The Dilemma of HIV Clinical Trial Participation—Guinea Pig or Positive Experience

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The Dilemma of HIV Clinical Trial Participation - Guinea Pig or Positive Experience

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Introduction

- HIV remains a threat to global health and economic stability
- Shifts in demographics—↑ rates among blacks, heterosexuals, IVDU, youth, women
- Women now account for ½ of world’s HIV/AIDS cases (Mills et al, 2006)
- In last 15 yrs research has contributed to major advancements—↓ AIDS related deaths where HAART is available—now have issues related to tolerance, viral drug resistance, long-term metabolic complications, dosing schedules (Mills et al, 2006)
- Justifies need for HIV clinical research!!!!
- Successful HIV clinical research = ability to successfully enrol adequate # of subjects + retention & compliance of subjects recruited!
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Introduction

Benefits of participating in an HIV clinical trial are not always obvious to subjects. In fact it can be a difficult decision!!!

A brief literature review of barriers to HIV clinical trials will be presented followed by case studies that draw on our own experiences as research nurses at a McGill university based HIV clinic in Montreal and the challenges we face with our diverse, multicultural population.
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Literature Review

*Lancet Infectious Disease 2006 Journal (Mills et al)*

- Researched qualitative + quantitative studies that addressed anxieties & barriers to HIV clinical trial participation.
- 14 studies reviewed which consisted of 2 open-ended questionnaires, 3 semi-structured, 9 structured questionnaires or interviews.
- Extracted themes from qualitative studies & determined which of these were in quantitative studies.

**Major barriers** to HIV participation included fear of side effects, distrust of researchers, concerns about study design, interference in everyday life or changes in routine, social discrimination. Suspicions of drug 53%, not informed/not eligible 38%, travel 39%, clinical effectiveness 1%.
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Emergent Themes:

- **Safety**
  - Suspicion of drug, fear of side effects, doubts about effectiveness

- **Concerns about Research design**
  - Not informed or misinformed-some subjects thought they weren’t eligible because too sick or not sick enough!
  - Placebo concern.
  - Pill burden & dosage.
  - #appointments.
  - Regular bloods drawn/injections.
  - Seeing other sick patients with HIV.
  - Concerns with clinic setting.
  - Wanting to maintain control.
  - Wanting to be drug free.
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- **Practical concerns**
  - Interference with ADL/changes in routine, childcare/family responsibilities, family dynamics/lack of support, travel, lack of time.

- **Discrimination/social issues**
  - Confidentiality, lack of anonymity, seeing past partners, inadvertent disclosure of HIV status, being perceived as gay.

- **Fear or mistrust**
  - Impact on long-term treatment, experimentation, distrust in researchers/research, treated as a # or guinea pig.

** No quantitative study looked at the following barriers: seeing other sick people with HIV, perception of being treated as guinea pig, concerns about clinic setting, desire to maintain control, family dynamics/lack of support, being perceived as gay, seeing past partners.
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Literature Review

Limitations

- All studies done on medium – high income nations. Greatest burden of epidemic in low-income countries which were not studied.
- Need to focus on hard-to-enrol populations such as women, children, minorities.
- Focusing on common themes may discount the importance of barriers that might be valid for an individual. Therefore, cannot generalize!!
- Quantitative studies did not identify issues that qualitative studies did.
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*Applied Nursing Research Journal 1995 (Morse et al)*

- Site specific socio-demographic recruitment, retention, compliance data was collected at 2 time points.
- HIV care nurses at each site identified factors functioning as barriers to protocol participation.
- Clinicians described strategies used to enhance recruitment, retention & protocol compliance.
- Telephone interviews were conducted.
- Barriers were divided as structural and client centered factors.
- Populations targeted were minorities, substance users, IVDU, sexual partners of HIV infected men, homeless, subjects living in remote areas. 79% men, 21% women, 45% white, 55% non-white.
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Subject centered barriers

