Adherence support approaches in iPrEx and iPrEx OLE

NIH Optimization of Adherence after VOICE meeting

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Roadmap

- Transition in Counseling Approaches: iPrEx to iPrEx OLE
  - Next Step Counseling → Integrated Next Step Counseling
- PrEP education
- Drug level feedback in iPrEx OLE
- Pilot of iText messaging support
- Summary of Lessons learned

Adherence Counseling in iPrEx RCT

- iPrEx RCT enrolled 2,499 MSM and transgender women, completed enrollment in December 2009 and on-drug follow-up in August 2010[1]
- Demonstrated 42% efficacy overall, >90% if drug detected in blood[1,2]
  - Subsequent analyses showed drug detected in ~55% (week 8), varied significantly by site, age, & sexual risk[3]
- Early formative work suggested adherence challenges and participant concerns about reporting missed doses[4]
- iPrEx Adherence Working Group (AWG) identified site practices for adherence counseling and recommended areas for change[5]
  - Next Step Counseling and Neutral Assessment implemented in Sept 2009 during final year of iPrEx

[1]Grant NEJM 2010; [2]Anderson Science Translational Medicine 2012; [3]Liu JAIDS 2014; [4]Vargas IAPAC 2010; [5]Amico AIDS and Behavior 2012

iPrEx OLE

- Prior iPrEx participants offered enrollment into a 72-week Open Label Extension (OLE) beginning June 2011[1]
  - **Participants choice to take or not take PrEP** (allowed to start PrEP within 1st 48 weeks)
  - All participants receive HIV testing, condom provision, STI screening
  - Monthly visits x 3 months, then quarterly
  - Evaluate PrEP uptake, adherence, sexual practices, HIV incidence
- Revisions to adherence counseling approach in OLE:
  - **Combine discussion of behavioral strategies and PrEP in a <u>single</u>, brief, client-centered conversation**
    - Evidence of PrEP as a risk reduction strategy → promote prevention synergies
    - Model comprehensive sexual health protection approach
    - Commonalities in conversations allows merging them to reduce redundancy, streamline, discussion, and save time
    - Feasible to incorporate in clinical practice / PrEP implementation programs
- Revisions to training and support
  - Inclusion of counseling procedures into protocol SSP *from beginning*
  - Shorter training workshops (2-3 days in iPrEx → ½ to 1 day in OLE with boosters)
  - Briefer manual
  - Address confusing steps (needs vs. strategies; examples of tailoring step)
  - Counseling participants in maintenance – how to keep things fresh

