The HPTN Scholars Program:

Enabling independent investigators in the HIV prevention research field.

Linda-Gail Bekker
The Desmond Tutu HIV Centre
UCT CTU, Cape Town.
Combination, tailored, population/risk specific
Protection and justice

Male circumcision
- Auvert BPloS Med 2005
- Gray R, Lancet 2007

Treatment of STIs
- Grosskurth H, Lancet 2000

Female Condoms

Male Condoms +Lube

HIV Counselling and Testing
- Coates T, Lancet 2000
- Sweat M, Lancet 2011

Microbicides for women
- Abdool Karim Q, Science 2010

Oral pre-exposure prophylaxis
- Grant R, NEJM 2010 (MSM)
- Baeten J, NEJM 2012 (Couples)
- Paxton L, NEJM 2012 (Heterosexuals)
- Choopanya K, Lancet 2013 (IDU)

Post Exposure prophylaxis (PEP)
- Scheckter M, 2002

(Un)conditional cash transfers
- Kohler HP, 2002

Behavioural Intervention
- Abstinence
- Be Faithful

PMTCT
- Cohen M, NEJM, 2011
- Donnell D, Lancet 2010
- Tanser, Science 2013

INNOVATION

Kohler HP, 2002

Karim S, 2014
Exciting clinical science attracts new young talent

“Fred, rumor has it you’re closing in on some profound, elemental truths about the universe, and I wanted to remind you that our research funding specifically prohibits that!”
Odds of Success: first R01

The NIH’s long tail

Although investigators aged 41–45 won more R01 and equivalent grants than did any other age group in 2016, the majority of awards go to researchers over the age of 45.

New investigator: Modular ▼ Non-modular
Established investigator: ▬ Modular ▮ Non-modular

AVERAGE SUCCESS RATES AT NIGMS

- NIH GRANTS AWARDED IN 2016
  - 816 (14.2%)
  - 771 (13.4%)
  - 2,550 (44.2%)
  - 1,629 (28.3%)

- 23.2%* modular
- 24.8%* non-modular
- 17.7% modular
- 19.9% non-modular

*Rates for researchers classified as early-stage investigators
Desperate need for opportunities to:

• Participate in “interim” funding opportunities
• Less fiercely competitive
• Practice some skills
  – Grant writing, project management, budget management, manuscript writing.
• Develop a network
• Give a “leg up” to get pilot data
• Build CV

Without giving up the “day job”!
EPICENTRE OF TUBERCULOSIS AND HIV
<table>
<thead>
<tr>
<th>UCTCTU CRSs</th>
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<tr>
<td><strong>GSH CRS</strong></td>
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<tr>
<td>HPTN 083</td>
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<tr>
<td>AMP/HPTN 081</td>
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<tr>
<td>HVTN 702</td>
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<td><strong>EMA CRS</strong></td>
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<td>HPTN 084</td>
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<td>HVTN 702</td>
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<td>HVTN 705</td>
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<td>ASPIRE</td>
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<td>ECHO</td>
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<td><strong>CIDRI CRS</strong></td>
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<td>HVTN 702</td>
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<td><strong>Protocol Specific</strong></td>
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<td><strong>SATVI CRS</strong></td>
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<td>TB Drugs</td>
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<td>Drug Resistance</td>
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<td><strong>MASI CRS</strong></td>
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Choice!

- More people get their preferences met
- Choice is important from a behavioral perspective – leads to better uptake and persistence
- Allows reach to the whole population, including traditionally hard-to-reach populations
- Mimics what toolbox approach to prevention may be like.....

Atujuna M et al., 2016

HPTN 067, AMP, 075, 076, 082, 083, 084

Questionnaire: TUPP study, CT
So, you would like to be an HPTN scholar?

Making a successful application:
Choosing a project
Choosing a mentor
Increasing the chances of success
Choosing a project

- Get to know what studies are “out there”
- Attend the HPTN meetings ......hear about the studies- understand the project objectives and get familiar with the protocol chairs, protocol numbers and protocol project support.
- Protocols are on the HPTN web sites
- Make contact with chair and discuss possibilities
- Think what interests you, what your capabilities are and when your “cycle” would be
- Consider projects that are
  - 1. recently finished
  - 2. will have data available in your cycle
Think about topics.....

• That are not the primary objectives – protocol team has first tabs on those!
• Explore angles or ideas with existing data
  • Review exploratory objectives
• Explore sub-populations within the data
  • Particular age group, sub-population
• Use the data in new ways
  • Use the data in modeling study
Challenges

• Timing, timing, timing......
• Steer away from primary objectives and discuss secondary objectives- think about exploratory objectives.
Think about mentor....

• Where are they located?
  • Co-located, at another site, another time zone?

• What is their role on the parent study?
  • Will they be able to influence decisions and do they know the parent study?

• How available are they?
  • How busy? How expert? Able to offer mentorship?
  • May still need assistance in particular areas

• How supportive are they?
  • Willing to go out to bat for you?
The case of Dr. Jesne Kistan and ADAPT/HPTN 067 in Cape Town

An International HPTN Scholar in Cycle 1.
A Phase II, Randomized, Open-label, Pharmacokinetic And Behavioral Study Of The Use Of Intermittent Oral Emtricitabine/Tenofovir Disoproxil Fumarate Pre-exposure Prophylaxis (Prep)

Alternative Dosing to Augment PrEP Pill Taking
Overall Purpose:

A Behavioral study to evaluate the feasibility of non daily PrEP regimens.

