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*)

Rolling Stone, 2014

- **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?**

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Interim Buprenorphine Treatment

- 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

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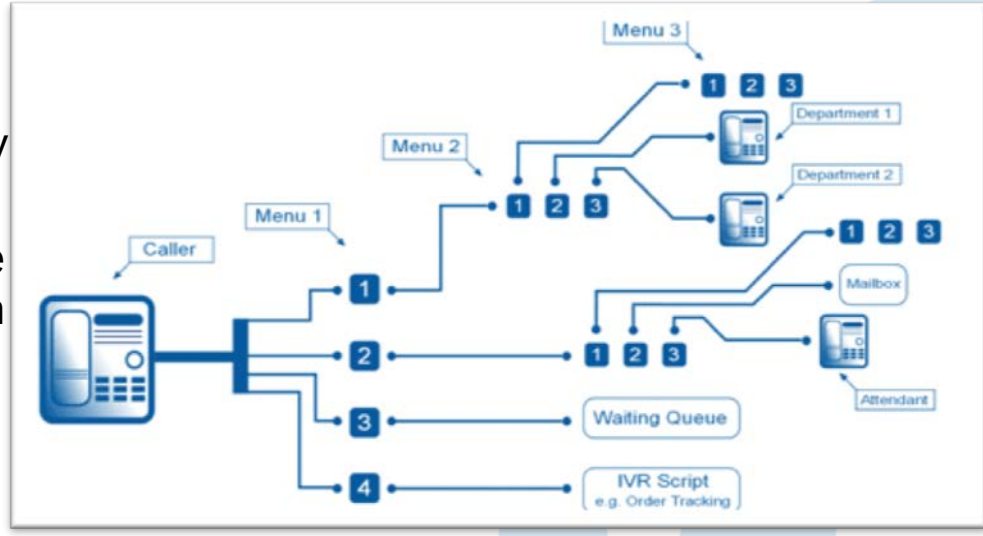
2. Nightly calls from an automated Interactive Voice Response (IVR) phone system to assess any drug use, withdrawal and craving:

- 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

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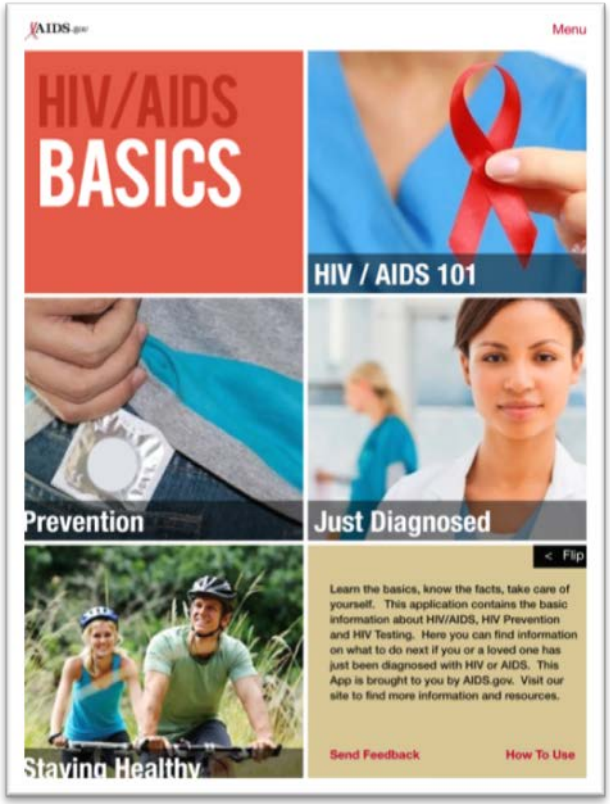
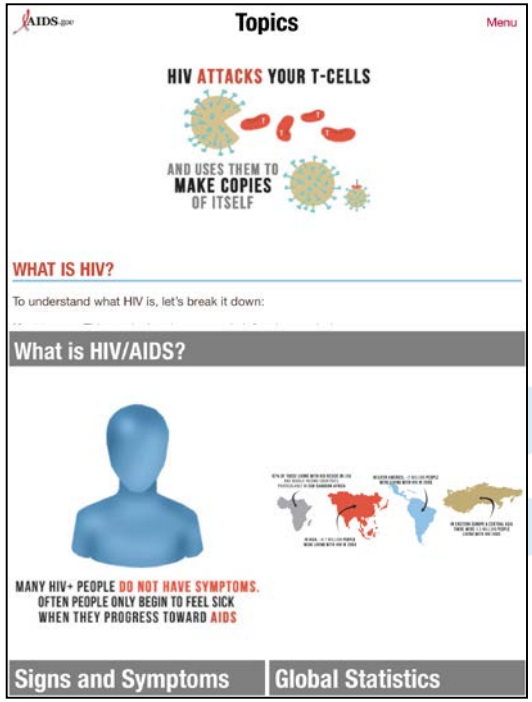
4. Automated HIV+HCV Education delivered via iPad