[1]**Grant Lancet ID 2014**

Global iPrEx

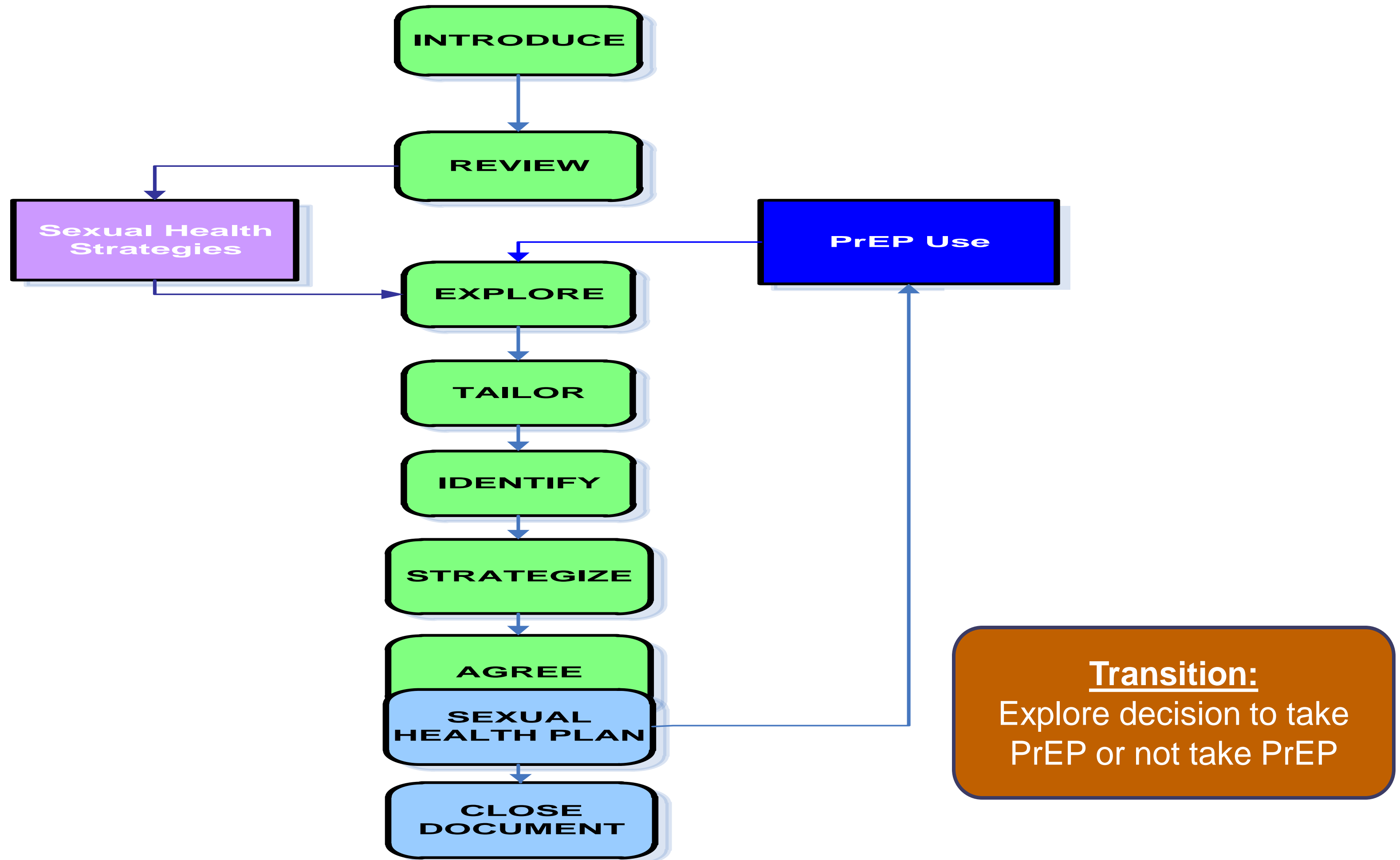
INTEGRATION CHALLENGES

The behaviors (behavioral risk reduction strategies and PrEP adherence) are very different and yet share similarities

- Unique
  - Specific strategies differ
  - Context of implementing difference strategies differ
  - Information, aspects of motivation and skill set for each discrete behavior differ

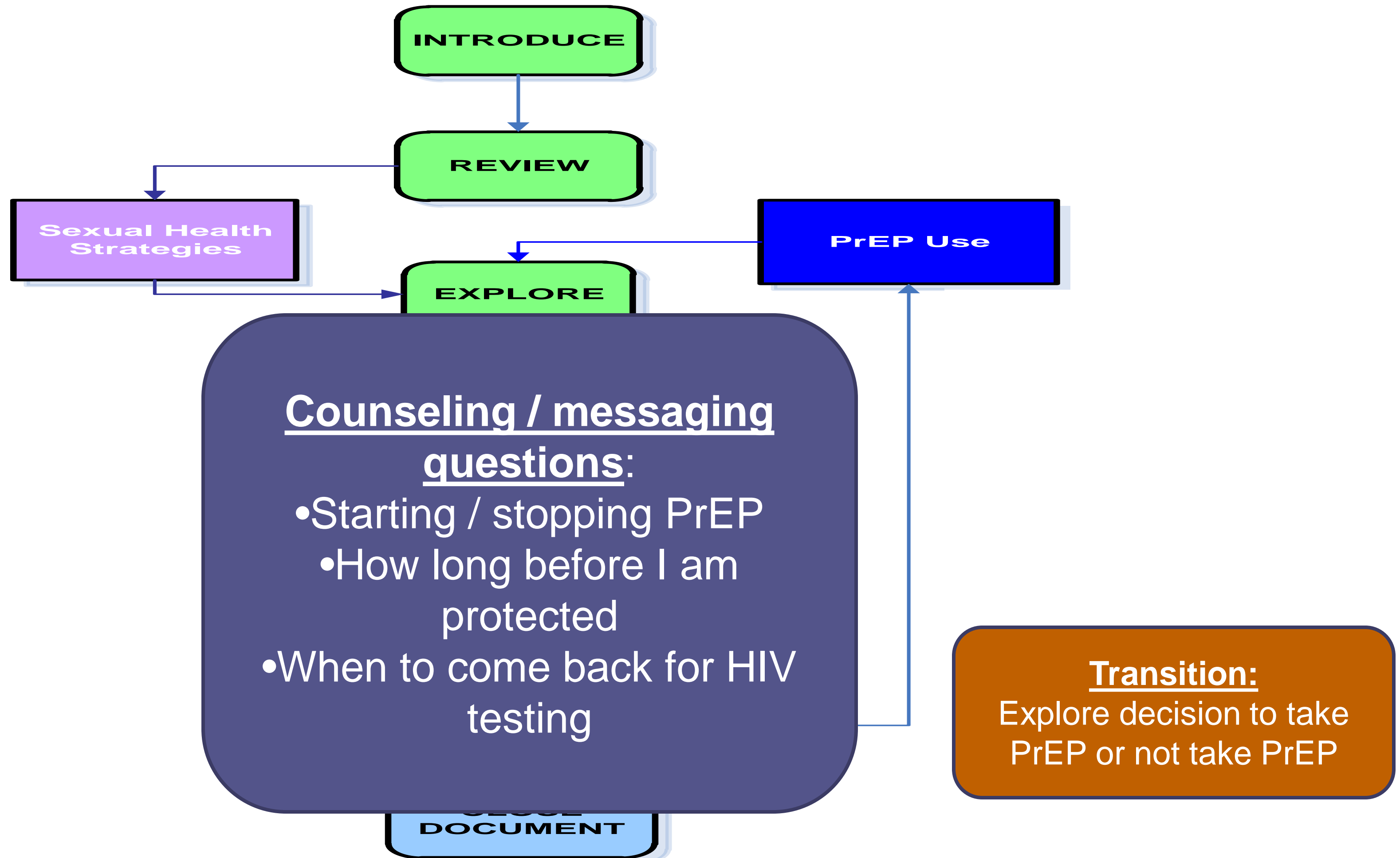
- Common
  - Motivation, commitment or desires for protecting sexual health may be shared
  - Perceived risk for acquiring HIV is consistent; as are perceived benefits of remaining HIV negative
  - Using behavioral strategies and PrEP are part of one's sexual health protection "plan"

