"This house believes that pre-exposure prophylaxis (PrEP) will have a major impact on the UK HIV epidemic"

Against…..

Martin Fisher
Brighton and Sussex University Hospitals NHS Trust
NHIVNA, Manchester, June 2012

Brighton and Sussex University Hospitals NHS Trust

brighton and sussex medical school

National HIV Nurses Association

Against PrEP

- Does it work?
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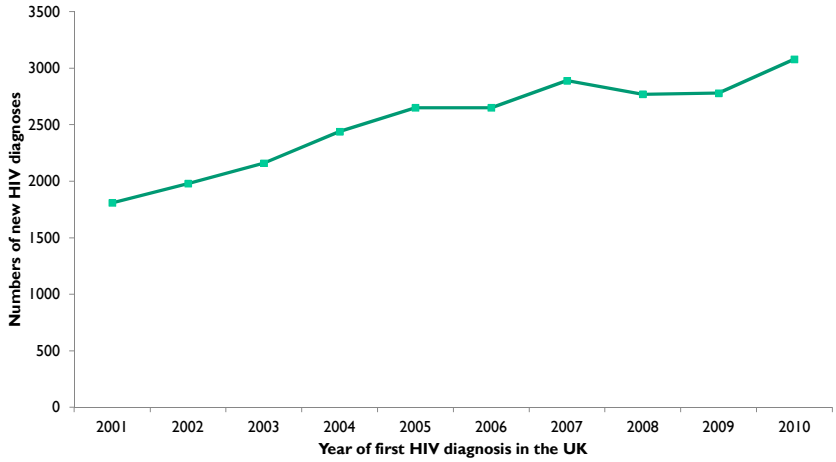
New HIV diagnoses (Adjusted) among MSM, UK, 2001-2010



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Study	Population	N	Results
CAPRISA 004 South Africa	Women	889	39% efficacy vaginal TFV gel
iPrEx Brazil, Ecuador, Peru, S Africa, Thailand, US	MSM	2499	44% efficacy FTC/TDF
TDF2 Study Botswana	Young men women	1200	62% efficacy FTC/TDF
Partners PrEP Study Kenya, Uganda	Heterosexual couples	4758	67% efficacy TDF 75% efficacy FTC/TDF
FEM-PrEP Kenya, S Africa, Tanzania	Women	1950	FTC/TDF = futility
VOICE S Africa, Uganda, Zimbabwe	Women	5029	TDF = futility Vaginal TFV gel = futility FTC/TDF ongoing
Bangkok Tenofovir Study Thailand	IDUs	2400	TDF ongoing
FACTS001 South Africa	Women	2200	TFV gel enrolling

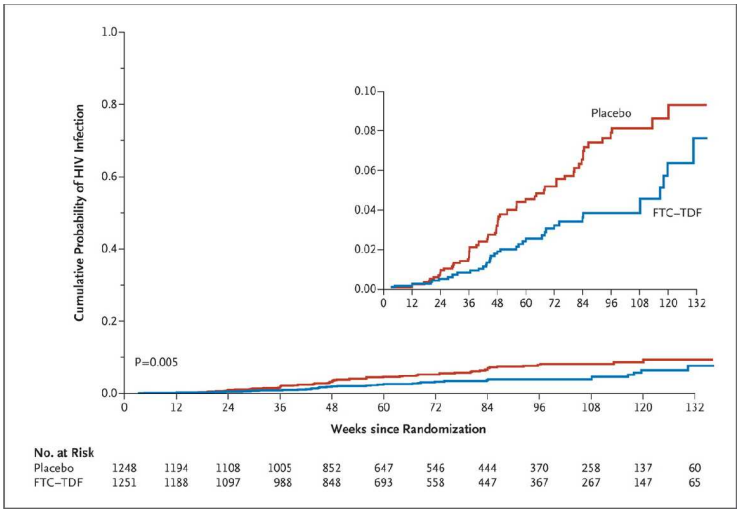
iPrEX Study


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

Robert M. Grant, M.D., M.P.H., Javier R. Lama, M.D., M.P.H., Peter L. Anderson, Pharm.D., Vanessa McMahan, B.S., Albert Y. Liu, M.D., M.P.H.,



•44% reduction in HIV (95% CI: 15-63%) (p=0.005)
•58%reduction (95% CI: 32-74%)(p=0.01) if reported URAI in 6m preceding enrolment

Fem PrEP: Primary effectiveness analysis

	TDF/FTC (N = 1025)	Placebo (N = 1031)
HIV infections	27	34
Incidence rate	4.2 per 100 P-Y	5.0 per 100 P-Y

Estimated effectiveness: 18% reduction in risk
Hazard ratio = 0.82 (0.49, 1.36); *p*-value = 0.44

