PEP and PrEP

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Consultant in HIV
Brighton & Sussex University Hospitals NHS Trust
UNAIDS 90-90-90:
HIV Treatment Targets for 2020 with Global Estimates (2014)

Target 1:
90% of HIV+ people diagnosed

Target 2:
90% of diagnosed people on ART

Target 3:
90% of people on ART with HIV RNA suppression

HIV Positive People | 36.9 million
--- | ---
Diagnosed | 33.2 million
On ART | 29.5 million
Viral Suppression | 26.9 million

Ref: The Joint United Nations Programme on HIV/AIDS. 90-90-90 An ambitious treatment target to help end the AIDS epidemic. 2014; JC2684
Global Estimates (2014-15) vs the Gap to reach 90-90-90 Targets

HIV Positive People: 36.9 million

Breakpoint 1: 13.4 million Undiagnosed
53%

Breakpoint 2: 14.9 million not treated
41%

Breakpoint 3: 15.3 million Not Virally Suppressed
32%*

Diagnosed: 19.8 million

On ART: 15.0 million

Viral Suppression <1000 (ITT)*: 11.6* million


www.ias2015.org
Global Estimates (2014-15) vs the Gap to reach 90-90-90 Targets

HIV Positive People: 36.9 million

Diagnosed: 19.8 million

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Viral Suppression <1000 (ITT)*: 11.6 million

Breakpoint 1: 13.4 million Undiagnosed

Breakpoint 2: 14.9 million not treated

Breakpoint 3: 15.3 million Not Virally Suppressed


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Post Exposure Prophylaxis
PEP
Post Exposure Prophylaxis

oPEP: PEP after occupational exposure

PEPSE or nPEP: PEP after Sexual Exposure
nPEP: PEP after non occupational exposure
What is considered substantial risk?

**Substantial Risk**
- Exposure of Vagina, rectum, eye, mouth or other mucous membrane, non intact skin, or percutaneous contact
- With Blood, semen, vaginal secretions, rectal secretions, breast milk, or any body fluid that is visibly contaminated with blood
- When The source is known to be HIV infected

**Negligible risk**
- Exposure of Vagina, rectum, eye, mouth or other mucous membrane, intact or non intact skin, or percutaneous contact
- With Urine, nasal secretions, saliva, sweat, or tears if not visibly contaminated with blood
- Regardless Of the known or suspected HIV status of the source
<table>
<thead>
<tr>
<th>Type of exposure</th>
<th>Estimated risk of HIV transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receptive anal intercourse</td>
<td>1.1 (0.042–3%)</td>
</tr>
<tr>
<td>Receptive vaginal intercourse</td>
<td>0.1 (0.004–0.32%)</td>
</tr>
<tr>
<td>Insertive vaginal intercourse</td>
<td>0.082 (0.011–0.38%)</td>
</tr>
<tr>
<td>Insertive anal intercourse</td>
<td>0.06 (0.06–0.065%)</td>
</tr>
<tr>
<td>Receptive oral sex</td>
<td>0.02 (0–0.04%)</td>
</tr>
<tr>
<td>Insertive oral sex</td>
<td>0</td>
</tr>
<tr>
<td>Needle-stick injury</td>
<td>0.3 (0.2–0.5%)</td>
</tr>
<tr>
<td>Sharing injecting equipment</td>
<td>0.67%</td>
</tr>
<tr>
<td>Mucous membrane exposure</td>
<td>0.63 (0.018–3.47%)</td>
</tr>
</tbody>
</table>
In addition to PEP

- Education about risk
- Hepatitis vaccinations
- Occupational Exposure
  - Washing of wound with soap and water in occupational exposure
  - No squeezing of wound
- Sexual Exposure
  - Identification of high risk individuals
  - Use of condoms
Post Exposure Prophylaxis

• No randomized, placebo-controlled clinical trial of PEPSE has been conducted

• Data relevant to PEP guidelines are evolved from
  1. Animal transmission models
  2. Perinatal clinical trials MTCT
  3. Observational studies of health care workers receiving prophylaxis after occupational exposures
  4. Observational and case studies of PEPSE use
1. Animal Model Data
Effectiveness of Tenofovir PEP in Macaques