Integrated Next Step Counseling



Amico IAPAC 2012

Integrated Next Step Counseling



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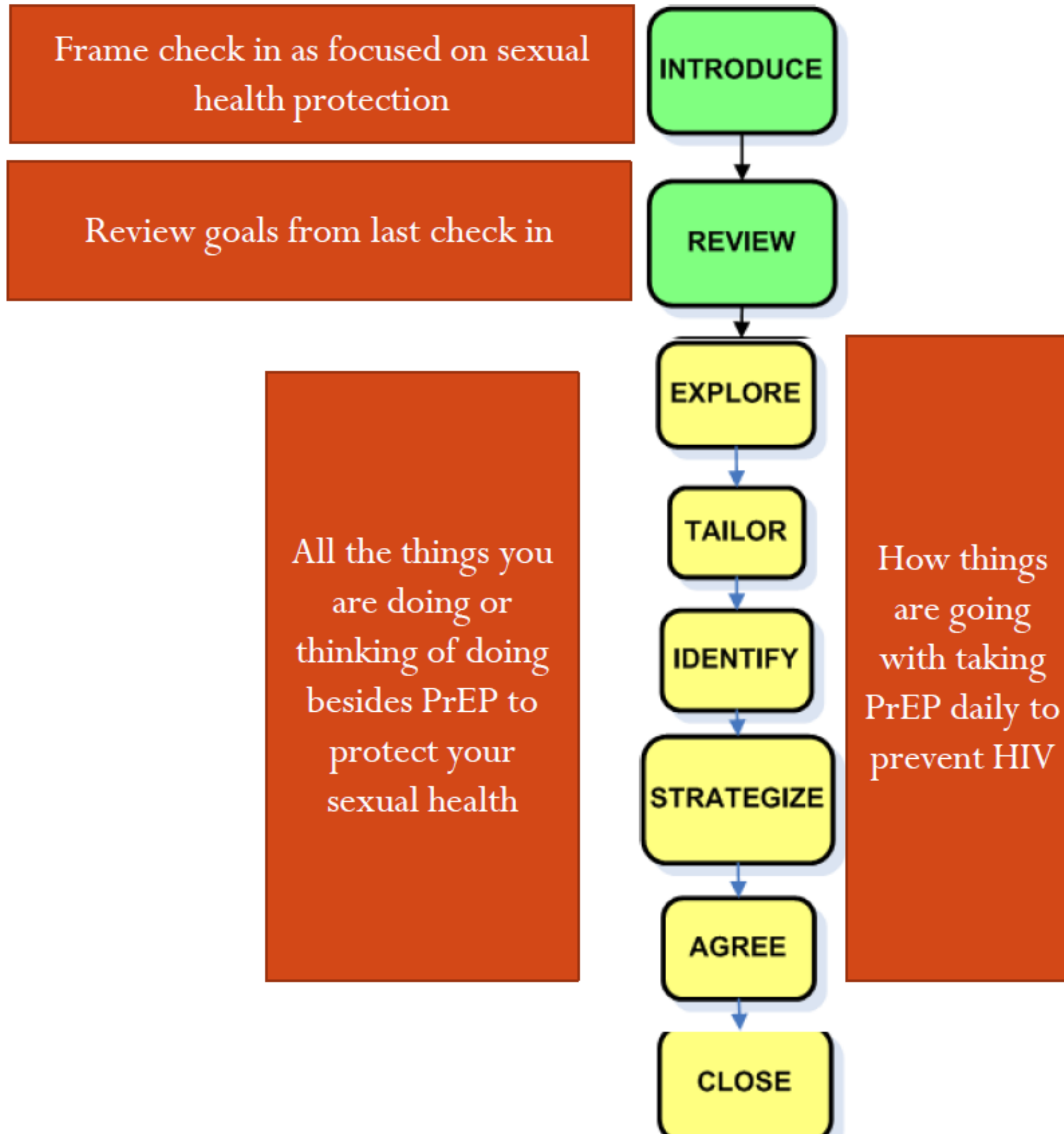

