Interim buprenorphine dosing for reducing illicit drug use and associated risks among waitlisted opioid-dependent adults

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Barriers to treatment

- Methadone and buprenorphine are efficacious and reduce illicit drug use, morbidity, mortality and spread of infectious disease.

- Demand for treatment exceeds available capacity in many areas of the country, with 96% of states having opioid dependence rates that exceed their capacity (Jones et al., 2015).

- Insufficient treatment capacity is especially urgent in rural areas:
  - Methadone clinics: lengthy waitlists, especially for subsidized treatment slots (~1.9 year waitlist; Sigmon, 2014, *JAMA Psychiatry*)
  - Office-based buprenorphine: insufficient number of providers and low density of patients among providers (~10% utilization rate; Sigmon, 2015, *JAMA Psychiatry*)

- Opioid-dependent individuals can remain on waitlists for extended periods and are at high risk for infectious disease, criminal activity, overdose and death during delays to treatment.

- How to reduce individual and societal risks when comprehensive treatment is not immediately available?
One effort to mitigate individual and societal risks during treatment delays may be to offer **interim medication dosing** to those awaiting enrollment into comprehensive opioid treatment.

Novel interim buprenorphine dosing regimen that includes several technology-assisted components to support delivery of pharmacotherapy while minimizing nonadherence:

1. **Automated medication dispensing**
   - Participants receive buprenorphine with bi-monthly, in-person clinic visits and the remaining doses dispensed at home via a secure computerized portable device:
     - Med-O-Wheel device (Addoz, Finland) holds up to a month of doses across individual secure cells
     - Each dose is available for a pre-programmed 3-hour window each day
     - Locks and alarms to prevent tampering and access to meds outside the predetermined dosing window
2. Nightly calls from an automated Interactive Voice Response (IVR) phone system to assess any drug use, withdrawal and craving:
   - Phone-based IVR systems offer advantages of low cost, consistent delivery, 24-hour availability, privacy and convenience.
   - Provides information about self-help meetings in the community and immediate connection with research staff if needed.

3. IVR-generated random call-backs to support abstinence and adherence:
   - IVR system contacts participants on a random schedule (~1 RCB per 2-week dosing interval)
   - Participant instructed to return to the clinic to
     - provide a staff-observed urine specimen
     - ingest their dose under nurse observation
     - present Med-O-Wheel for inspection and pill count
4. Automated HIV+HCV Education delivered via iPad

- Pre-test assessments of HIV- and HCV-related knowledge; automated corrective feedback
- Interactive HIV educational application and animated HCV educational video
- Post-test assessments of HIV and HCV knowledge immediately as well as at 4 and 12 weeks post-intake
Randomized trial

- 12-week outpatient randomized pilot trial to evaluate initial efficacy

Participants (n=50):
- >18 years old
- Meet DSM-V criteria for OUD
- Provide opioid-positive urine at intake
- Currently waitlisted for opioid treatment

**IBT**: Visited clinic every 2 weeks to ingest dose, provided UA, and received their remaining doses via Med-O-Wheel. Daily IVR monitoring of recent drug use, craving and withdrawal; random-call backs (~2x/mo). Monthly follow-ups at Weeks 4, 8, and 12.

