

Moving PrEP from clinical trials to implementation

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Adherence and HIV protection: oral PrEP

	% of blood samples with tenofovir detected	HIV protection efficacy in randomized comparison	HIV protection estimate with high adherence
Partners PrEP FTC/TDF arm	81%	75%	90% (tenofovir in blood)
TDF2	79%	62%	78% (prescription refill)
BTS	67%	49%	70% - 84% (tenofovir in blood / pill count)
iPrEx	51%	44%	92% (tenofovir in blood)
FEM-PrEP & VOICE	<30%	No HIV protection	N/A

When adherence was high, HIV protection is consistent and high.

Understanding lack of efficacy

- **Hypotheses for low adherence in FemPrEP & VOICE**
 - Motivation for daily prevention behavior?
 - Dynamic risk? Perceived risk is low? Perceived benefits are low?
 - Importance of partner engagement & support?
- **HIV incidence of 6%**
 - HIV prevention is not working in this group
 - Innovation & understanding are needed

Correlates of low adherence in oral PrEP trials

- Younger age (Partners PrEP, VOICE)
- Not partnered (VOICE, FEM-PrEP)
- Low perception of risk? Stigma? (FEM-PrEP, others?)
- Less sex (Partners PrEP, iPrEx)
- Alcohol use (Partners PrEP)
- Not attending appointments (Partners PrEP, VOICE, others?)

Key factors diminish adherence to daily preventative therapy (or to optimal clinical trial participation).

Good news about adherence

- In Partners PrEP, people 'self sorted' into consistent or non-consistent adherers
 - At month 1, 89% of controls had high tenofovir levels & 75% at month 12
 - Lower levels of adherence when not sexually active
- Adherence was high among IDUs in Bangkok
 - Even though adherence was not perfect with DOT
- Modeling from iPrEX shows high protection with 4+ doses/week

Donnell D CROI 2012

Haberer J et al PLoS Med 2013

Choopanya et al IAS 2013

Anderson Sci Trans Med 2013



Antiretrovirals for HIV prevention

From trials to implementation

- Populations
- Delivery
- Impact

Principles of PrEP implementation

Not lifelong but during 'seasons' of vulnerability

- HIV serodiscordant couples trying to conceive & before HIV+ partner is on ART
- Adolescents
 - Highest HIV incidence globally in young women in subSaharan Africa
- MSM with early syphilis, young MSM
- Other risk factors: Intimate partner violence, new partner, depression, alcohol & drug use

PrEP use in the US: 2011-13

- Little information about PrEP use in the US
 - Analysis of retail pharmacy records to identify TDF/FTC use (in patients not treated for HIV, HBV, or receiving PEP)

- Of 1774 probable PrEP prescriptions:
 - Use increased markedly in 2012
 - Highest number of PrEP prescriptions in southeast US
 - 14% were under age 25 & 48% were women
 - PrEP prescriptions under-represent highest risk group (young MSM)