Amico IAPAC 2012

Examples of Tailoring for Adherence Counseling in OLE

Context	Potential options
Reporting many challenging situations	• Keep conversation broad • Focus on 1 challenge • Focus on common themes between challenges
Reporting no challenges (“habit”)	• Ask what changes would break habit? • Ask ppt how they would share with others how to establish habit?
Counseling Fatigue	• Use own words • Be responsive and flexible in discussions to keep discussion fresh
Long-term maintainers	• Explore what’s needed to maintain adherence • Forecast potential challenges • Discuss staying motivated over time

Training: Providing clarifying examples of steps

Needs and Strategies Can Differ….a lot

NEED	STRATEGY
I need to remember dose time	Cell phone reminder
	Take pill with routine activity
I need privacy to take the study pills	Cell phone reminder
I need to feel less side effects	Take with Lunch
I need to make it part of an existing routine	Take with Dinner
I need to take it when I feel calm	Take with Lunch
I need to manage side-effects	Talk to study clinician

Documentation: Counseling CRFs

iPrEx Open Label Study — *Sexual Health Promotion Counseling - iNSC (SHPC)*

DF/Net (iPrEx - OLE) 199 (SHPC) 191

☐ off PrEP ☐ on PrEP ☐ seropositive — Visit Week: ENROLLMENT — *CRF not administered* ☐

Participant ID: ☐☐-☐☐☐☐☐-☐ (*Site*, *Participant Number*, *Chk*) Visit Date: ☐☐ ☐☐☐ ☐☐ (*dd*, *MMM*, *yy*)

Sexual Health Promotion Counseling - iNSC

1 **INTRODUCE:** Introduction to session provided? ☐ *yes* ☐ *no* ☐ *n/a*

2 **REVIEW:** Were the participant's experiences/decisions in the study reviewed? ☐ *yes* ☐ *no* ☐ *n/a* → ***Go to item 3.***

2a. Transition provided? ☐ *yes* ☐ *no*

3 **EXPLORE:** Facilitators ☐ *Not discussed*

3a. Categories: *mark all that apply*

- ☐ *being well informed*
- ☐ *partner(s) supports strategies*
- ☐ *having intimacy with my partners*
- ☐ *other, specify:* ____________
- ☐ *confidence in negotiating strategies with sexual partner(s)*
- ☐ *personal commitment (motivation) to staying HIV negative*
- ☐ *fits well into what I do sexually*
- ☐ *none could be identified*

EXPLORE: Challenges ☐ *Not discussed*

3b. Categories: *mark all that apply*

- ☐ *not feeling well informed*
- ☐ *partner(s) unwilling/reluctant/against to practice strategies*
- ☐ *thinking partners are HIV-negative without really knowing their status*
- ☐ *feeling down/sad (not caring about protecting self)*
- ☐ *drug or alcohol use (making decision making difficult)*
- ☐ *other, specify:* ____________
- ☐ *specific incentives to not use strategies (pay or trade)*
- ☐ *fearful of rejection or missed opportunity (ruining the mood)*
- ☐ *interferes with intimacy*
- ☐ *not thinking that getting HIV would be bad*
- ☐ *caught up in the moment*
- ☐ *none could be identified*

4 **TAILOR:** Level of engagement in this part of counseling: ☐ *low* ☐ *medium* ☐ *high*

5 **IDENTIFY needs:** (What) ☐ *Not discussed*

5a. Categories: *mark all that apply*

- ☐ *feel better informed*
- ☐ *have access to strategies (condoms, HIV testing, lube)*
- ☐ *feel more motivated*
- ☐ *social support*
- ☐ *other, specify:* ____________
- ☐ *be assertive/confident*
- ☐ *have strategies that are sexy/fit into sexual life*
- ☐ *have better concrete skills around negotiating strategies with partners*
- ☐ *basic living needs met (housing, food, safety)*
- ☐ *none could be identified*