Lut Van Damme, M.D. on behalf of the FRM-PrEP; CROI 2012; Abst 32LB

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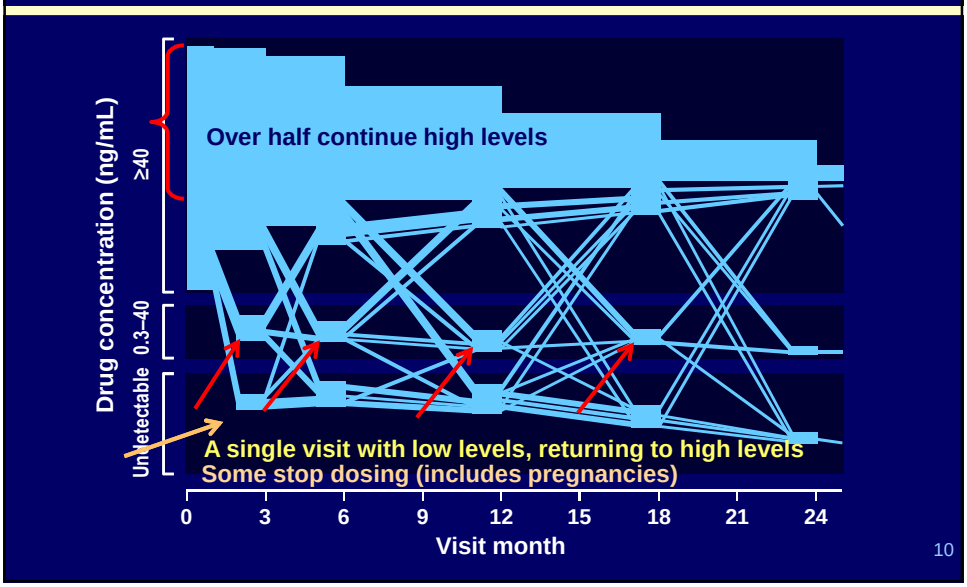
Drug levels during follow-up in cohort: Initially high levels



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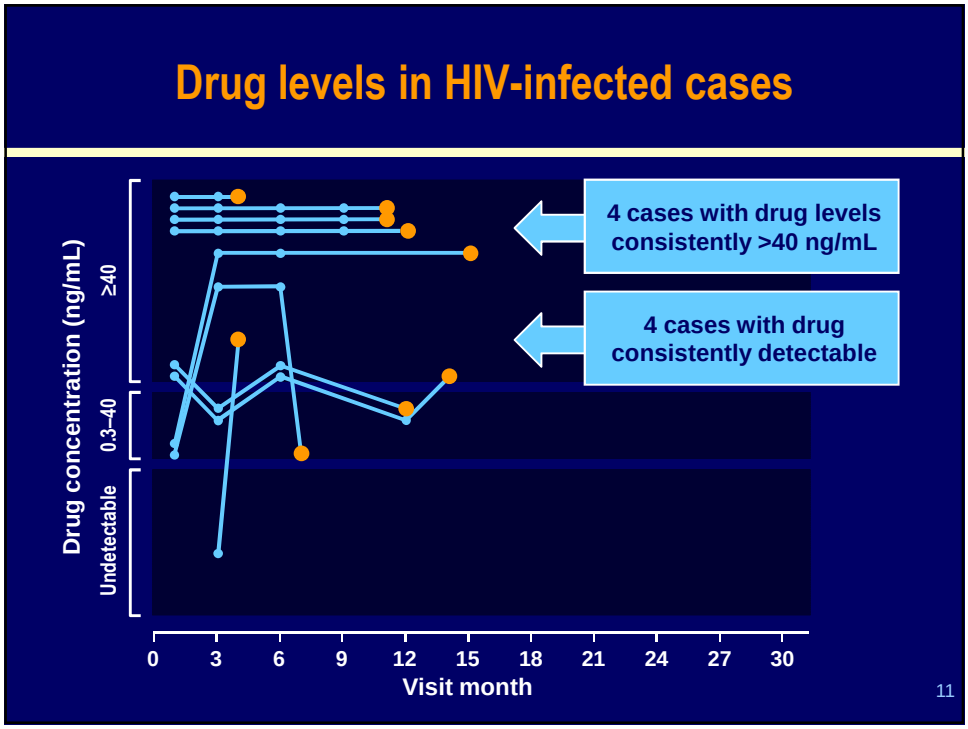

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HIV-1 infection risk reduction & dosing

STRAND dosing	iPrEx model estimate for HIV risk reduction (95% CI)
2 doses/wk	76% (56 to 96%)
4 doses/wk	96% (90 to >99%)
7 doses/wk	99% (96 to >99%)

Intermittent PrEP

Fixed / Time-based dosing

Event-based dosing

Fixed dosing with event-based supplementation

Periodic PrEP

Patient preference: daily > event-based

- But adherence patterns in trials….

