Developing and implementing a mobile health (mHealth) adherence support system for HIV-uninfected men who have sex with men (MSM) taking pre-exposure prophylaxis (PrEP): the iText Study

A Liu, K Stojanovski, R Lester, KR Amico, V McMahan, P Goicochea, L Vargas, D Lubensky, K Koester, J Brothers, S Buchbinder, K Mayer, S Hosek, R Grant, J Fuchs

8th International Conference on HIV Treatment and Prevention, Miami, FL

The views expressed herein do not necessarily reflect the official policies of the City and County of San Francisco; nor does mention of the San Francisco Department of Public Health imply its endorsement.
Adherence is the “Achilles’ heel” of PrEP

• Adherence is critical for PrEP efficacy
  • In iPrEx, efficacy rose from overall 42% to an estimated >90% among those with detectable drug
  • Lack of efficacy in FEM-PrEP and VOICE (low rates of drug detection)

• Developing strategies to support PrEP adherence in real-world settings is critical to maximizing the public health impact of PrEP
Mobile phone strategies successful in supporting ART adherence: 2 RCTs in Kenya

Almost all MSM in US own a cell phone (>90%), with few sharing phones, and infrequent service discontinuations in 2010 internet-based survey (N=1568) (Fuchs IAS Rome 2011)
iText study aims

• Develop an SMS-based support system (iText) to support PrEP adherence in HIV-negative individuals, based on the Weltel SMS model in HIV-positive pts

• Evaluate the feasibility, acceptability, and preliminary effectiveness of iText among MSM taking PrEP in iPrEx Open Label Extension (OLE)
Methods: Formative work and pilot study

**Qualitative interviews**
In-depth interviews (IDIs) with 59 iPrEx OLE ppts in SF, Boston, Chicago to assess interest and recommendations for iTex

**Develop platform**
iText developed in iterative process with Capito Life Technologies

**3-mo. iTex pilot (iPrex OLE)**
Weekly SMS check-in Phone support as needed Post-intervention survey, focus groups in subset

**iText Eligibility:**
- Dispensed PrEP for at least 12 weeks, with a plan to continue for an additional 12 weeks
- Have an SMS-capable phone or active email account
Evaluating impact on adherence: Regression discontinuity analysis

If there is a treatment effect, there will be a... discontinuity... in the regression lines... at the cutoff

- Primary model included all pre- and post-observations, adjusting for age, race, site, start date, and duration in study

Adapted from http://www.socialresearchmethods.net
Phase 1 Results: Formative work

- Substantial interest in SMS support, particularly among young MSM of color in Chicago; many in SF felt they had already established pill taking routines
- Some prefer other modes of communication (email, Facebook)
- Participants wanted some level of personalization (choose timing of messages, rotation of messages)
- Range of message preferences:
  - How are you?
  - Are you OK?
  - How is PrEP working for you?
Registration

<table>
<thead>
<tr>
<th>Question</th>
<th>Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hi, how are you doing?</td>
<td>Fine/Not Fine</td>
</tr>
<tr>
<td></td>
<td>Well/Not Well</td>
</tr>
<tr>
<td></td>
<td>Ok/Not Ok</td>
</tr>
<tr>
<td>Hi, are you ok?</td>
<td>Yes/No</td>
</tr>
<tr>
<td>Hi, how is PrEP going?</td>
<td>Ok/Not Ok</td>
</tr>
<tr>
<td></td>
<td>Fine/Not Fine</td>
</tr>
<tr>
<td></td>
<td>Good/Not Good</td>
</tr>
</tbody>
</table>

Semantics

<table>
<thead>
<tr>
<th>Doing Well</th>
<th>Not Well</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fine</td>
<td>Not Fine</td>
</tr>
<tr>
<td>Well</td>
<td>Not Well</td>
</tr>
<tr>
<td>Good</td>
<td>Not Good</td>
</tr>
<tr>
<td>Ok</td>
<td>Not Ok</td>
</tr>
<tr>
<td>Okay</td>
<td>Not Okay</td>
</tr>
<tr>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Yah</td>
<td>Nay</td>
</tr>
</tbody>
</table>

Response

- Doing Well
  - Thanks!