6 **STRATEGIZE:** Strategies discussed? ☐ *yes* ☐ *no*

7 **AGREE on:** Strategy and Action Plan

7a. Strategy selected? ☐ *yes* ☐ *no* → ***End of form.***

7b. Action Plan? ☐ *yes* ☐ *no*

Version 1.0, 01-APR-11 — Completed by: ____________ *(initials/date)*

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iPrEx Open Label Study — *Study Pill Counseling - iNSC (SPC)*

DF/Net (iPrEx - OLE) 199 (SPC) 190

☐ off PrEP ☒ on PrEP ☐ seropositive — Visit Week: ENROLLMENT — *CRF not administered* ☐

Participant ID: ☐☐-☐☐☐☐☐-☐ (*Site*, *Participant Number*, *Chk*) Visit Date: ☐☐ ☐☐☐ ☐☐ (*dd*, *MMM*, *yy*)

Study Pill Counseling - iNSC

1 **INTRODUCE:** Introduction to session provided? ☐ *yes* ☐ *no* ☐ *n/a*

2 **REVIEW:** Were the participant's experiences/decisions in the study reviewed? ☐ *yes* ☐ *no* ☐ *n/a* → ***Go to item 3.***

2a. Transition provided? ☐ *yes* ☐ *no*

3 **EXPLORE:** Facilitators ☐ *Not discussed*

3a. Categories: *mark all that apply*

- ☐ *mobile/carry tools (e.g pill boxes)*
- ☐ *commitments/protecting self or others*
- ☐ *access*
- ☐ *other, specify:* ____________
- ☐ *match with routine/event*
- ☐ *memory aids/tools (e.g calendar, alarm)*
- ☐ *social support (family, friends, partners)*
- ☐ *none could be identified*

EXPLORE: Challenges ☐ *Not discussed*

3b. Categories: *mark all that apply*

- ☐ *partying/drugs/alcohol*
- ☐ *disruption in routine*
- ☐ *side effects*
- ☐ *other, specify:* ____________
- ☐ *medication (too big, tastes bad)*
- ☐ *forgetting/no doses available*
- ☐ *lack of privacy*
- ☐ *none could be identified*

4 **TAILOR:** Level of engagement in this part of counseling: ☐ *low* ☐ *medium* ☐ *high*

5 **IDENTIFY needs:** (What) ☐ *Not discussed*

5a. Categories: *mark all that apply*

- ☐ *access (have available)*
- ☐ *motivation*
- ☐ *privacy*
- ☐ *other, specify:* ____________
- ☐ *remember*
- ☐ *manage side effects*
- ☐ *social support*
- ☐ *none could be identified*

6 **STRATEGIZE:** Strategies discussed? ☐ *yes* ☐ *no*

7 **AGREE on:** Strategy and Action Plan

7a. Strategy selected? ☐ *yes* ☐ *no* → ***End of form.***

7b. Action Plan? ☐ *yes* ☐ *no*

Version 1.0, 01-APR-11 — Completed by: ____________ *(initials/date)*

iNSC implementation data

- 4371 sexual health promotion and 3345 PrEP use discussions occurred*
- Nearly all iNSC sessions are documented as containing key ingredients (94-99% of steps completed)
- Preliminary data suggest feasibility and acceptability

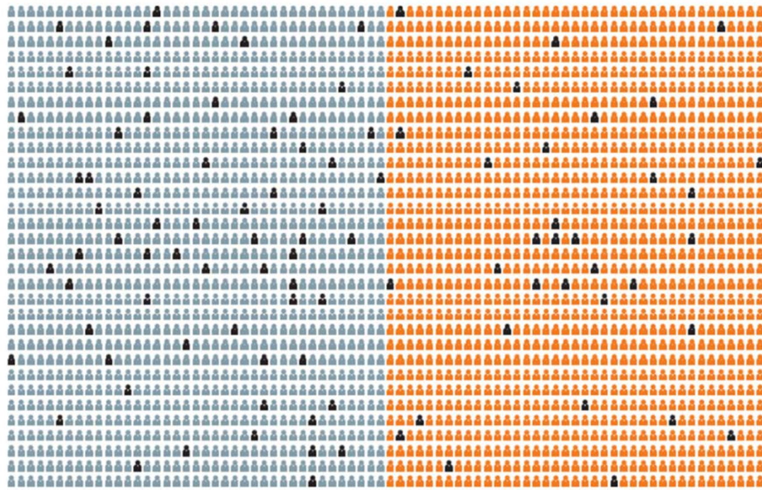
Top 3 most common	Behavioral strategies	PrEP adherence
Facilitators	**1. Personal commitment / motivation (53%)** 2. Feeling well informed (42%) 3. Confidence (31%)	1. Match to existing routine (81%) 2. Carry doses (22%) **3. Personal commitment; memory aids (17% each)**
Barriers	1. Caught in moment (21%) 2. Assuming partner is HIV neg (14%) **3. Drug / Alcohol**; interference with intimacy (11% each)	1. Forgetting dose time or to bring doses; Routine disruptions (31% each) 2. Side effects (9%) **3. Drug / alcohol** (8%)
Needs	**1. Consistent/better access** (41%) 2. More confidence (15%) 3. Motivation; Fit (12% each)	1. Remember / cue (46%) **2. Consistent/better access (27%)** 3. Side effects management (8%)