THE NEW YORKER

OCTOBER 1, 2013

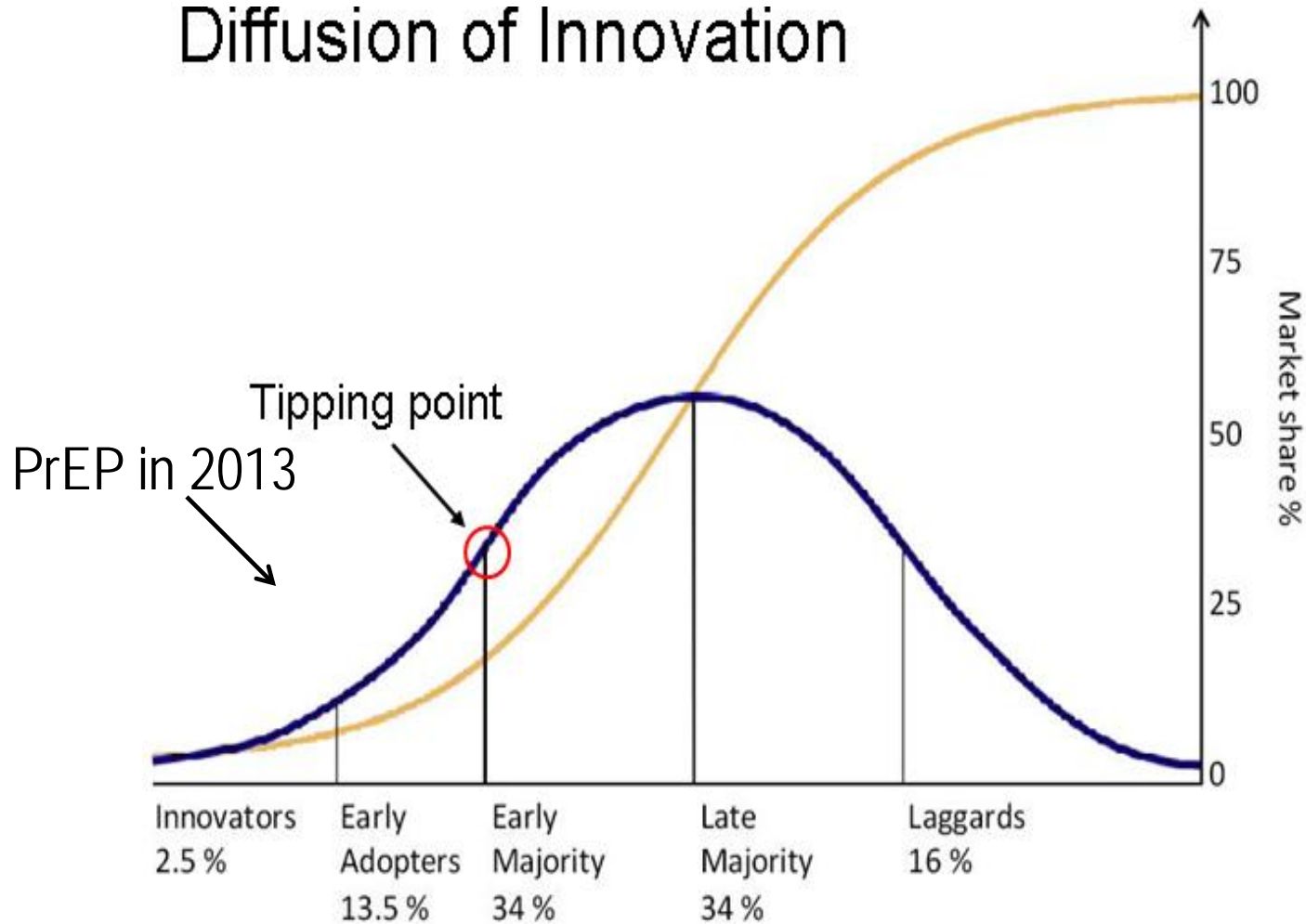
WHY IS NO ONE ON THE FIRST TREATMENT TO PREVENT H.I.V.?

POSTED BY CHRISTOPHER GLAZEK



Diffusion of Innovations theory

Diffusion of Innovation



PrEP should be a 'fast idea'

- Learning from new ideas that flourish quickly (surgical anesthesia) vs slowly (antiseptics)
 - Slower uptake with interventions for invisible outcomes
- Realism about HIV prevention for those most at risk
 - Can't just wish condom use will increase
- Do not have luxury of having PrEP be a 'slow idea'

Gawande New Yorker 2013

Evans & Van Gorden, Huffington Post Oct 4, 2013



Thinking about PrEP from the framework of ‘diffusion of innovation’

“Evidence-based interventions are often not adopted because they are too difficult to understand or “*too complex to use*”

Dearing et al Am J Prev Med 2013

- Need ‘push’ interventions
 - Disseminate information to providers & potential users
 - Demand stimulation (different for early & late adopters)
- Need ‘pull’ strategies
 - Provider training
 - Address structural barriers (access, costs)

PrEP: Looking through the 'lens' of *providers*

- Concerns about PrEP implementation
 - How to reach most at risk populations
 - Assessing risk & targeting use
 - Costs
 - Provider time & reimbursement
 - Ease of prescribing, counseling & monitoring
- Need for
 - Risk assessment tools (Smith et al JAIDS 2012)
 - Simple prescribing guidelines & reimbursement
 - Identify best practices & models for delivery

Looking through the ‘lens’ of potential *PrEP* users

- Who is at high risk & motivated to use PrEP when counseled that it works (*well*) when taken regularly?
- Will people who initiate PrEP ‘self-sort’ into regular users and non-users?
- How to support adherence with brief adherence counseling, text messages, drug levels?

