

Bioethical issues in clinical trials for life-threatening illnesses



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Background

- We are all confronted with and consider how best to make our research 'ethical'
- What should constitute the standard of care in a clinical trial is not always well defined
- In dynamic research contexts with limited access to therapeutics the standard of care in a clinical trial may be superior to that which is routinely available
- Other benefits of participation too - medical care; diagnostics; ancillary care and reimbursements – concerns around structural coercion and the 'empty choice'¹
- Participants are sometimes described as having a ***therapeutic misconception***²
- How does this all impact the decision-making process?

Setting and Methods

- Focus on people living (and hospitalised) with advanced HIV disease
- Ethnographic research within the AMBITION-cm trial for cryptococcal meningitis
- In AMBITION-cm the control arm was the WHO recommended first-line regimen which was not routinely available due to issues with flucytosine access (since resolved)
- Better outcomes in cryptococcal meningitis trials than routine care
- In-depth interviews and observations with 89 participants in Botswana and Uganda – trial participants, surrogate decision makers and researchers¹



Pathways to care

- Heavily contextualised by the severity of the illness and the pathway to care
- Prospective participants have often been through a lot before we meet them
 - **Symptoms of underlying disease**
 - **Impact of HIV and/or cryptococcal meningitis diagnosis**
 - **Convoluted pathways to care**
- Caregivers and surrogate decision-makers have been there too

Previous experience

- Limited/no previous experience with clinical research
- Unaware of concepts such as equipoise and randomisation
- Not aware of the nuanced differences in AMBITION-cm versus routine care
- Difficulty in disentangling research and routine care

Decision making



- Not highly motivated by additional benefits, ancillary care or reimbursements
- Significant fear that diagnostic and therapeutic lumbar punctures would kill them
- Trust placed in trial team, routine care staff, other participants and caregivers who advocated for enrolment
- The trial offered the best possible chance of survival
- Decisions were made based on a ***therapeutic expectation*** from the trial¹
- Researchers highly motivated to recruit participants and want broad inclusion criteria

¹Lawrence DS et al (2022) *Social Science & Medicine*

Therapeutic Expectation

- This is a therapeutic expectation, not a misconception
- We have a responsibility as researchers to acknowledge this and to meet and/or manage these expectations
- What is our role in elevating the standard of care before, during and after a trial?
- Can our aspirations fit within current funding frameworks and how would they impact equity in global health research?
- Qualitative methods research can and does add value +++ to our clinical trials

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