**Waitlist Control**: Remain on waitlist but completed Week 4, 8, and 12 follow-ups

*Interim Buprenorphine vs. Waiting List for Opioid Dependence*

## IBT Participant characteristics

<table>
<thead>
<tr>
<th>Participant Characteristics</th>
<th>IBT (n=25)</th>
<th>WLC (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>33.6 ± 10.0</td>
<td>35.7 ± 10.7</td>
</tr>
<tr>
<td>Male, %</td>
<td>60</td>
<td>56</td>
</tr>
<tr>
<td>Employed full-time, %</td>
<td>48</td>
<td>40</td>
</tr>
<tr>
<td>Education, yrs</td>
<td>12.4 ± 2.4</td>
<td>12.7 ± 1.7</td>
</tr>
<tr>
<td>Primary past year opioid of abuse, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heroin</td>
<td>64</td>
<td>40</td>
</tr>
<tr>
<td>Prescription opioids</td>
<td>36</td>
<td>60</td>
</tr>
<tr>
<td>Primary route of administration, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral/sublingual</td>
<td>28</td>
<td>44</td>
</tr>
<tr>
<td>Intranasal</td>
<td>16</td>
<td>24</td>
</tr>
<tr>
<td>Inhalation</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Intravenous</td>
<td>56</td>
<td>28</td>
</tr>
<tr>
<td>Duration of regular opioid use, yrs</td>
<td>6.4 ± 5.8</td>
<td>8.0 ± 6.3</td>
</tr>
<tr>
<td>Ever used IV, %</td>
<td>80</td>
<td>76</td>
</tr>
<tr>
<td>Past-month cocaine use, %</td>
<td>28</td>
<td>32</td>
</tr>
<tr>
<td>Duration on treatment waitlist, mos</td>
<td>3.3 ± 2.5</td>
<td>3.4 ± 2.6</td>
</tr>
<tr>
<td>Buprenorphine dose, mg</td>
<td>13.2 ± 1.1</td>
<td>n/a</td>
</tr>
</tbody>
</table>
Primary outcome: Illicit opioid abstinence

- Primary outcome: % of participants in each condition providing urine specimens testing negative for illicit opioids.

- IBT participants achieved greater illicit opioid abstinence:
  - At 4-, 8- and 12-week assessments, 88%, 84% and 68% of IBT participants abstinent vs. 0%, 0% and 0% of WLC participants (p<.0001).

- Similar picture seen at IBT participants’ scheduled bi-monthly study visits, with 81% of specimens testing negative for illicit opioids.
Secondary outcomes: IV drug use, IBT adherence & satisfaction

- IBT participants demonstrated greater reductions in past-month frequency of IV opioid use (p<.001)

- IBT participants’ adherence & satisfaction:
  - took 99% of scheduled doses
  - completed 96.2% of IVR check-in calls
  - completed 96.3% of random call-backs
    - 85.3% of urine specimens collected at those random visits tested negative for illicit opioids
  - rated satisfaction with IBT at 4.6 ± 0.6 (range: 1-5)
Secondary outcomes: Psychiatric distress

- At Intake and weeks 4, 8, 12, all participants complete the ASI, Beck Depression Inventory, Beck Anxiety Inventory and the Brief Symptom Inventory.

- Participants in both groups presented with elevated depression severity.

- Following randomization, changes over time in BDI scores were group dependent ($F(3,125)=11.26, p<.01$)

- BDI scores decreased among IBT participants ($F(3,125)=26.62, p<.01$), with mean scores significantly lower than baseline at Weeks 4, 8 and 12 ($p’s<.01$)

- No change in depression severity in WLC participants.

- Similar outcomes seen on Beck Anxiety Index, Brief Symptom Inventory and ASI Psychiatric subscale.


![Beck Depression Inventory Graph](image-url)
Secondary outcome: HIV & HCV knowledge

- The *m*Health HIV+Hepatitis Education intervention was associated with significant improvements in knowledge of HIV and HCV transmission and risk behaviors.

- Knowledge improvements persisted throughout the 12-week study period, without additional educational sessions.

Conclusions

- Innovative strategies are needed to eliminate barriers to treatment access, as well as to reduce risks to the patient and society during delays to treatment entry.

- Providing interim, technology-assisted buprenorphine dosing to waitlisted opioid-dependent individuals was associated with:
  - greater illicit opioid abstinence
  - reductions in IV use
  - improvements in psychological distress
  - significant and sustained improvements in HIV and Hepatitis risk knowledge

- Ongoing RCTs to replicate and build further upon these promising results
  - over longer intervention duration
  - in rural, underserved populations

- Interim Buprenorphine Treatment, without formal psychosocial counseling, may substantially reduce drug use and related risks during delays to comprehensive treatment.
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