- Not Well
  - Thanks for letting me know, I'll be calling you within 24 hours when I'm in my office

- No Response (24h)
  - I didn't hear from you. How are you? I'll give you a call if I don't hear back in 24 hours.

Follow-up

- Mon 9 AM-Fri 12PM
  - Thanks for letting me know, I'll be calling you within 24 hours when I'm in my office

- Fri 12:01 PM-Mon 8:59 AM
  - Thanks for letting me know. I'll call you on Monday when I'm in my office.

System programmed for SMS and email message delivery
## All Participants Dashboard

![Dashboard Image](image)

### Tasks
- Participant Search
- Participant Registration
- All Participants Dashboard
- My Participant
- Calls Needed
- Calls Made
- Study Metrics

### Reports
- Captio2A Access DB

#### All Participants

<table>
<thead>
<tr>
<th>ID Number</th>
<th>Assigned Counselor</th>
<th>Activation Date</th>
<th>Week of Participation</th>
</tr>
</thead>
<tbody>
<tr>
<td>9470455</td>
<td>AD</td>
<td>11-07-2012</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13</td>
</tr>
<tr>
<td>9470097</td>
<td>RG</td>
<td>11-09-2012</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13</td>
</tr>
<tr>
<td>9470145</td>
<td>RG</td>
<td>03-01-2013</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13</td>
</tr>
<tr>
<td>9470636</td>
<td>AD</td>
<td>12-06-2012</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13</td>
</tr>
<tr>
<td>FTEST002</td>
<td>Steve Conwin</td>
<td>05-09-2013</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13</td>
</tr>
</tbody>
</table>

- **Doing Well**
- **Not Doing Well**
- **No Response**
- **A=Call Attempted**
- **C=Call Completed**

---

[Logo and Branding]

Where science meets community™
Phase 2 Results:
High uptake among eligible participants

<table>
<thead>
<tr>
<th>Recruitment stage</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approached</td>
<td>68</td>
</tr>
<tr>
<td>Ineligible</td>
<td>6</td>
</tr>
<tr>
<td>Eligible (% approached)</td>
<td>62    (91%)</td>
</tr>
<tr>
<td>Refused</td>
<td>6</td>
</tr>
<tr>
<td>Enrolled (% eligible)</td>
<td>56    (90%)</td>
</tr>
</tbody>
</table>
# iText Pilot Study Participant Characteristics (N=56)

<table>
<thead>
<tr>
<th></th>
<th>San Francisco N=48</th>
<th>Chicago N=8</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤30 yrs</td>
<td>2%</td>
<td>100%</td>
</tr>
<tr>
<td>&gt; 30 yrs</td>
<td>98%</td>
<td>0%</td>
</tr>
<tr>
<td><strong>Race/Ethnicity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>79%</td>
<td>0%</td>
</tr>
<tr>
<td>Black</td>
<td>6%</td>
<td>50%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>8%</td>
<td>25%</td>
</tr>
<tr>
<td>Other</td>
<td>6%</td>
<td>25%</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completed some college</td>
<td>94%</td>
<td>51%</td>
</tr>
<tr>
<td><strong>Living situation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alone</td>
<td>27%</td>
<td>25%</td>
</tr>
<tr>
<td>w/male sexual partner</td>
<td>42%</td>
<td>13%</td>
</tr>
<tr>
<td>w/ family/friends</td>
<td>8%</td>
<td>63%</td>
</tr>
<tr>
<td><strong>Cell-phone plans</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have an unlimited SMS plan</td>
<td>78%</td>
<td>100%</td>
</tr>
<tr>
<td>Send/receive text messages daily</td>
<td>90%</td>
<td>86%</td>
</tr>
</tbody>
</table>
About 2/3 of participants elected SMS, 1/3 email
Majority of participants wanted PrEP specific messaging