PrEP demonstration project questions


Topic	Question
Targeting	Who to prioritize for PrEP? How to <i>deliver</i> ?
Uptake	Do those who might benefit most from PrEP <i>want</i> it?
Adherence	<i>Who</i> takes PrEP? Do they take it <i>often enough</i> to be effective?
Sexual behavior	Is PrEP use associated with <i>risk compensation</i> ?
Impact	<i>HIV incidence? Resistance? Incremental cost effectiveness?</i>

Types of PrEP demonstration projects

	Experimental types		Exemplary types	
	Open-label studies	Implementation pilot studies	Single-sponsor demonstrations	Integrated demonstrations
Type-specific questions	Acceptability (patients); medication adherence; longer-term safety	System acceptability; retention in prevention care; sustainability (cost, reimbursement); practice variation effects on outcomes	Interest, adoption, adaptation, implementation, sustained use	Partnership, coordination, interest, adoption, adaptation, implementation, sustained use
Setting(s)	Research clinics	Usual clinical sites	Usual clinical sites	Public health and clinical sites
Population(s)	Clinical trial participants (or similar)	Broad population that may benefit	Potential adopters	Potential adopters
Incentives	Money for time and effort	Clinical services only	Nonmonetary	Nonmonetary
Protocol	Strict research protocol	Practice guidelines	Dissemination guidelines, implementation guidelines	Dissemination guidelines, implementation guidelines
Provider(s)	Research staff	Community providers	Community providers	Community providers
Funding	Research funds	Insurance (public, private, or self)	Innovation sponsor	Combined sponsorship

PrEP Open label studies

- Provide *research participants* access to PrEP for 1 year
- In context of known efficacy, assess adherence, risk behavior, HIV seroconversion, resistance & AEs

Study	Location	Population	Status
Bangkok Tenofovir Study Follow-Up	Thailand	People who inject drugs	500 expressed interest, with expected completion late 2014.
iPrEx OLE 	Brazil, Peru, Ecuador, South Africa, Thailand, US	MSM/TGW	1529 (65% enrolled; results expected 2014.
TDF-2 Follow-Up	Botswana	Heterosexual men and women	Enrolled 232 people; results expected mid- 2014

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PrEP Implementation Studies

- Objectives: Assess targeted delivery & uptake, in *research-naïve populations*, involving:
 - Recognition of risk
 - Challenges: denial, stigma, & dynamic nature of risk
 - Need tools for providers & potential users
 - Motivation to use products
 - Acceptability to populations
 - In different contexts & partnerships
 - Ease of delivery
 - Simplify steps in the 'prevention cascade'