- Study Features
- N = 24 macaques
- Randomized to 6 treatment arms
- SIV inoculated intravenously
- SIV dose 10x 50% infective dose
- PEP started at 24, 48 or 72 hours
- PEP duration: 3, 10, or 28 days
- PEP regimen: tenofovir (TDF) SQ
- Analyzed for antibody and viremia

Macaque animal models – timing of PEP

- Systemic viral dissemination does not occur immediately → window of opportunity

Macaque animal models – timing of PEP

1. Animal Model Data

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Dynamics following exposure to HIV

24 hours

Regional lymph node

48 – 72 hours

CD4

CCR5

5 days

Mucosa

blood

Dynamics following exposure to HIV

- **24 hours**
- **48 – 72 hours**
- **5 days**

- **Mucosa**
- **CD4**
- **CCR5**
- **Regional lymph node**
- **Blood**

2. Perinatal Studies MTCT

Zidovudine significantly reduces MTCT

PACTG 076 Study

- Placebo (n): 183
- Zidovudine (n): 180

- Probability of transmission (%)
  - Placebo: 25.5%
  - Zidovudine: 8.3%

- Weeks: 0, 24, 48, 72

66% reduction in transmission rate

Connor EM et al. NEJM 1994;331:1173–1180
HIVNET 012: HIV transmission
Intrapartum/postpartum nevirapine vs zidovudine

<table>
<thead>
<tr>
<th>Time</th>
<th>ZDV (n = 308)</th>
<th>NVP (n = 311)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3 days</td>
<td>10.4</td>
<td>8.2</td>
</tr>
<tr>
<td>6-8 weeks</td>
<td>21.3</td>
<td>11.9</td>
</tr>
<tr>
<td>14-16 weeks</td>
<td>25.1</td>
<td>13.1</td>
</tr>
</tbody>
</table>

Stat dose NVP for mother and infant vs ZDV for mother in labour and neonate 1/52

3. Occupational PEP (oPEP) study

- An observational case-control study
- HCW with occupational percutaneous exposure to HIV infected blood
- The case patients (n=33) were those who became seropositive after exposure to HIV, as reported by national surveillance systems in France, Italy, the United Kingdom, and the United States
- The controls (n=665) were HCWs in a prospective surveillance project who were exposed to HIV but did not seroconvert
- The case patients were significantly less likely than the controls to have taken zidovudine after the exposure (odds ratio=0.19; 95 percent confidence interval, 0.06 to 0.52)
- The first study to describe the efficacy of oPEP

4. MSM PEPSE Observational study Brazil

- 2-year prospective study in Brazil
- 200 seronegative MSM at high risk of HIV were provided with
  - education regarding PEPSE
  - a 4-day starter pack with instructions to initiate its use for a suspected eligible exposure
  - a follow-up 24-day pack (to complete a 28-day course) but only for those men with eligible exposures
  - 68/200 MSM initiated PEPSE
  - Adherence to PEPSE medications was estimated on the basis of questions at the 28-day visit and remaining pill counts
  - The entire 28-day PEPSE regimen was completed by 89% of men with eligible exposures including 1 participant who seroconverted
  - Ten of 11 seroconversions occurred among men who did not initiate PEPSE despite risk exposure

PEPSE failure in Men who have Sex with Men (MSM)

- 49 seroconversions were reported after PEPSE use based on 1 case report and 6 studies.

- The case report from Italy described a PEPSE failure in an MSM despite:
  - self-reported 100% adherence
  - Use of a 3-drug medication regimen consisting of ZDV, lamivudine (3TC), and indinavir (IDV)
  - denial of ongoing HIV risk transmission behaviors after completing PEPSE
  - concomitant hepatitis C virus (HCV) seroconversion was also diagnosed


PEPSE failure in Men who have Sex with Men (MSM)

