The Ethics of HIV Cure Research

HIV Cure Research Training Curriculum

Ethics of HIV Cure Research Webinar

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CUREiculum

The HIV CURE research training curriculum is a collaborative project aimed at making HIV cure research science accessible to the community and the HIV research field.

Session Overview

- Understanding research ethics in HIV cure research
- A brief overview of HIV cure strategies
- Selected ethical challenges in HIV cure research
- Potential ethical challenges for specific cure strategies

What is

Ethics?

What is Ethics?

- *What ought to be done?*
- Identifying, analyzing and resolving conflicts of value
- Research with human participants involves values and they can conflict

Ethics is NOT

- Regulations/Law
  - Practice of setting regulations and determining if those regulations are met (e.g. Ethics Review Committee)

Why Do We Care About

Research Ethics?

Nazi Medical Experiments in WWII

Nuremberg Military Tribunal

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15 of 23 guilty, 7 hanged, 5 life sentences

What Are the Values in Research Ethics?

- **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 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?

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

What Are the Values in Research Ethics?

- **Favorable Risk/Benefit Ratio**
  - Are risks to participants minimized and acceptable in view of personal or social benefits?
- **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?

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

Ethics of Prevention, Treatment and Cure Research

Research type	Participant status	Research goal	Selected ethical issues
HIV treatment	HIV positive	Effective suppression of virus, boosting immune system	Risk of drug side-effects; adherence problems
HIV prevention	HIV negative	Effective methods of preventing HIV acquisition	Seroconversion of participants during trial; behavioral disinhibition
HIV cure	HIV positive	Interventions to produce permanently suppress or eradicate HIV	Risk of intervention side-effects; **existence of known effective treatment**

Current Cure Strategies

Examples of Strategies

- **Gene Alteration/Modification**: modifying cells so they are less susceptible to HIV or are better able to kill HIV; modifying the virus so it's less effective
- **Kick and Kill**: approach that stimulates virus production from latent cells and then kills virus particles outside the cell and infected cells
- **Immune Modulators**: category of research that harnesses the innate and adaptive immune system to better recognize and/or fight HIV

Selected Ethical Challenges

What is the Potential Social Value of an HIV Cure?

- For people living with HIV
  - Suspension of cART- daily pill burden and side effects
  - Potential reduction in stigma
- For public health
  - Lower HIV transmission
  - Reduce global spending on HIV care and treatment

What is the Social Value of HIV Cure Research?

- Considerations
  - Burdens and limitation of HIV treatment
  - Cure ≠ the 'end of AIDS' (e.g. TB)
  - Cure research where treatment access is partial?
  - Research on acute infection vs. global burden is chronic
  - Reasons to pursue HIV cure vs. reasons to improve ART or prevention methods

Informed Consent in HIV Cure Research

A free decision to participate in research based on adequate understanding

- **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 Research

HIV cure 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 stakeholders' lives

Favorable Risk/Benefit Ratio

- 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) but are not the focus of the study

What Do We Call Cure Research?

- Study vs. trial. vs experiment
  - Much of the in human research currently has little to no benefit. *Would calling a trial an "experiment" lead to less therapeutic misconception?*
- Control vs remission vs cure
  - The term "cure" has deep emotions that come with the word. Can participants truly give consent in early trials if they believe there is a cure?
- Patient vs participant vs subject
  - What do we call individuals in clinical research that have little to no chance of personal benefit.

Determining Risks

Determining risks

- Risks of study interventions in each approach
- Not all risks known
- All risks, not just physical
  - Identity, social, emotional

Determining *acceptability of* risks

- Studies involving serious co-morbidities
- Studies with competent adults vs. children

Who decides what's acceptable?

- Participants? Ethics committees? Communities?

Ethical Highlight: Treatment Interruption

- Analytic treatment interruptions (ATI) are currently an important part of many cure studies.
- ATIs may have notable risks, but there's much uncertainty. Examples include:
  - Expansion of reservoir?
  - More durable inflammation?
  - Increased risk of transmission?

Ethical Highlight: Treatment Interruption

- Risks can be reduced by:
  - Selection of participants less likely to be harmed by ATI: e.g., co-morbidities, higher CD4, no history of resistance
  - Careful monitoring of viral load and immediate resumption of ART
  - Counseling on barrier protection; consider PrEP for partner(s)

Potential Ethical Challenges of Specific Cure Strategies

Gene Alteration/Modification- Ethical Considerations

- Scalability of the approach
- Off targeting
- Hereditability

Kick and Kill: Ethical Considerations

- Current studies have not shown a substantial reduction in the size of the reservoir
- Possible spread of the reservoir because of reactivation of latently infected cells
- Several therapies being explored are known carcinogens
- Benefits of early phase research accrue to science and society and not the individual

Immune Modulators: Ethical Considerations

- Development of autoimmunity
- Potential to spread the reservoir by mobilizing additional viral targets to activated cells
- Antibodies used in passive immunization have a half life so are not a sustained treatment

Operationalizing Ethics

Protection BEFORE the trial process

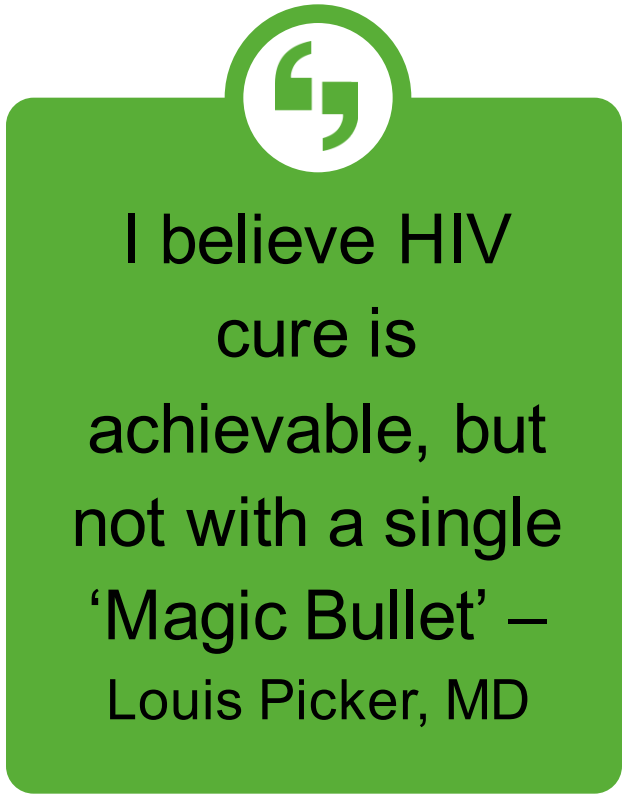
- IRBS/Ethics Review Committees
- CIOMS Guidelines
- WHO Guidelines

Protection DURING the trial process

- Good Clinical Practice
- Data Safety & Monitoring Boards

Conclusions

- HIV cure research is an evolving field and ethical considerations need to be managed throughout the research process with substantial and consistent community participation.



Discussion Questions

- What are your biggest ethical concerns with HIV cure research?
- How concerned are you about the risks of cure research despite the current lack of direct benefit?
- To what extent should HIV cure research be a priority?
- Other questions?

Questions

For additional information visit: **www.avac.org/CUREiculum**

Acknowledgement

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