- Unemployment
- Hospitalization
- Transportation
- Hospitalization for substance abuse
- Victim of violent crime
- Homelessness
- Incarceration
- Arrested
- Fear of research trials
- Hospitalized for mental illness
- Negative staff attitude
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Structural barriers
- Lack of financial resources
- Lack of staff
- Lack of space
- Restrictive protocols
- Types of protocols
- Lack of medical staff
- Protocol variety

Important points
* The sites that had identified barriers had the most participants because innovative strategies were developed to overcome the barriers!
* Since 1995, no advancements have been made in addressing barriers in vulnerable populations!
Case Study 1

Clarissa is a 40-year-old woman accountant from Burundi, refugee in Canada since September 2005. Patient was gang raped in refugee camp by military officers. Father and 4 brothers were murdered in 1995-2004. She came to Canada leaving behind several children she cared for. Living at the YMCA until November 2005 when she finally finds an apartment. Lives alone and is relatively isolated. Has two African friends she met at YMCA. Friends are unaware of HIV status.

She is very knowledgeable of risks of mutations and resistance if medications are not taken properly.
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Case Study 1

Medical History:
- HIV positive since June 2004. Received antiretroviral in Africa but had to stop them because of immigration to Canada. No opportunistic infections. Started on Septra.
- Hepatitis B surface antigen positive.
- Hepatitis C antibody negative.
- Negative PPD.
- Negative Toxo IgM.
- CD4 count 87.9%.
- Viral load 32,532 copies.
- No known allergies.
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Case Study 1

Which barriers would you anticipate to encounter?

- Immigration status
  - Preoccupied with refugee hearing.
  - Need to evaluate if she has immigration lawyer who is knowledgeable of HIV/refugee issues and conflicts in her country to assist her to prepare for hearing. Protocol initially not her priority!
  - Need to consider the immense losses she has experienced and is presently coping with!!! Is she emotionally and psychological stable to embark on a protocol? Risk for Post Traumatic Stress!!!
  - New country with different social structure and rules! Need to establish trust first & therapeutic relationship!!!
  - Has refugee status & most meds are covered. Unlike in Burundi, she has far more treatment options via commercial route. Not dependant on a clinical trial for access to medication.
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Case Study 1

** Some refugee patients have shown concern about participating in clinical trials for fear that it would affect their refugee hearing. Immigration Canada would know details of their chart because of the access to their medical chart. Confidentiality issues!

- **Education/Literacy level**
  - She was a professional in her country.
  - Has had previous experience with meds and had good general HIV information unlike other refugees.
  - No previous experience with clinical trials! Not aware that had option commercial route vs. clinical trial. Options very limited in her country!
  - Required explanation of treatments available via commercial route vs. clinical trial route.
  - Requires explanation of clinical trials and phases of clinical trials before even discussing details of the trial being offered to her.
  - Knowledgeable of importance of adherence unlike other refugees.
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Case Study 1

Study designs and terms can be complicated!

Housing
- Concerned with finding a home first!
- Preoccupied with living expenses.
- Is it accessible to public transit? How far is it from the medical facility? Remember, clinical trials have frequent visits!!
- Is it in her community?

Employment/Financial
- Recent refugee no work permit yet. Remember, accounting degree not recognized in Quebec!
- Medications are covered by refugee status, if not need to apply for Federal Interim Health Program.
- A clinical trial offers free meds.
Cultural values

- Remember, different ethnic backgrounds, languages, historical experiences and levels of education contribute to mistrust and fears of the clinical trial intentions.
- Need to be culturally sensitive!
- Need to be clear about the purpose of clinical trial, risks, benefits.
- HIV is very taboo in African cultures! Stigma still associated with illness!
- Rape not spoken about openly. Clinical trial participation requires access to their chart! Fear that rape details will be divulged!
- Frequent visits with protocol could mean encountering other Africans from the community. Patients have been known to hide from each other.
- Need to assess cultural values that affect compliance and understanding of HIV.
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Case Study 1

**Cultural values**
- African women tend to be passive in decisions about their health. Value physician’s opinion.
- Require reassurance that participation is voluntary and that they have withdrawal options. Care not affected if decide not to participate!
- Fertility is very valued in African cultures. Not accustomed to using contraception or even condom. Most clinical trials require double barrier methods! Teaching required as to why pregnancy should be avoided while on a trial.

