **HIV will come back?**
    - More durable **inflammation?**
    - **Increased risk** of HIV transmission?

ethical considerations

Social and Ethical Considerations of ATIs

See separate ATI module for further details

REVIEW *Journal of Virus Eradication* 2017; 3: 82–84

Interrupting antiretroviral treatment in HIV cure research: scientific and ethical considerations

Samual A Garner[1]*, Stuart Rennie[2], Jintanat Ananworanich[3], Karine Dube[2], David M Margolis[4,5], Jeremy Sugarman[6], Randall Tressler[7], Adam Gilbertson[2] and Liza Dawson[8]

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[2] University of North Carolina at Chapel Hill, NC, USA
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[7] Division of AIDS, National Institute of Allergy and Infectious Diseases, Bethesda, MD, USA; Contractor, Columbus Technologies and Services Inc, Bethesda, MD, USA
[8] Division of AIDS, National Institute of Allergy and Infectious Diseases, Bethesda, MD, USA

Recommendations for analytical antiretroviral treatment interruptions in HIV research trials—report of a consensus meeting

Boris Julg, Lynda Dee, Jintanat Ananworanich, Dan H Barouch, Katharine Bar, Marina Caskey, Donn J Colby, Liza Dawson, Krista L Dong, Karine Dubé, Joseph Eron, John Frater, Rajesh T Gandhi, Romas Geleziunas, Philip Goulder, George J Hanna, Richard Jefferys, Rowena Johnston, Daniel Kuritzkes, Jonathan Z Li, Udom Likhitwonnawut, Jan van Lunzen, Javier Martinez-Picado, Veronica Miller, Luis J Montaner, Douglas F Nixon, David Palm, Giuseppe Pantaleo, Holly Peay, Deborah Persaud, Jessica Salzwedel, Karl Salzwedel, Timothy Schacker, Virginia Sheikh, Ole S. Søgaard, Serena Spudich, Kathryn Stephenson, Jeremy Sugarman, Jeff Taylor, Pablo Tebas, Caroline T Tiemessen, Randall Tressler, Carol D Weiss, Lu Zheng, Merlin L Robb, Nelson L Michael, John W Mellors, Steven G Deeks, Bruce D Walker

- **Scientific utility of ATIs**
- **Risk thresholds**
- **Equitable participant selection**
- **Fostering agency of participants**
- **Study design and monitoring, considering sexual partners**
- **Meaningful and contextual Informed consent**

ethical considerations

Image credit: Michael Louella

In other words…

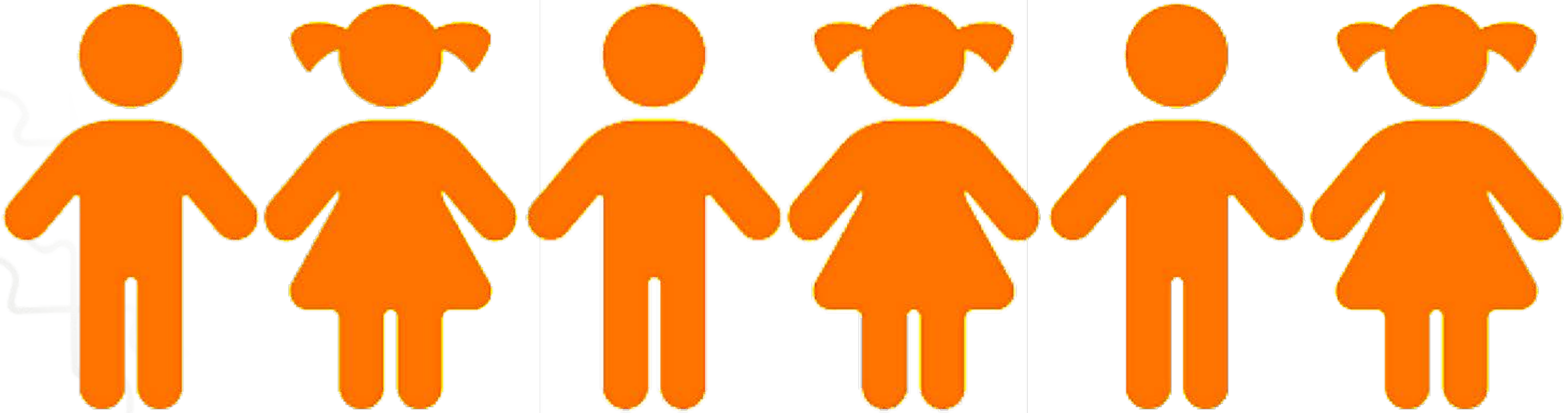
- Cure trials will **ultimately require an interruption** of antiretroviral drugs in order to **determine** if a participant has been cured
- Ideally, there will be a useful biomarker (a molecule in our bodies, found through blood tests) that can be used to predict success ***BEFORE*** interrupting treatment
- This could limit the risks associated with ATI studies, including periods of uncontrolled virus replication

CUREiculum

ethical considerations

Other HIV Cure-Related Issues

- **Development for special populations (e.g., pediatrics)**
  - *Ethics and regulations require that studies are safe and effective in adults before studies can be done with children.*



Other HIV Cure-Related Issues

- **Trial durations may be very long**
  - *It is not known how long virus will need to remain undetectable once off of antiretroviral treatment before a person can be considered cured*
  - *It is also unclear how long people should be followed for safety in order to detect slowly developing adverse events that may be related to the HIV cure treatment; e.g., cancer risks*

Other HIV Cure-Related Issues

- **Special risks for partners**
  - *Because an ATI study may increase a participant's detectability viral load, it may be more possible to transmit HIV to sexual partners.*

  - *This risk can be addressed through very frequent monitoring of viral load, as well as by giving sexual partners access to PrEP, use of barrier protection, or abstaining from sexual relations during the ATI.*

Part 4:
Conclusions and Take-Aways

ethical considerations

Community and Patient Engagement

- Creation of relationships
- Management of expectations
- Sharing of information
- Meaningful dialogue
- Mutual literacy and understanding

Community Advisory Boards

- Input into research process
- Sounding board
- Protocol or research review
- Critical safeguard in research process

Recruitment for Clinical Research

- Populations of interest
- Eligibility screening
- Enrollment in clinical research
- Meaningful dialogue

Research

- Systematic work
- Generalizable knowledge
- Research methods
- Informed consent

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AIDS treatment ATAC activists coalition

AIDS ACTION BALTIMORE

MARTIN DELANEY COLLABORATORIES COMMUNITY ADVISORY BOARD

TAG Treatment Action Group

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Michael Louella, *defeatHIV CAB*

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ethical considerations