- 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





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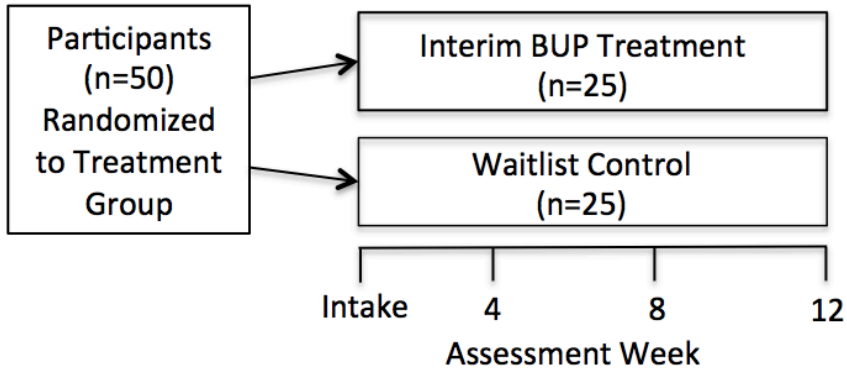
Randomized trial

- 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:** Remained on waitlist but completed Week 4, 8, and 12 follow-ups

The NEW ENGLAND JOURNAL of MEDICINE

Interim Buprenorphine vs. Waiting List for Opioid Dependence

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IBT Participant characteristics

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

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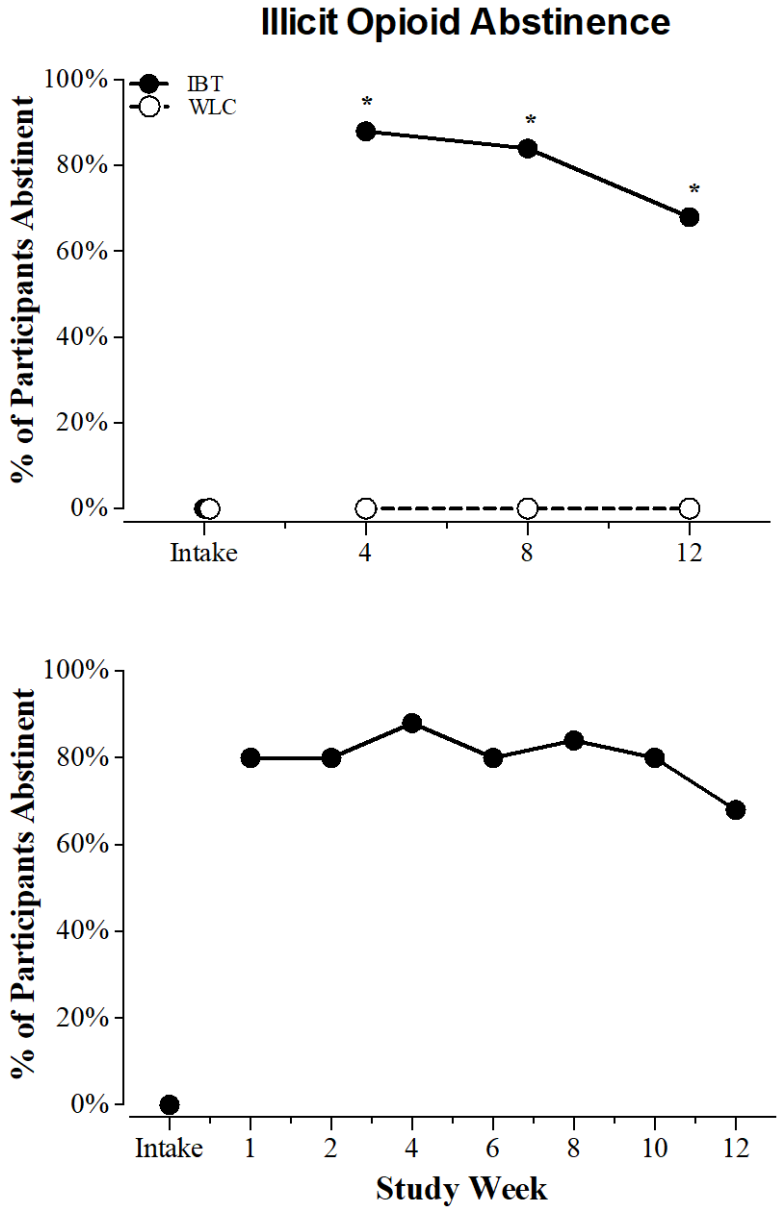
Primary outcome: Illicit opioid abstinence



- **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.