**Isolation/support**
- Refugees are isolated! Family support either in their country or members have been killed!
- At risk for depression!
- A clinical trial offers more structure and closer follow up.
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Case Study 2

Alain is a 28 year old HIV positive male with a long history of IVDU. Diagnosed HIV+ 8 yrs ago & a carrier of the Hepatitis C virus (HCV) which was diagnosed at the same time. He has no allergies, he smokes and drinks alcohol occasionally. Long history of being on the streets – no stable home. Frequent incarcerations. Four years ago, he was started on HAART which he is failing. Has multi-drug resistant virus. Being referred to you for a clinical protocol for salvage therapy.

His lab results were as follows:
- Hep B surface antigen -
- Anti HCV +
- CD4 : 115 cells/µL (11%), ratio 0.1%
- Viral load : 320,000 copies/mL
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Case Study 2

Which barriers would you anticipate to encounter?

- **Arrest/Incarcerations**
  - Before patient was screened for protocol which offered him a low pill burden & simple formulation, he was arrested & incarcerated.
  - Needed to work with outreach nurse at our site & court to request permission to allow the patient to come to protocol visits.

- **Homelessness**
  - Required collaborative work with outreach nurse at our site to help the patient with placement issues once is gets out of jail.
  - At risk for violent crimes, non-compliance & other risks if remains homeless.
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Case Study 2

- **Active Drug Use**
  - Would not be eligible if he continues to actively use. Referral required to Detox. Program.
  - Compliance issues! Poor compliance will affect validity & reliability of data.
  - Potential interactions with study drug!
  - Potential adverse events related to IVDU!

- **Unemployment**
  - Unable to pay for medications via commercial route until applies for welfare & stops spending on drugs!
  - Outreach nurse + social worker required.

- **Transportation Issues**

- **Family support**
  - No friends except has support from mother who is willing to house him.
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Case Study 3

Francois is a 50yr.old businessman, MSM, diagnosed HIV+in 1987. Has been on several extensive HAART regimens in the past and now has a multi-drug resistant virus. He is currently failing his salvage treatment which consists of the following: Fuzeon, Combivir, Videx Ec, Atazanavir, Norvir, Forotovase. His CD4 count is at 84, 8% and viral load at 31, 300 copies. He has participated in several clinical trials in the past. He is very knowledgeable of HIV treatments and HIV. He frequents HIV support groups and has a very supportive boyfriend and family. He is very eager to start a new treatment. He fears his immune system will further weaken and he will become ill.

Which barriers would you anticipate to encounter?
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Case Study 3

- Fear of placebo
  - The patient will still receive standard therapy or study drug. In salvage regimens, it is unethical to receive no treatment at all!

- Safety
  - Need to address safety issues openly & thoroughly ex. DSMB, safety reports.

- Fear of side effects

- Fear of effectiveness and progression of illness

* There are a lot less barriers with an educated, well informed, clinical trial experienced, supported patient!
Future studies should focus on hard-to-enroll populations such as vulnerable populations, ex. women, refugees and minorities.

The barriers highlighted from the literature review should be considered by nurses when involved in the implementation of informed consent process & when considering potential protocol patients. But still cannot generalize!

Nurses need to be culturally sensitive and adopt strategies to enhance recruitment, retention & compliance that are specific to the needs of the population they are treating.

Nurses are well positioned to identify the structural and client barriers specific at their sites and to design strategies to address them in order to successfully enroll & retain more subjects.
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