Partners Demo Project

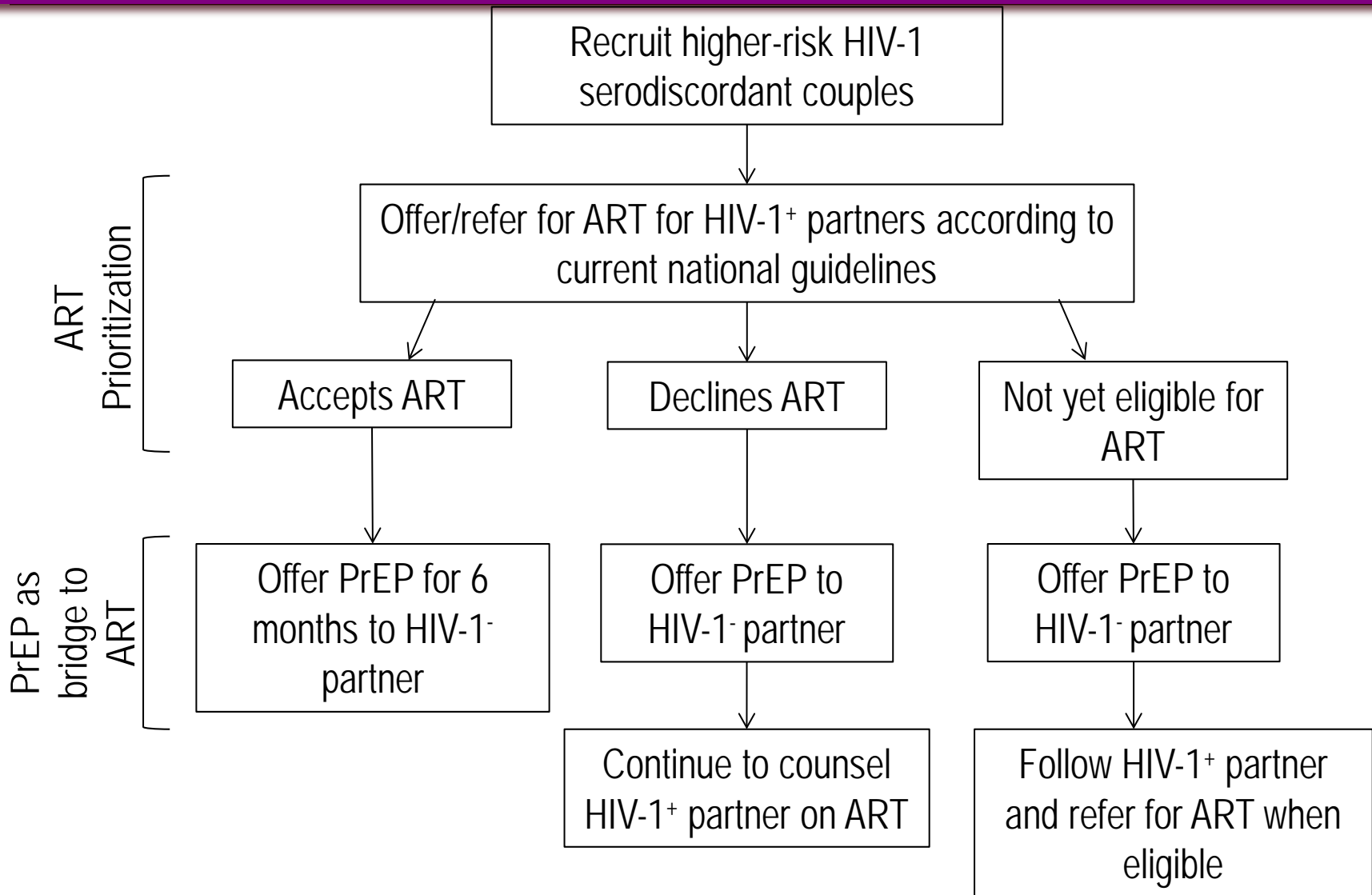
- **Goal:** to understand prevention preferences, uptake of ART and PrEP, adherence, & risk behavior among high risk HIV serodiscordant couples
- **Design:** Prospective observational study of 1000 HIV serodiscordant couples in Kenya and Uganda with quarterly follow up for 2 years
- **Setting:** Kenyan and Ugandan HIV care centers
- **Delivery:** PrEP is offered as a 'bridge' to ART use
 - PrEP discontinuation recommended after 6 months of sustained ART use the HIV infected partner



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Partners Demo Project

PrEP as bridge to ART in couples





Partners Demo Project Status

- Enrollment since November 2012
 - 419 couples enrolled as of Oct 2013
- High interest and uptake of PrEP at enrollment: >90% of participants
- ART willingness is high among eligible participants at enrollment: >70% accept a referral or onsite ART
- Retention rates: ~90% for HIV uninfected partners, ~88% for HIV infected partners
- PrEP and ART can work together to provide couples with maximum protection against HIV transmission

PrEP for serodiscordant couples: Opinions

New Vision

UGANDA'S LEADING DAILY

New HIV policy spells doom for discordant couples - activists Publish Date: Sep 13, 2013

Couples who had hoped to benefit from pre-exposure prophylaxis will have to look to other means for protection against HIV
newvision

TRUTH EVERYDAY

By Francis Kaseke

New Vision

UGANDA'S LEADING DAILY

Daily Monitor

NATIONAL

Study shows HIV treatment in discordant couples successful

Uganda needs HIV prevention pill as addition

Even for couples where PrEP efficacy was highest, need implementation projects & advocacy



PrEP Demo Projects in the US

Study	Population (N)	Sites	Timeline
Demo Project	600 MSM/trans women	San Francisco Miami Washington DC	Enrollment Sept 2012, results 2015
CCTG 595	700 MSM/trans women	San Diego Long Beach, LA Torrance	Enrollment Q2 2013, results 2016
PATH-PrEP	375 MSM/trans women	Los Angeles	Enrollment April 2013, results 2017
CRUSH	150 young MSM of color, high risk women	Oakland	Enrollment Q1 2013
ATN 110 and 113	300 young MSM age 15-22	14 sites in US	Enrollment Dec 2012, results Q4 2014
HPTN 073	225 Black MSM	Washington DC, LA, Chapel Hill	Enrollment June 2013, results 2017
SPARK	~300 MSM and trans women	New York	Enrollment Q4 2013