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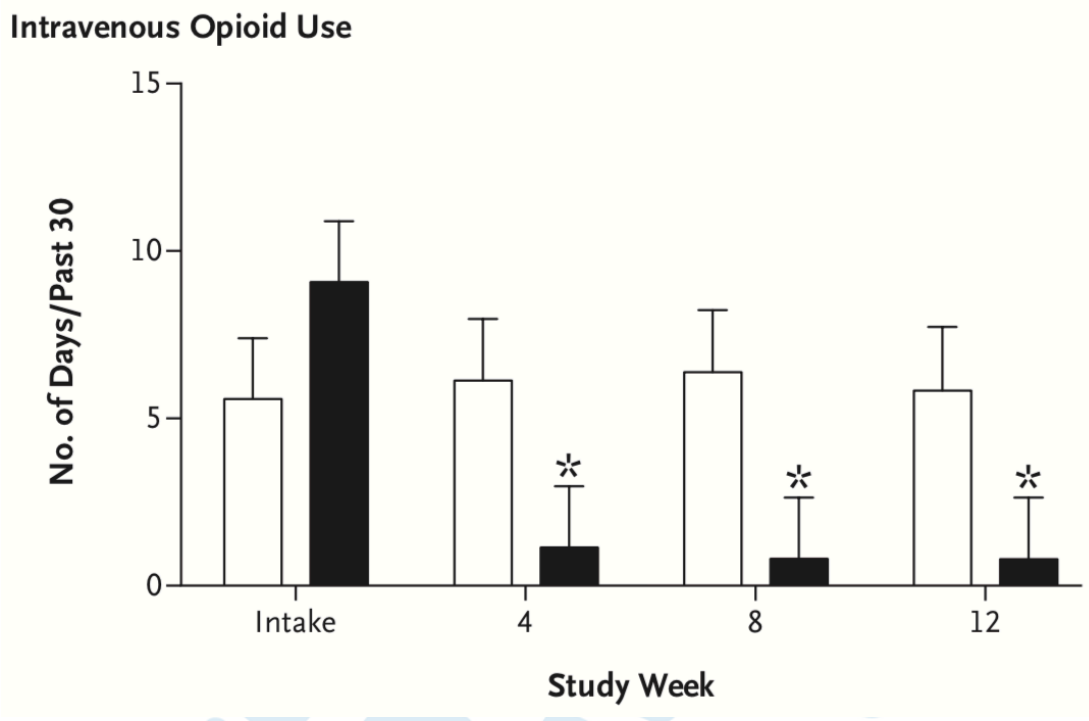
Secondary outcomes: IV drug use, IBT adherence & satisfaction

- 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)



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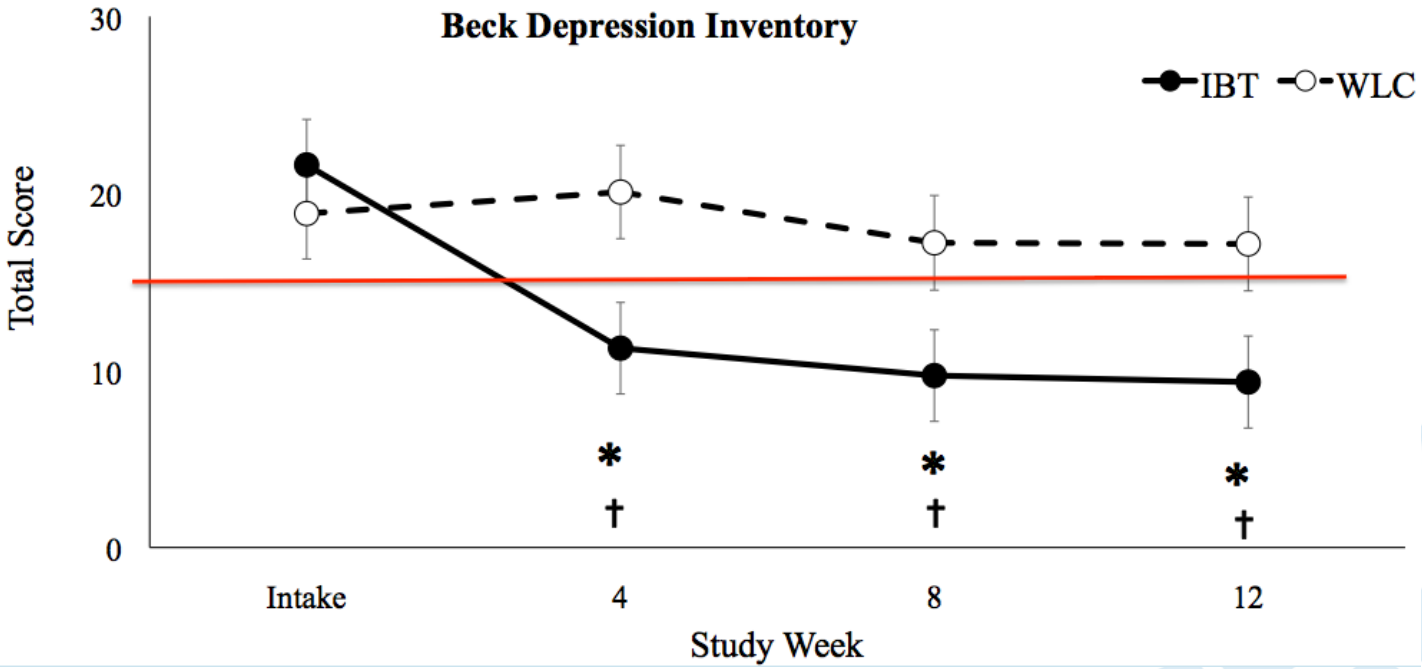
Secondary outcomes: Psychiatric distress