• 6 studies of 1535 MSM with 48 HIV seroconversions despite PEPSE use (31.3 seroconverions/1,000 persons)
• At least 40 of the 48 seroconversions likely resulted from ongoing risk behavior after completing PEPSE
  – 35/40 seroconversions occurred ≥ 180 days subsequent to PEPSE initiation and are unlikely to constitute failures
• The remaining 8 seroconverters among 1,535 MSM participants (5.2 seroconverions/1,000 persons) may be classified as potential PEPSE failures
  – This included 1 recipient with an indeterminate HIV test result and isolation of an M184 mutation resistant virus on the last day of his 28-day regimen despite initiating PEPSE ≤ 48 hours after exposure indicating...??
  – 4 patients seroconverted at 91 days, 133 days, 160 days, and 168 days after PEPSE initiation, including 3 who reported completing the 28-day regimen; however, there was no description regarding ongoing sexual risk behaviors after PEPSE completion
  – Among the remaining 3 men who seroconverted after taking PEPSE no information was reported regarding the PEPSE regimen prescribed, adherence to PEPSE, delay in PEPSE initiation or timing of HIV-positive results
Tenofovir-Emtricitabine (TDF-FTC) plus Raltegravir for PEPSE in MSM

- 100 participants enrolled at Fenway Health
- 98% male, 83% MSM, mean age 33 yrs
- Prescribed TDF-FTC plus raltegravir for PEPSE
- 85/100 had 3-months follow-up
- None were HIV infected
- 57% finished the regimen as prescribed
- Comparable to historic controls (AZT-3TC or TDF-FTC + PI/r)
- Biggest limitation = missed second dose of raltegravir by 27%
- Well tolerated and fewer side effects than historic controls

Considerations of PEP

- Adherence
- Side effects
- Dosage
- Missed doses
- Prescribed medication
- Other drugs
Potential risks of offering PEP

- Toxicity
- Resistance
- Service Provision
- Cost
- Impact on sexual behaviour
PEPSE and sexual behaviour

- UK nonoPEP Study:
  - 77% reported reduced high-risk activity with casual partners

- Brazil:
  - Baseline: 57% reported high-risk behaviour; 24 months: 40%

- San Francisco:
  - 74% reported reduction in high-risk behaviour; 10% reported an increase

Benn et al, BHIVA 2006; Schecter et al, JAIDS 2004; Roland et al, CID 2005
### BASHH PEPSE Guidelines 2015

**Table 4** Situations when post-exposure prophylaxis (PEP) is considered (IV, grade C)

<table>
<thead>
<tr>
<th>Source HIV status</th>
<th>HIV-positive</th>
<th>Unknown from high prevalence group/area</th>
<th>Unknown from low prevalence group/area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral load detection</td>
<td>Recommend</td>
<td>Recommend</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>Receptive anal sex</strong></td>
<td>Recommend</td>
<td>Consider</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>Insertive anal sex</strong></td>
<td>Recommend</td>
<td>Consider</td>
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<td><strong>Receptive vaginal sex</strong></td>
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<td>Consider</td>
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<tr>
<td><strong>Insertive vaginal sex</strong></td>
<td>Recommend</td>
<td>Consider</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>Fellatio with ejaculation</strong></td>
<td>Consider</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>Fellatio without ejaculation</strong></td>
<td>Not recommended</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>Splash of semen into eye</strong></td>
<td>Consider</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>Cummingus</strong></td>
<td>Not recommended</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>Sharing of injecting equipment</strong></td>
<td>Recommended</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>Human bite</strong></td>
<td>Not recommended</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>Needlestick from a discarded needle in the community</strong></td>
<td>Not recommended</td>
<td>Not recommended</td>
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</tr>
</tbody>
</table>

- **High prevalence groups within this recommendation are those where there is a significant likelihood of the source individual being HIV-positive. Within the UK at present, this is likely to be men who have sex with men and individuals who have immigrated to the UK from areas of high HIV prevalence (particularly sub-Saharan Africa).**
- **More detailed knowledge of local prevalence of HIV within communities may change these recommendations from consider to recommended in areas of particularly high HIV prevalence.**
- **PEP is not recommended for individuals receiving fellatio, i.e., inserting their penis into another’s oral cavity.**
- **A bite is assumed to constitute breakage of the skin with passage of blood.**

Factors PEPSE *should not* be prescribed when the exposure is an undetectable plasma viral load. In light of this evidence...
EACS PEP Guidelines