Participant selected messaging question

<table>
<thead>
<tr>
<th>Messaging type</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>How are you?</td>
<td>23%</td>
</tr>
<tr>
<td>How is PrEP going?</td>
<td>61%</td>
</tr>
<tr>
<td>Are you okay?</td>
<td>11%</td>
</tr>
<tr>
<td>Not activated</td>
<td>5%</td>
</tr>
</tbody>
</table>
Most preferred messages earlier in the week

- **Monday**: 29%
- **Tuesday**: 16%
- **Wednesday**: 16%
- **Thursday**: 13%
- **Friday**: 5%
- **Saturday**: 4%
- **Sunday**: 14%
- **Not activated**: 5%

**Participant selected messaging day**
Morning messages were most desired

**Participant selected time of messaging**

<table>
<thead>
<tr>
<th>Messaging time</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning</td>
<td>63%</td>
</tr>
<tr>
<td>Afternoon</td>
<td>30%</td>
</tr>
<tr>
<td>Evening</td>
<td>2%</td>
</tr>
<tr>
<td>Not activated</td>
<td>6%</td>
</tr>
</tbody>
</table>

Morning messages were most desired among participants, with 63% preferring them in the morning.
Majority of responses were “ok” (N=667 messages)

iText support strategy messaging responses

- Ok: 77%
- Not ok: 0.4%
- No response: 22%

Reasons for non-response: travel, phones were disconnected, no credit on phones, phone turned off, changing phones, just didn’t feel like responding
Impacts on adherence: pill count

Mean missed # days pre and post iTxt, by pill count

 RR=0.5 (95% CI 0.29-0.84, p=0.008) in model adjusted for age, race, site, duration in study, and start date
Impacts on adherence: self-report

**Self reported missed days pre and post iText**

- Pre: 2.7
- Post: 2.5*

RR=0.52 (95% CI 0.29-0.91, p=0.023) in model adjusted for age, race, study site, start date, and duration in study
How helpful, overall, would you rate the iText support strategy for you?

- San Francisco:
  - Not helpful: 48%
  - Somewhat helpful: 45%
  - Very helpful: 88%
  - Don't know: 0%

- Chicago:
  - Not helpful: 2%
  - Somewhat helpful: 12%
  - Very helpful: 5%
  - Don't know: 0%
To Whom should iText be offered?

**Offered to PrEP users with problems:**
- San Francisco: 36%
- Chicago: 12%

**Offered to all PrEP users:**
- San Francisco: 52%
- Chicago: 88%

**Not sure:**
- San Francisco: 10%
- Chicago: 0%

**Not offered to anyone:**
- San Francisco: 2%
- Chicago: 0%
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.”[C-FG]
HELPFUL
It's just my whole attitude was just so much better and I just felt like I was so --
I was like really in control when I started getting the text messages. [C-FG]

NOT/LESS HELPFUL...
And I mean I take the pill every morning religiously. It doesn't... it didn't help
me. I mean it just didn't help me. [SF-FG]

BUT WOULD BE FOR THOSE JUST STARTING PrEP...
So if you're starting out and maybe you would have some symptoms or
something you wanted talk to somebody about it, maybe that makes sense. [SF-FG]
iText: post pilot focus groups

Other recommendations – greater personalization and interactivity:
• Allow additional tailoring of frequency and timing of text
• Addition of online social network strategies (Black Gay Chat, Jack’d, Facebook) to add human element
• Open-ended “text discussion” vs. phone call

Operational guidance:
• Fix glitches!
• Emphasize purpose of texts more clearly and offer reminder texts as an add in feature
Limitations

1) Pre and post study design has limitations for determining the effects of the iText intervention.