- 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.**

Streck, J., Ochalek, T., & Sigmon, S.C. (in press). Interim buprenorphine treatment during delays to comprehensive treatment: Changes in psychiatric symptoms. *Experimental and Clinical Psychopharmacology*.

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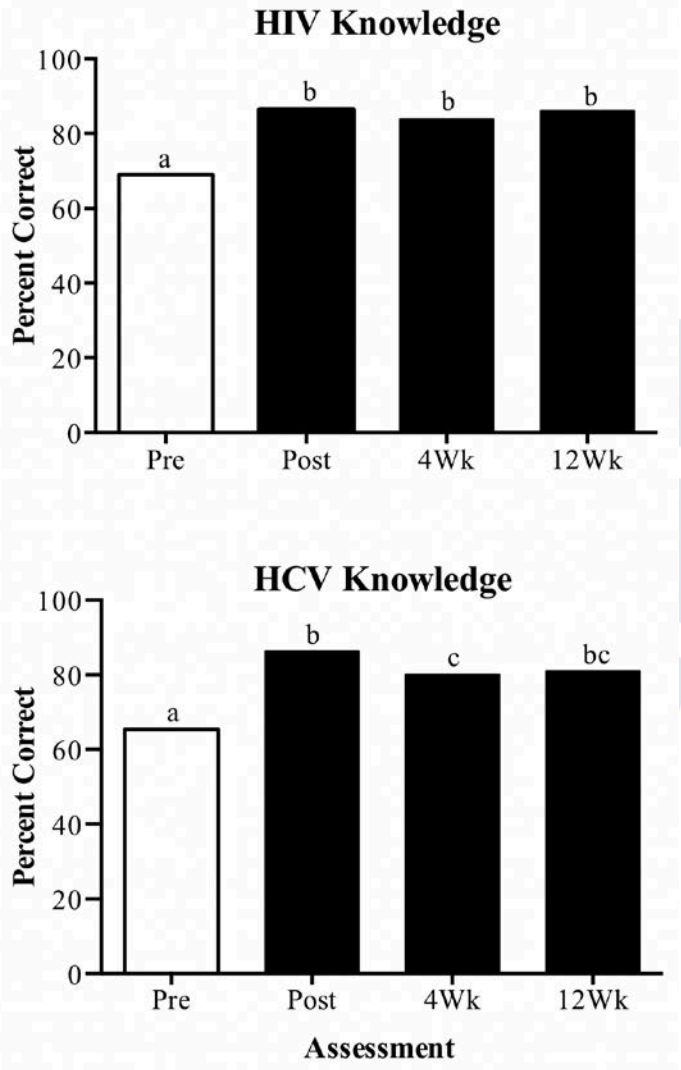
Secondary outcome: HIV & HCV knowledge

- 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.



Ochalek, T., Heil, S.H., Higgins S.T., Badger, G.J. & Sigmon, S.C. (submitted). A novel *m*Health application for improving HIV and Hepatitis C knowledge in individuals with opioid use disorder: A pilot study. *Drug and Alcohol Dependence*.

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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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