- Rapid testing of the source person for HCV and HIV (if HIV-status unknown) recommended
- If source person HIV-positive on ART, order resistance testing if HIV-VL detectable
- Individualise PEP according to the source’s treatment history and previous resistance tests
- **For sexual exposure, if HIV-positive source has documented undetectable HIV-VL, PEP is no longer recommended**
- PEP to be started ideally < 4 hours after the exposure and no later than 48/72 hours
- Duration of PEP: 4 weeks
- PEP regimens: TDF/FTC (alternative: ZDV/3TC) + RAL bid, or + DRV/r qd or + LPV/r bid. TDF/FTC + DTG qd may be also considered as an alternative.
- Full sexual health screen in case of sexual exposure
- Follow-up: HIV serology + HBV and HCV, pregnancy test (women) within 48 hours of exposure
- Re-evaluation of PEP indication by HIV expert within 48-72 hours
- Assess tolerability of PEP regimen
- Transaminases, HCV-PCR and HCV serology at month 1 if source person HCV-positive (observed or suspected)
- Repeat HIV serology after 2 and 4 months, syphilis serology after 1 month if sexual exposure
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Assess need for PrEP!
Pre Exposure Prophylaxis
PrEP
Previous Prevention Trials

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<th>Study</th>
<th>Effect size (95% CI)</th>
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<td>Medical male circumcision</td>
<td>54% (38; 66)</td>
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<tr>
<td>Truvada for MSMs</td>
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<tr>
<td>Prime boost Vaccine</td>
<td>31% (1; 51)</td>
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<tr>
<td>Truvada for women</td>
<td>0% (-69; 41)</td>
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<tr>
<td>Tenofovir gel (daily) for women</td>
<td>0% (-49; 34)</td>
</tr>
</tbody>
</table>
All PrEP trial participants received a comprehensive HIV prevention package.
Previous Prevention Trials

**Study**

- Treatment for prevention
  - HPTN 052
- Medical male circumcision
- Truvada for MSMs
  - iPrEx
- Tenofovir vaginal (coital)
  - Caprisa 004
- Prime boost Vaccine
- Truvada for women
  - FEM PrEP
- Tenofovir gel (daily)
  - for women
  - VOICE

**Effect size (95% CI)**

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<38% of HIV-ve had any drug
How do we know oral PrEP is effective?

1. Animal studies

2. Major PrEP trials
   - iPrEx
   - PROUD
   - Ipergay
1. Animal Studies

Local and systemic drug concentrations after oral administration of Truvada

Graphs showing TFV and FTC concentrations over time in rectal secretion and plasma, and TFV-DP concentrations in various tissue samples over 7 days.
Efficacy of intermittent PrEP with Truvada in the repeat low-dose macaque model: design

Slides courtesy of Gerardo Garcia-Lerma*1 CROI 2010 Paper # 83
Efficacy of intermittent PrEP with Truvada in the repeat low-dose macaque model: design

Slides courtesy of Gerardo Garcia-Lerma*1 CROI 2010 Paper # 83
2. iPrEx

2007-2011 NIH interventional double-blind, placebo controlled trial

TRUVADA PREP in sexually active MSM & TG

The study enrolled 2,499 HIV uninfected participants in six countries
# iPrEx Results

<table>
<thead>
<tr>
<th>Prevention of HIV acquisition from PREP</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRUVADA</td>
</tr>
<tr>
<td>All participants</td>
</tr>
<tr>
<td>Took 4/7 days</td>
</tr>
<tr>
<td>Took 7/7 days</td>
</tr>
</tbody>
</table>

Daily TRUVADA prevents HIV infection in MSM/TGW who take it

Could be used as part of broader prevention strategy for HIV in high risk groups
2. Pragmatic Open-Label Randomised Trial of Pre-Exposure Prophylaxis: the PROUD study

- To determine whether PrEP worked as well as iPrEx in this setting (44% reduction in HIV)
- Possibility that effectiveness might be less in real world
Main endpoints in Pilot: HIV infection in first 12 months
PROUD: new HIV infections