Amico IAPAC 2012; *based on data through June 2012

Adherence in iPrEx OLE

- Proportion of participants with tenofovir detected in blood plasma was similar in iPrEx OLE vs. iPrEx randomized phase (week 8), varied significantly by site
- Higher drug detection in Peru (44% in RCT to 63% in OLE, p=0.02), similar across other sites
- PrEP drug concentrations in DBS were higher among people of older age, higher education, and higher reported risk
- No randomized evaluation of iNSC – difficult to assess impact

PrEP Education: understanding iPrEx results



Placebo Group
64 HIV Infections

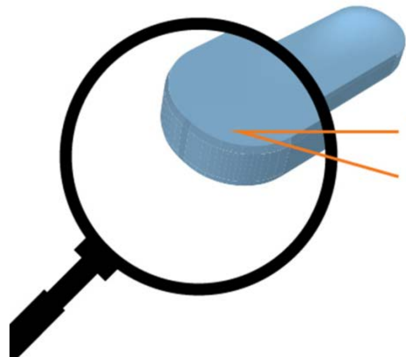
Truvada Group
36 HIV Infections

A reduction of
44%

Placebo Group
64 HIV Infections

Truvada Group
36 HIV Infections

Drug Level Testing checks the levels
of tenofovir and emtricitabine
in the blood of participants taking Truvada
around the time of the blood draw.

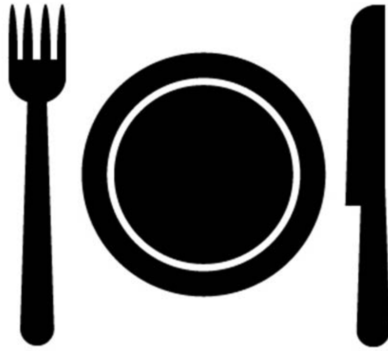


Tenofovir and
emtricitabine are the
two components
of Truvada

Truvada appears to provide protection when it is taken consistently

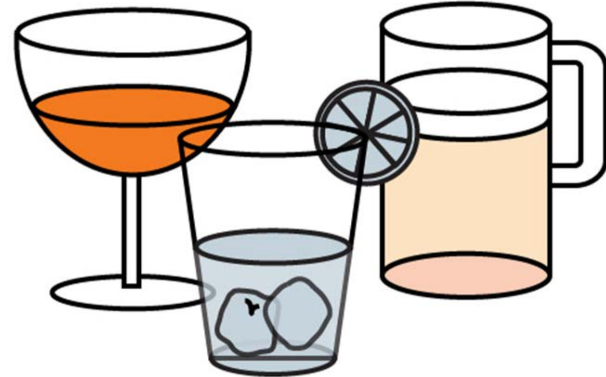
PrEP education: Addressing misconceptions and promoting choice

People can take Truvada...



With or without food

People can take Truvada...



With or without alcohol

Personal choice

Everyone has a choice to take Truvada

or not to take it
as one of their HIV prevention strategies

iPrEx Open Label Extension is about choice
and understanding what helps people
to promote their sexual health
with or without Truvada
as part of their sexual health plan

GLOBAL iPrEx

Single time-point drug-level feedback

- Providing patients with results of PK lab results may promote adherence and/or foster more accurate reporting of adherence
- Blood plasma samples collected in first 12 weeks of study were tested for presence of TFV and FTC
- Study clinicians shared results (detectable/undetectable) with participants at week 24, as part of disclosing lab results
  - Handle negative detection results with care (not penalizing)
- Acceptability of receiving results evaluated through in-depth interviews with subset of OLE ppts in US (n=59)

Koester AIDS Care 2015

Drug level feedback: results

- Half experienced feedback as “non-event”
  - Drug level detection expected (no new information / added value)
  - Information not intended for study ppts
  - “It doesn’t make me feel anything…I know it’s in me. It’s just for their records”
- Other half found results encouraging and affirming
  - Some felt protected, empowered
  - Helped establish they were not on a placebo, metabolism not interfering with absorption
  - “You know it’s working. You know it’s there. You know you’re not doing it just in vain.”
- Reactions from ppts with “no drug detected”
  - Not perceived as threatening or penalizing
  - More likely to provide accurate information
  - Motivated one participant to take PrEP
  - “I guess really after hearing that, that made me really wanna make sure I take it every day”