Recommendations for intermittent usage, compared with daily usage, to provide comparable coverage of risk exposures with pre- and post-exposure dosing, decreased pill requirements, and decreased symptoms.
Overall PI: Robert Grant

Silom Community Clinic
178 HIV-uninfected at risk
MSM/TGW
Bangkok, Thailand
March 2014

Emavundleni Prevention Centre
179 HIV-uninfected at risk WSM
Cape Town, South Africa
June 2013

Harlem Prevention Centre
179 HIV-uninfected at risk
MSM/TGW
NYC (Harlem), USA
Dec 2014
Primary Objective:

To test the hypothesis that recommending non-daily PrEP, compared with recommending daily usage, will be associated with:

- Equivalent **coverage** of sex events with pre- and post-exposure dosing
- Lower **number of pills** needed for coverage and fewer pills used
- Decreased self-reported **symptoms/side effects** (both severity and frequency) during 24 weeks of self-administered use
Secondary Objectives

• To describe safety outcomes including adverse events among all participants and drug resistance and plasma HIV RNA levels among participants who seroconvert

• Assess differences between arms in the acceptability of different PrEP regimens and in perceptions of advantages and disadvantages of different regimens

• Assess differences by arm in adherence

• Develop objective measures of drug exposure by obtaining steady state pre-dose “trough” drug concentration in several biological matrices for participants during a lead-in period of weekly DOT

• Evaluate the potential influence of PrEP usage on:
  – changes in sexual behavior, planning for sex, prediction of risky situations, and recognition of possible HIV exposure from baseline to final on-drug assessment in relation to PrEP optimism
HPTN 067 Design

- **Screening Enrollment**: PK steady state
- **Sex coverage**: IDIs and FGs
- **Qualitative**: Staff, 60 Participants

**Stage 1**: 6 weeks DOT
- 1 dose Weekly for 4 weeks

**Stage 2**: Randomized
- 24 weeks self-administered dosing
- Daily: Once daily dosing
- Time driven: 2 doses/week with post coital boost
- Event driven: pre and post coital dosing
- No more than 1 dose daily and 7 doses/week

**Stage 3**: 4 weeks off drug
- Final Study Visit

**Stage 4**: Wk 34

**Wk 0**
- TDF/FTC

**Wk 34**
294 screened

191 enrolled

179 randomized

103 not enrolled*

- HIV + rapid: 7/6.8%
- Pregnant: 3/2.9%
- Lab abnormality: 3/2.9%
- Not Hep B immune: 29/28.2%
- Other medical/mental: 12/11.7%
- Low HIV risk: 26/25.2%
- Withdrew consent: 1/1%
- Not enrolled in window: 14/13.6%
- Other: 10/9.7%

12 not randomized

- HIV + rapid: 2/16.7%
- Relocated: 3/25%
- Pregnant: 1/8.3%
- Lost contact: 2/16.7%
- Other: 4/33.3%

60 Daily usage

59 Time-driven usage

60 Event-driven usage
PrEP for Younger Women? Jesne’s question.....

- To assess differences in **adherence** between young African women (age: 18-24) and older African woman (age ≥ 25) within the different PrEP dosing regimens.

**ADAPT HPTN 067**: An open label of oral PrEP use by 179 women in Cape Town, South Africa.

- **Majority of women** took oral PrEP when made available in open label.
- **Daily dosing** resulted in good adherence (higher drug levels) & better **coverage** of sex acts, compared to intermittent use.
- **Daily dosing** may foster better habit formation and provide the most forgiveness for missed doses at observed adherence levels.

Bekker, et al Lancet HIV 2017
Tips to a successful application

• Sit down with protocol chair and mentor preferably face to face....
• Consider feasibility, timing, scope
• Clarify which permissions, approvals will be needed and time line for these
• Start **early** to allow time for :
  • Initial drafting of proposal
  • Back and forth with mentor- use this feedback
  • Submission to protocol team – see if mentor can endorse
  • Further potential back and forth - using mentor support
  • Be politely persistent and engaged
  • Trouble shoot with mentor support if things get “stuck”
In the application, articulate

• How this proposal plays to your strengths and capabilities
• Make a compelling case for: Why this? Why you? Why now?
• How it will enhance the overall study, site, HPTN? Be honest about any risks and provide mitigating solutions
• In the mentorship plan: show feasibility, compatibility, realistic expectations
During the project

- Remain in touch and engaged with mentor
- Watch timelines carefully
- Be politely persistent and seek help early if things seem stuck
- Use networking opportunity to seek help in other quarters keeping mentor informed
- Try for F2F mentorship sessions where possible but skype and tele calls also ok
  - Long distance mentorship possible but more challenging
- Take responsibility: Remind mentor, others about timelines, tasks and milestones
- Give enough time for inputs, be responsive to guidance and apologise when timelines are tight!
- Leave sufficient time for report backs and manuscript writing
Good luck!!!!!
Extraordinary opportunity....

To make a difference and translate good ideas into great work ........and saved lives!

Your ordinary acts of love and hope point to the extraordinary promise that every human life is of inestimable value.
Thanks

- The UCTCTU and its CRSs
- Giuseppe, Jill, Christie, Ntando, Lulu, Danielle, Zoh, the CRS leaders
- Other CTUs: PHRU, Aurum, CAPRISA
  - Kathy, Fatima, Glenda, Gavin
- The Networks and Core teams: HVTN, HPTN, MTN, INSIGHT, ACTG, IMPAACT
- Their support teams: LAB, SHARP, FHI
- The DAIDS, NIH program

COMMUNITIES OF VOLUNTEERS IN SOUTH AFRICA