<table>
<thead>
<tr>
<th>Weeks since enrolment</th>
<th>Immediate PrEP</th>
<th>Deferred PrEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Immediate PrEP: N=3
Deferred PrEP: N=19
**PROUD: STIs**

**Caveat**
Number of screens differed between the groups:
e.g. Rectal gonorrhoea/chlamydia
974 in the IMM group and 749 in the DEF

![Bar chart showing the percentage of different STIs in Immediate and Deferred groups with p-values for each comparison.](chart_image)
PROUD: conclusions

- Daily PrEP with Truvada was highly effective in preventing HIV infection – 86% reduction
- HIV incidence was much higher than predicted in the deferred arm
  - despite extensive use of PEP in the deferred period
- Concerns about PrEP being less effective in the real world unfounded
- There was no difference in STIs, which were common in both groups
3. Ipergay

**Ipergay : Event-Driven iPrEP**

- 2 tablets of Truvada® or placebo before sex (2 to 24 hours before)
- 1 tablet of Truvada® or placebo 24 hours later
- 1 tablet of Truvada® or placebo 48 hours later
Study Design

Double-Blinded Randomized Placebo-Controlled Trial

- HIV negative high risk MSM
- Condomless anal sex with > 2 partners within 6 m

TDF/FTC before and after sex
N=199

Placebo before and after sex
N=201

- Follow-up visits: month 1, 2 and every two months thereafter
Ipergay : Event-Driven iPPrEP

- 2 tablets (TDF/FTC or placebo) 2-24 hours before sex
- 1 tablet (TDF/FTC or placebo) 24 hours later
- 1 tablet (TDF/FTC or placebo) 48 hours after first intake
Ipergay clinical trial results

- 400 participants with a mean follow-up of 13 months

- 16 subjects infected
  - 14 in placebo arm (incidence: 6.6 per 100 PY),
  - 2 in TDF/FTC arm (incidence: 0.91 per 100 PY)

- 86% relative reduction in the incidence of HIV-1 (95% CI: 40-98, p=0.002)

- NNT for one year to prevent one infection: 18
- 133 STIs diagnosed in the TDF/FTC arm
Conclusions

- “On Demand” oral PrEP with TDF/FTC was very effective with a 86% (95% CI: 40-99) reduction in HIV-incidence
- Adherence was good
- Safety of “on demand” TDF/FTC was overall similar to placebo except for gastrointestinal AEs
- Intermittent PrEP may reduce longer term toxicity
Regimens

**PROUD**
- Daily TRUVADA
- Takes 14 days to reach steady state
- Missing 5 doses makes PrEP less effective

**IPERGAY**
- ON DEMAND TRUVADA
- 2 doses between 2-24 hours before sex
- 1 dose at 24 hours
- 1 dose at 48 hours
Missed Doses

**PROUD**
- Take as soon as remember if within 12 hours. May mean 2 doses in 1 day
- Remind if misses 5 days drug levels fall to concerning level
- Discuss resistance

**IPERGAY**
- If not taken double dose before sex, as soon as possible: should take within 12 hours of sex
- If they missed the second dose/third dose they should take TRUVADA if they are within 3 days of the missed dose
Case Report: Multiclass Resistant HIV Infection Despite High Adherence to PrEP

- 43-yr-old MSM acquired multiclass resistant HIV-1 infection following 24 mos of oral once-daily TDF/FTC PrEP
- Pharmacy records, blood concentration analyses, and clinical history support recent and long-term adherence to PrEP
- PrEP failure likely result of exposure to PrEP-resistant, multiclass resistant HIV-1 strain

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Mutations Detected on Day 7 Following p24-Positive Test</th>
<th>Estimated Fold-Change in IC\textsubscript{50} or Change in Response (Drug)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRTI</td>
<td>41L, 67G, 69D, 70R, 184V, 215E</td>
<td>1.9x (ABC), 61x (3TC), 38x (FTC), 1.3x (TDF)</td>
</tr>
<tr>
<td>NNRTI</td>
<td>181C</td>
<td>43x (NVP)</td>
</tr>
<tr>
<td>PI</td>
<td>101</td>
<td>No relevant change</td>
</tr>
<tr>
<td>INSTI</td>
<td>51Y, 92Q</td>
<td>Reduced (RAL), resistant (EVG), reduced (DTG)</td>
</tr>
</tbody>
</table>
PrEP assumptions