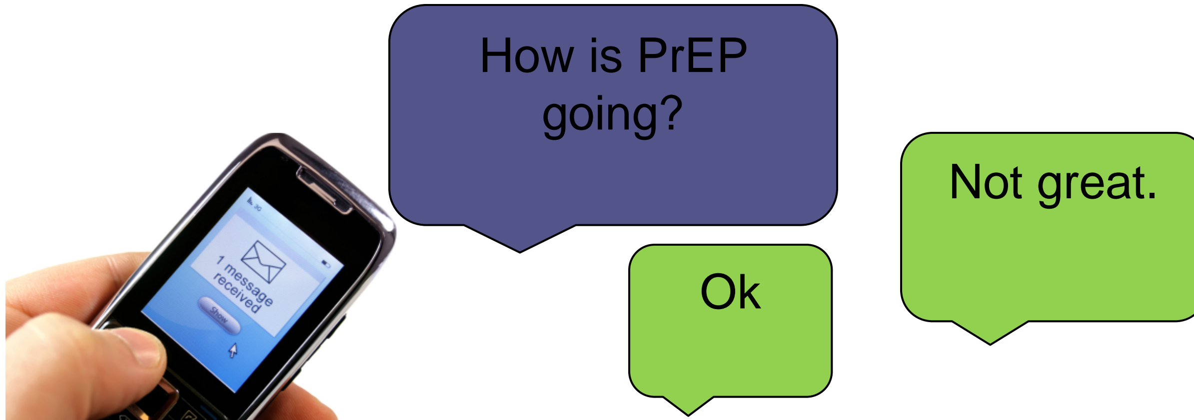
Koester AIDS Care 2015

Drug level feedback: lessons learned

- Need to increase salience of results
  - Reduce time between testing and provision of results
  - Provide results in the context of adherence counseling
  - Provide quantitative results
    - Include information on level of drug needed for protection
    - DBS and hair levels are promising biomarkers

Koester AIDS Care 2015

iText Pilot in iPrEx OLE: SMS/Email Check-ins



- Weekly SMS check-in
  - Are you okay?
  - How are you?
  - How is PrEP going?
- Staff call pt if "not OK"

- Weltel SMS study showed improved adherence and virologic suppression in Kenya for HIV treatment[1]
- 3 month pilot study in iPrEx OLE (SF and Chicago)[2]
- 50% reduction in missed doses comparing periods before/after intervention (self-report and pill count)
- High acceptability among young MSM of color
- Participants: more interactivity, customization, 2-way texting
- Providers: recommend integration into existing clinic flow

[1]Lester Lancet 2010; [2]Liu IAPAC 2013

EPIC
Enhancing PrEP in Community

iText: post-pilot focus groups

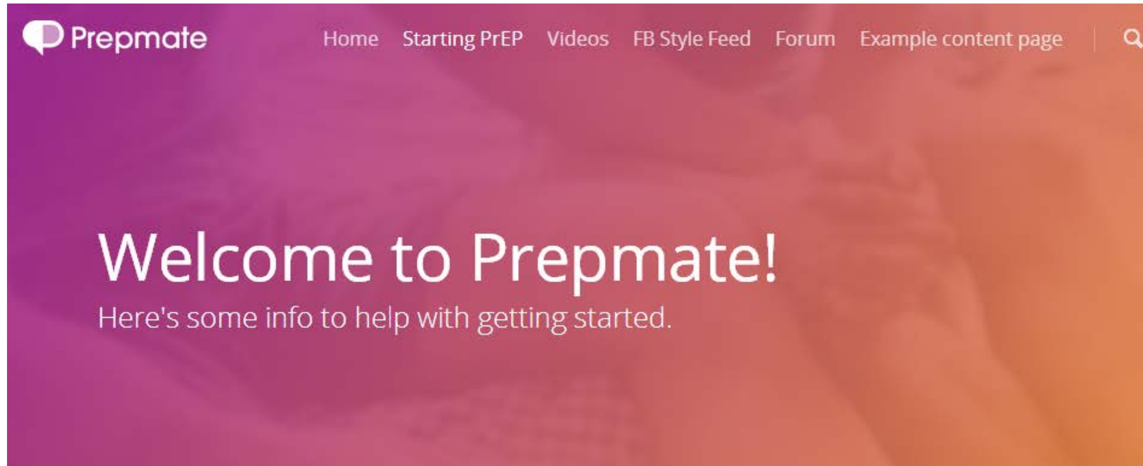
PROVIDED ADDITIONAL SUPPORT AND SENSE OF SECURITY

- …[You know when I wasn't on the I-Text study, I feel like I didn't really have a lot of support because I really didn't want to put too many people into my life, at that kind of level. So like just getting those messages made me feel like there was always kind of somebody there just in case something went wrong … It's kind of like I was on my own before iText."[Chicago MSM ppt]

Liu IAPAC 2013

EPIC
Enhancing PrEP in Community

Revised SMS system (Prepmate) developed and being tested in young MSM (EPIC-2 RCT)



We know starting PrEP can be exciting and overwhelming, and we're here to help you out in any way we can. Here's how we've got your back:

Real people, real support.