Demand high
in SF;

PROUD Pilot, United Kingdom

MSM reporting UAI
Willing to take a pill now or in 12M



Randomize 500 HIV negative eligible MSM
(exclude if on treatment for hepB)



Risk reduction includes
Truvada **NOW**

Risk reduction includes
Truvada **in 12M**



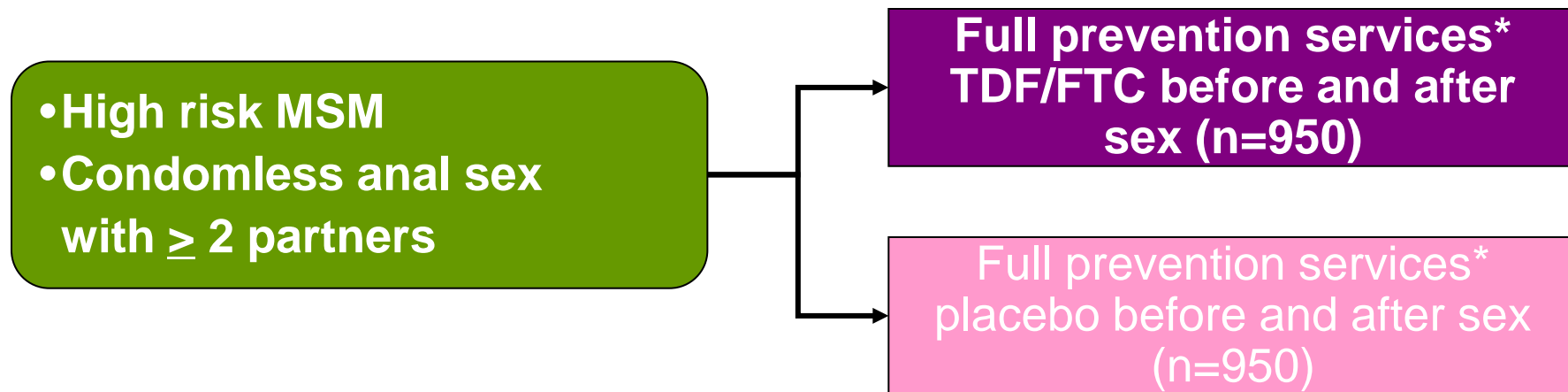
Follow **3 monthly** for up to 24 months (+**1m** after start truvada)

Outcomes: Whether or not a large trial is feasible; who takes up offer of PrEP; adherence; risk behaviour; uptake of behavioural interventions

IPIRGAY, France

Study Design

Effectiveness of “on demand” PrEP Randomized placebo-controlled trial



- Counseling, testing for STI, condoms, vaccination, PEP
- Primary endpoint : HIV infection, 64 events expected
- Incidence of HIV-infection: 3%PY, 50% efficacy, ~ 2000 pts

What about PrEP for...?

- Young African women

- Sex workers
 - Women in subSaharan Africa
 - *Men (?Kenya, Latin America)*

- Fishing communities around Lake Victoria

Critical questions about PrEP for young African women

- Risk perception
 - How to understand it, measure it, influence it?
- Willingness & motivation for HIV prevention
 - Can self-efficacy & locus of control be modified?
 - Uptake & adherence may be higher in context of known efficacy
- Adherence to PrEP & other prevention behaviors
 - Role for behavioral 'nudges', incentives, & peer support?

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PrEP in combination HIV prevention

- The future is offering PrEP in integrated HIV prevention delivery
- Combination prevention studies with PrEP in development in HPTN:
 - MSM & transgender women in the Americas
 - Young women in southern Africa
 - HIV serodiscordant couples in Africa

Moving PrEP from trials to implementation requires...

- Not being paralyzed by inconsistent efficacy results
 - Understanding low adherence in some populations
- Demonstration projects of targeted PrEP to populations with high HIV incidence
 - Define who wants it, how long they use it, when & how to discontinue PrEP
- Development of longer acting, less user dependent PrEP strategies



Thank you

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