2) Adherence outcomes are currently only available from self-report and pill count data -> will analyze drug level data

3) Late implementation within OLE, with participants having been on PrEP for several years (including randomized phase)
Conclusions and next steps

- iTxt PrEP support found to be feasible and acceptable in iPrEx OLE –
  - Young MSM of color in Chicago >> older, more PrEP-experienced MSM in SF
  - May be most helpful when starting PrEP

- Formative work and pilot testing critical

- Next steps will be to refine intervention and evaluate the efficacy of iTxt in an RCT in a real-world setting (PrEP demonstration project)
Acknowledgements

**EPIC Study Team**
- Kristefer Stojanovski
- Richard Lester
- Rivet Amico
- Eric Vittinghoff
- Kim Koester
- David Lubensky
- Susan Buchbinder
- Jonathan Fuchs

**iPrEx OLE Study Team**
- Vanessa McMahan
- Pedro Goicochea
- Lorena Vargas
- Kenneth Mayer
- Sybil Hosek
- Jennifer Brothers
- Robert Grant

**Capito Life Technologies**
- Steve Corwin

**Med Adherence LLC**
- Jonathan Katz
3 participants responding not okay

1) **San Francisco**
   - Participant had 1 week of sore throat, cough, body aches, feeling feverish -> decided to stop study drug
   - Spoke with clinician – low suspicion for ARS
   - Participant instructed to come in for rapid HIV test prior to restarting study drug.

2) **Chicago**
   - Unable to contact ppt by phone, but reached through Grindr (IRB-approved outreach strategy)

3) **San Francisco**
   - Responded not okay to test the system
   - Participant contacted the same day and appreciated quick follow-up.
Higher acceptability of iTText as a support strategy in younger MSM of color, bivariate analyses

<table>
<thead>
<tr>
<th>Domain</th>
<th>Comparison</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Helpful for them</td>
<td>Non white vs white*</td>
<td>7.3</td>
</tr>
<tr>
<td></td>
<td>&lt; 30 years vs &gt; 30 years**</td>
<td>7.3</td>
</tr>
<tr>
<td></td>
<td>Chicago vs SF **</td>
<td>10</td>
</tr>
<tr>
<td>Future use</td>
<td>Non-white vs white*</td>
<td>4.7</td>
</tr>
<tr>
<td></td>
<td>&lt; 30 years vs &gt; 30 years*</td>
<td>12.5</td>
</tr>
</tbody>
</table>

*p<0.05, p<0.01
Faster response time to SMS (text) messages

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Mean</th>
<th>Std Dev</th>
<th>Range</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMS (in hours)</td>
<td>370</td>
<td>4.4</td>
<td>8.6</td>
<td>(0.001, 46.7)</td>
<td>0.03</td>
</tr>
<tr>
<td>Email (in hours)</td>
<td>139</td>
<td>6.1</td>
<td>9.4</td>
<td>(0.02, 43.8)</td>
<td></td>
</tr>
</tbody>
</table>
Did getting these messages help you take PrEP?

- **San Francisco**
  - Yes: 63%
  - No: 25%
  - Don’t know: 10%

- **Chicago**
  - Yes: 76%
  - No: 12%
  - Don’t know: 10%

Helpful for taking PrEP?
If you were to continue taking PrEP, either in the study or elsewhere, and iText was available to you, would you use it?

Would you iText?

<table>
<thead>
<tr>
<th>Would you iText?</th>
<th>San Francisco</th>
<th>Chicago</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>38%</td>
<td>100%</td>
</tr>
<tr>
<td>No</td>
<td>57%</td>
<td>0%</td>
</tr>
<tr>
<td>Don't know</td>
<td>5%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Would you iText? (San Francisco vs. Chicago)
iText: post pilot focus groups

Some confusion over purpose of iText

REMEMBER

That was my impression that it was supposed to be a reminder ... to take the pill. [SF-FG]

CHECK-IN

...[it was to] provide some form of communication, consistent communication with the participants that would allow them to seek -- to get help...outside the [days between visits] [C-FG]
Almost all MSM in US own a cell phone

Internet-based survey among 1568 HIV-uninfected MSM (2010)

**Own a Cell Phone**  
(Base: total MSM Sample)  
- Yes, 90%  
- No, 10%  

n=1568

**Share Cell Phone**  
(Base: have cell phone)  
- Yes, 10%  
- No, 90%  

n=1374

**Times Service Disconnected in Past Year**  
(Base: have cell phone)  
- Never: 79%  
- Once: 9%  
- Twice: 5%  
- 2-5 times: 4%  
- More than 5 times: 3%

Fuchs IAS Rome 2011