• Adherence
• May have periods not requiring PrEP
• Patients need to be aware not protective against STIs (hep C)
• Require regular HIV tests
• Discordant partners of HIV+ on treatment may need (HPTN-052)

• **PrEP is not recommended in**
  – Unable to tolerate TRUVADA
  – Hepatitis B infection
PrEP-C with Tenofovir
n=22

All women HIV negative 3/12 after last exposure
Maximum attempts 12*
Fertility investigations after 6 attempts*

Vernazza, et al. 4th IAS, 2007
* Personal communication from P Vernazza
Efficacy in Partners PrEP[1]

Table 2: Kaplan-Meier curve for the primary modified ITT analysis

38% HIV neg partners were women.

<table>
<thead>
<tr>
<th></th>
<th>HIV+</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>75% TDF/FTC</td>
<td>52</td>
<td>13</td>
</tr>
<tr>
<td>67% TDF</td>
<td>13</td>
<td>17</td>
</tr>
</tbody>
</table>

31% vs 81%
detectable TNF at seroconversion visit in HIV+ vs HIV-


Funding: Bill & Melinda Gates
<table>
<thead>
<tr>
<th></th>
<th>FTC/TDF</th>
<th>TDF</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1 or 2</td>
<td>15%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Grade 3 or 4</td>
<td>4%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>phosphorus abnormalities</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAEs</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deaths</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Modest GI and fatigue in active arms during month 1.

Previous Prevention Trials

**Study**

- Treatment for prevention
  - HPTN 052
- Medical male circumcision
- Truvada for MSMs
  - iPrEx
- Tenofovir vaginal (coital)
  - Caprisa 004
- Prime boost Vaccine
- Truvada for women
  - FEM PrEP
- Tenofovir gel (daily)
  - for women
  - VOICE

**Effect size (95% CI)**

- 96% (73; 99)
- 54% (38; 66)
- 44% (15; 63)
- 39% (6; 60)
- 31% (1; 51)
- 0% (-69; 41)
- 0% (-49; 34)
MTN-020/ASPIRE & IPM-027: Dapivirine Vaginal Ring for HIV Prevention in Women

- Silicone elastomer vaginal matrix ring containing NNRTI dapivirine 25 mg; ring replaced every 4 wks
- Randomized, double-blind phase III trials
  - MTN-020/ASPIRE\textsuperscript{[1,2]}: Malawi, South Africa, Uganda, Zimbabwe
  - IPM-027 (The Ring Study)\textsuperscript{[3]}: South Africa, Uganda
  - Primary endpoints: efficacy and safety

Sexually active HIV-uninfected adult women
(ASPIRE: N = 2629; IPM-027: N = 1959)

Dapivirine 25 mg Vaginal Ring every 4 wks
+ HIV Prevention Service Package
(ASPIRE: n = 1313; IPM-027: n = 1300)

Placebo Vaginal Ring every 4 wks
+ HIV Prevention Service Package
(ASPIRE: n = 1316; IPM-027: n = 650)


Slide credit: clinicaloptions.com
MTN-020/ASPIRE & IPM-027: Efficacy and Safety of Dapivirine Vaginal Ring

- Efficacy for HIV prevention similar in both studies
- No clinically relevant safety differences between arms

<table>
<thead>
<tr>
<th>Outcome</th>
<th>ASPIRE[^1,^2]: 15 Sites</th>
<th>ASPIRE[^1,^2]: 13 Sites*</th>
<th>The Ring Study[^3]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dapivirine (n = 1308)</td>
<td>Dapivirine (n = 1198)</td>
<td>Dapivirine (n = 1300)</td>
</tr>
<tr>
<td></td>
<td>Placebo (n = 1306)</td>
<td>Placebo (n = 1197)</td>
<td>Placebo (n = 650)</td>
</tr>
<tr>
<td>HIV infections, n</td>
<td>71</td>
<td>54</td>
<td>77</td>
</tr>
<tr>
<td>HIV incidence (per 100 PYs)</td>
<td>3.3</td>
<td>2.8</td>
<td>4.1</td>
</tr>
<tr>
<td>HIV protection efficacy, %</td>
<td>27 (P = .046)</td>
<td>37 (P = .007)</td>
<td>31 (P = .040)</td>
</tr>
</tbody>
</table>