50% MSM last AI “planned”; but……

Concerns regarding pharmacokinetics

- ?need to achieve steady-state before intermittent dosing

Buchbinder, #68

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PEPSE ineffective in MSM

- **"Praca Onze" Study**
  - MSM in Rio, Brazil
  - Given PEP pack to start after risk exposure
  - N=200, follow-up 24 months
  - 10 seroconversions in "non-PEP users" (4.2%); 1 seroconversion in "PEP user" (0.6%); $p<0.05$
  - However…overall HIV incidence 2.9/100py compared to 3.1/100py expected; $p>0.97$
  - *"PEP did not appear to substantially affect HIV transmission"*

Schechter M et al; JAIDS, 2004

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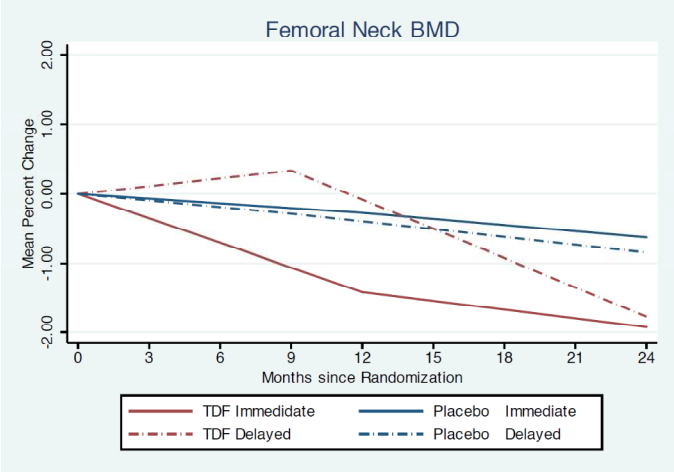
Toxicity: Effect of TDF on BMD over time: Femoral Neck



Net BMD Effect: -1.1% (95% CI -0.4 to -1.9%), p = 0.004

Resistance

- Synopsis of PrEP studies:
  - No resistance in those HIV negative at baseline
  - FTC resistance in all of those "undetected" as positive
  - Monthly HIV testing in a clinical trial
  - Clinical reality?

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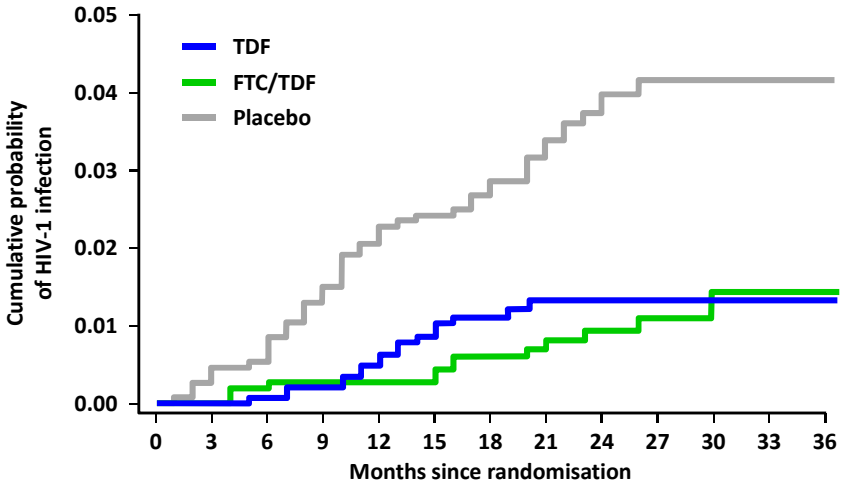
Partners PrEP: Primary Efficacy Results



No. at risk:													
TDF	1572	1559	1547	1498	1350	1223	1062	902	735	510	287	108	15
FTC/TDF	1568	1557	1546	1493	1371	1248	1059	901	743	525	291	114	16
Placebo	1568	1557	1544	1487	1347	1224	1061	902	744	523	295	120	18

Baeten et al., 19th CROI; Seattle, WA; March 5-8, 2012. Abst. 29

PrEP: which drug(s) to use?

- Truvada?
- Tenofovir?
- Maraviroc?
- Other?

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PrEP studies and sexual behaviour

- No increase in “risk” behaviour but….
- Clinical trial population
- Placebo-controlled
- Before efficacy data
- Equipoise is now lost????

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How affordable is PrEP?

- PrEP may not be affordable
  - Overall
    - Brighton:
    - Total population: 250,000
    - Gay population: 25,000
    - MSM population: 12,500
    - HIV negative, at-risk: 2,500
    - Cost of regular HIV tests, monitoring, Truvada
      - Cost of Truvada alone: £12,500,000
  - Truvada in London: affordable for prevention but not for treatment?

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Principles of Biomedical Ethics

- Beneficence
- Non-maleficence
- Autonomy
- Justice

Principles of Biomedical Ethics

- Beneficence ?
- Non-maleficence ?
- Autonomy √
- Justice ?/X

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- Is it ethical? ?

Who will Dr McCormack prescribe PrEP for?

- MSM only?
- MSM with1 episode of UPAI?
- 2 episodes?
- 3 episodes?
- 4 episodes?
- Another STI?
- Post PEP?

BHIVA / BASHH Position Statement on PrEP in the UK

Fidler S, Fisher M, McCormack S

- *"It is imperative to gather evidence for the value of PrEP in the UK, in order to achieve universal access should it prove cost-effective as part of a combination prevention package. There are important concerns, and we recommend that ad-hoc prescribing is avoided, and that PrEP is only prescribed in the context of a clinical research study in the UK. Ideally this would be a randomised controlled trial, which is embedded in a broader concerted effort to intensify HIV prevention and implement the existing guidelines"*