Anytime you need a question answered, some help with PrEP, or just someone to talk to, text us. We'll get back to you as soon as we can, and always within 24 hrs.

Reminders that don't suck.

We'll send reminders (disguised as pretty funny texts) for about 2 weeks to get you started. If you want more, just text to let us know, but we don't want to be annoying.

People like you.

We've got a little social network thing going on so you can talk to other PrEP users. You can find it under the menu at the top right.

Supported by NIMH R01 MH095628

EPIC
Enhancing PrEP in Community

GLOBAL iPrEx

Summary

- Key changes in transitioning adherence counseling from iPrEx RCT to iPrEx OLE
  - Integrate risk reduction and adherence discussions to streamline – highly feasible
  - Include counseling approach and procedures into protocol/SSP from the beginning
  - Address counseling challenges in trainings (e.g. no barriers, participants in maintenance)
  - Significant counseling / messaging needs around starting/stopping PrEP
- Participant education materials can be helpful for both staff and participants
  - Addressing product use misconceptions
  - Educating staff and ppts on the importance of choice
- Drug level feedback most useful if quick turnaround, delivered as part of counseling, and provide quantitative information
- SMS support strategies highly scalable, can provide support between study visits

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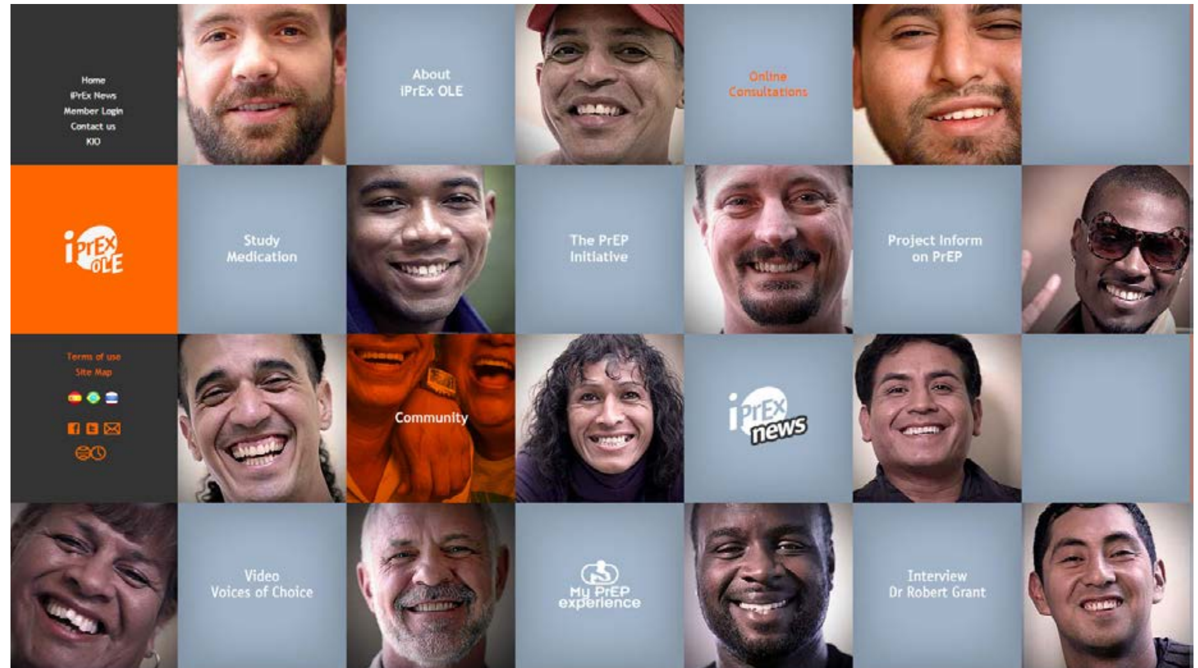

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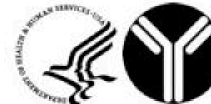

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The iPrEx Study: **Safety, Efficacy, Behavior, and Biology**

BridgeHIV™
San Francisco Department of Public Health