- Among women older than 21 yrs
  - 56 (P < .001)
  - 37 (P = .10)


*Excludes 2 sites with low adherence.
ÉCLAIR: Patient Satisfaction With IM Therapy vs Oral Phase

• Pt satisfaction assessed by questionnaire at Wk 18 of IM treatment; asked pts to compare satisfaction of current IM vs past oral therapy\(^1\)

How satisfied are you with your current treatment?

How satisfied would you be to continue with your present form of treatment?

- In separate macaque study, CAB LA conferred 88% protection (21/24 animals) against IV exposure to SIVmac251; results may be relevant to humans who inject drugs\(^2\)

HPTN-069/A5305: Maraviroc-Based PrEP for MSM 48w

- Randomized, double-blind phase II trial
  - Primary endpoints: safety (grade ≥ 3 AEs), tolerability (rate/time to discontinuation of study drug)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVC 300 mg (n = 101)</td>
<td>MVC 300 mg + FTC* (n = 106)</td>
</tr>
<tr>
<td>MVC 300 mg + TDF* (n = 99)</td>
<td>FTC + TDF* (n = 100)</td>
</tr>
</tbody>
</table>

HIV-uninfected men with condomless anal intercourse with ≥ 1 HIV+ or HIV unknown man in previous 90 days (N = 406)

- 67 grade 3/4 AEs; rates similar across arms
- 9% discontinued study drug early
  - Rates of study drug discontinuation (P = .6) and time to permanent discontinuation (P = .6) similar across arms
- 5 new HIV infections occurred during study for annual incidence rate of 1.4% (95% CI: 0.8-2.3);
  - 4xMVC, 1xMVC/TDF; all R5 tropic; no transmitted drug resistance

Where to buy PrEP online, now, in the UK

So far we have independently verified 4 different companies who reliably sell PrEP that you can trust. For full details on our independent verification process, click here.

**United Pharmacies Ltd** (£41 per month)

United Pharmacies UK is our personally recommended supplier of PrEP. If you do not need to upload a prescription for purchasing and they have some of the cheapest prices on the internet. In addition to independently verifying their product, we also use United Pharmacies to buy PrEP ourselves. The only minor issue is that due to running out of stock, orders occasionally have a delay of around 1 - 2 weeks.

1 month supply = £46.70 per month
2 month supply = £91.70 per month, (£45.17 each)
3 month supply = £137.85 per month, (£45.29 each)
Delivery to the UK costs £6.99 and takes 7 - 14 business days.

**All Day Chemist** (£42 per month)

All Day Chemist also does not ask you to upload a prescription for PrEP. Their website operates in US dollars but we converted the prices below to make them easier to compare. We have in fact anecdotal reviews of All Day Chemist being a popular choice for many PrEP users. Again, we have fully verified their sales process and reliability of their drugs, especially with All Day Chemist see below for information on any but potential import taxes.

1 month supply = £36.26
2 month supply = £72.28
3 month supply = £108.29
Delivery to the UK costs £8.99 and takes 7 - 14 days

**In House Pharmacy** (£46 per month)

In House Pharmacy does not ask you to upload a prescription for PrEP, but their prices are higher than most other sellers the others we have fully verified that they are a reliable supplier of PrEP.

1 month supply = £33.66
3 month supply = £99.45
Delivery to the UK is free and takes 10 - 21 days

**Aids Drugs Online** (£49 per month)

We have ourselves made a purchase from Aids Drugs Online with no problems. However they do require you to upload a prescription before they dispatch your order. For more information on prescriptions, their website also operates in US dollars and they ship from Singapore. Aids Drug Online is one of the least expensive out of any of the suppliers listed, which takes 2 - 3 business days to process before they dispatch your order.

1 month supply = £30.46 (US dollars) (around 389p)
3 month supply = £91.48 (US dollars) (around £76.40)
Delivery costs £8.00 and takes 7 - 14 business days after your prescription has been checked, which takes 2 - 3 business days.

Our Verification Process

Many people including doctors, who are very concerned about medication that is bought online. If you haven’t placed an order before you may not trust the company or be able to tell if they are operating legitimately. You may also not have the unhindered testing of the drugs you buy from them to make sure that they are genuine and working as they should.

One of the key objectives of this website is to try to assist with the above concerns. All of the PrEP that we list on this site are made by Gilead and have been officially approved by the United States Food and Drug Administration (US FDA). We do verify all suppliers so the drugs are lab-tested (to ensure that the supplier is working properly) and the process was smooth, easy and reliable. More importantly, the drugs purchased from each website have been tested by customers, who then rate and review them on this website. We are constantly working with new HIV organizations to establish a reliable and trustworthy platform to verify the quality of PrEP drugs available online.

There are numerous other online pharmacies that sell PrEP. If you do not trust them then this is the simple fact that we have not been able to personally verify them yet, nor because we have had a negative experience with them.

If you have bought PrEP from any other websites and been able to verify your purchase with a blood test then please let us know on info@prawan.co.uk so that we can investigate and add other reputable sites to our list for everyone else to use.
HIV prevention drug Truvada won't be subsidised in Australia
EACS PrEP Guidelines

- PrEP can be used in adults at high-risk of acquiring HIV infection.
- Recommended in HIV-negative men who have sex with men (MSM) and transgender individuals who are inconsistent in their use of condoms with casual partners or with HIV-positive partners who are not on treatment.
- A recent STD or use of post-exposure prophylaxis may be markers of increased risk for HIV acquisition.
- May be considered in HIV-negative heterosexual women and men who are inconsistent in their use of condoms and likely to have HIV positive partners who are not on treatment.
- PrEP is a medical intervention that may not provide full protection against acquiring HIV, does not protect against other STDs and should be used in combination with other preventive interventions, including the use of condoms.
- PrEP should be supervised by a doctor, experienced with sexual health and use of HIV medicines, possibly as part of a shared care arrangement.
- The following procedures are recommended:
  - Documented negative fourth generation HIV test prior to starting PrEP.
  - During PrEP, this test should be repeated every 3 months, and PrEP should be stopped immediately in case of early clinical signs of HIV seroconversion or a positive HIV diagnostic test and the person referred for evaluation to an HIV unit.
EACS PrEP Guidelines

- Before PrEP is initiated, HBV serology status should be documented.
- If HBsAg positive see Clinical Management and Treatment of HBV and HCV Co-infection in HIV-positive Persons.
- Counsel that PrEP does not prevent other types of STD; screen for STD (including HCV) when starting PrEP and regularly during use of PrEP.
- Counsel that PrEP may impact renal and bone health
- Check renal function and bone mineral density according to guidelines on TDF use.
- Counsel that PrEP, like other prevention methods, only works when it is taken. Adherence counselling is recommended.
- Counsel that PrEP can be prescribed long term but that each consecutive PrEP prescription should be for a period of **maximum 3 months (90 tablets) to ensure appropriate monitoring.**
- PrEP regimen
  - TDF/FTC 300*/200 mg 1 tablet qd. For MSM with high-risk sexual behavior PrEP may be dosed ‘on demand’ (double dose of drug 2-24 hours before each sexual intercourse, followed by two single doses of drug, 24 and 48 hours after the first drug intake). If dosed ‘on demand’, the total dose per week should not exceed 7 tablets.
  - In certain countries TDF is labelled as 245 mg rather than 300 mg to reflect the amount of the prodrug (tenofovir disoproxil) rather than the fumarate salt (tenofovir disoproxil fumarate).
Summary PEP and PrEP

- Assessment of risk and engagement in care
- Part of risk reduction strategy
- Highly effective
- Regimens well tolerated
- Newer agents/methodologies being assessed for PrEP
- Studies ongoing in heterosexual populations
- Clear guidelines on management and follow-up
- Essential part of HIV and Sexual Health Care