18th Annual Conference of the British HIV Association (BHIVA)

Dr David Dunn

MRC Clinical Trials Unit, London

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COMPETING INTEREST OF FINANCIAL VALUE ≥ £1,000:	
Speaker Name	**Statement**
Dr David Dunn:	None declared
Date	**April 2012**

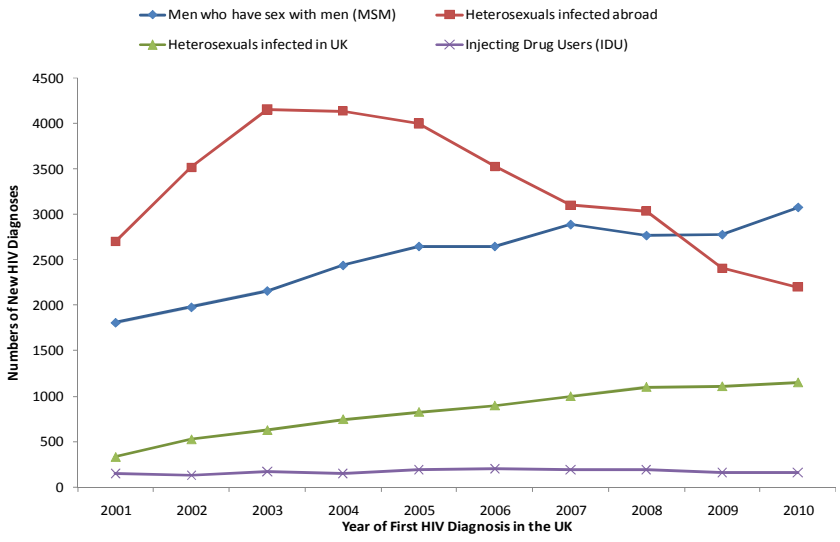
18-20 April 2012, The International Convention Centre, Birmingham

MRC Clinical Trials Unit

Optimising the use of Truvada as PrEP in the UK

David Dunn

New HIV Diagnoses (Adjusted) - UK



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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., Lorena Vargas, Pedro Goicochea, M.Sc., Martín Casapía, M.D., M.P.H., Juan Vicente Guanira-Carranza, M.D., M.P.H., Maria E. Ramirez-Cardich, M.D., Orlando Montoya-Herrera, M.Sc., Telmo Fernández, M.D., Valdilea G. Veloso, M.D., Ph.D., Susan P. Buchbinder, M.D., Suwat Chariyalertsak, M.D., Dr.P.H., Mauro Schechter, M.D., Ph.D., Linda-Gail Bekker, M.B., Ch.B., Ph.D., Kenneth H. Mayer, M.D., Esper Georges Kallás, M.D., Ph.D., K. Rivet Amico, Ph.D., Kathleen Mulligan, Ph.D., Lane R. Bushman, B.Chem., Robert J. Hance, A.A., Carmela Ganoza, M.D., Patricia Defechereux, Ph.D., Brian Postle, B.S., Furong Wang, M.D., J. Jeff McConnell, M.A., Jia-Hua Zheng, Ph.D., Jeanny Lee, B.S., James F. Rooney, M.D., Howard S. Jaffe, M.D., Ana I. Martinez, R.Ph., David N. Burns, M.D., M.P.H., and David V. Glidden, Ph.D., for the iPrEx Study Team*

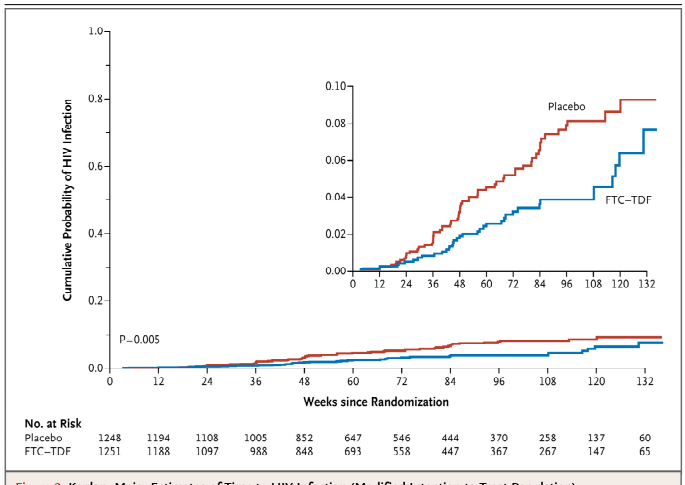

Figure 2. Kaplan–Meier Estimates of Time to HIV Infection (Modified Intention-to-Treat Population).

The cumulative probability of HIV acquisition is shown for the two study groups. The efficacy of preexposure prophylaxis with emtricitabine and tenofovir disoproxil fumarate (FTC–TDF) was 44%, as compared with placebo (P=0.005). The inset graph shows a more detailed version of the overall graph up to a probability of 0.10.

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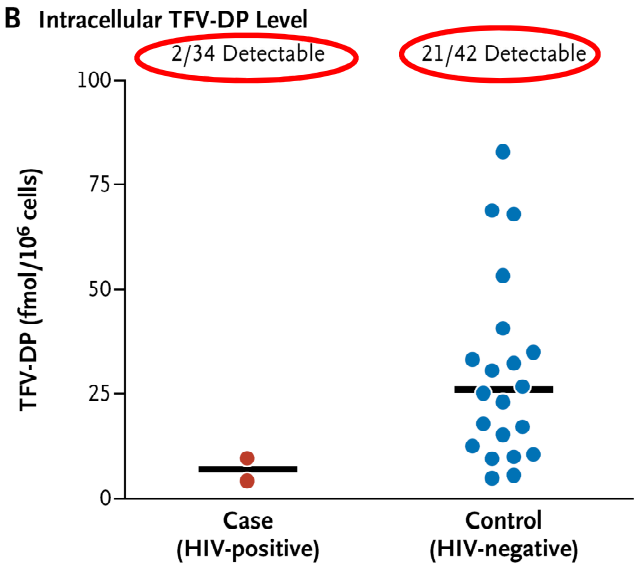

Efficacy versus Effectiveness (1)

- Major motivation for using a **placebo** controlled arm in PrEP trials is to ensure balance in sexual behavioural characteristics between arms
- This enables the observed difference between the arms to be ascribed to the pharmacological **efficacy** of PrEP
- But to assess the "real life" (public health) **effectiveness** of PrEP need to consider that patients knowingly taking an efficacious drug may have different sexual behaviour

Efficacy versus Effectiveness (2)

- To what extent might pharmacological efficacy of PrEP be counterbalanced by
  - Decreased use of condoms?
  - Increased risky sexual behaviour?
- Effectiveness can only be reliably assessed by a pragmatic **open-label** trial where subjects know if they are on active drug
- Such trials measure the **net effect** of
  - the direct effect of pharmacological efficacy, and
  - any indirect effect on "risk compensation"

BHIVA-BASHH Position Statement on PrEP

- 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

PROUD

- **Pr**e-exposure **O**ption for preventing HIV in the **U**K: an open-label randomisation to immediate or **D**eferred inclusion of Truvada as part of a comprehensive HIV prevention package
- Designed by colleagues from MRC CTU, HPA, expert clinicians, PrEP eGroup, NAM/THT
- PI: Sheena McCormack

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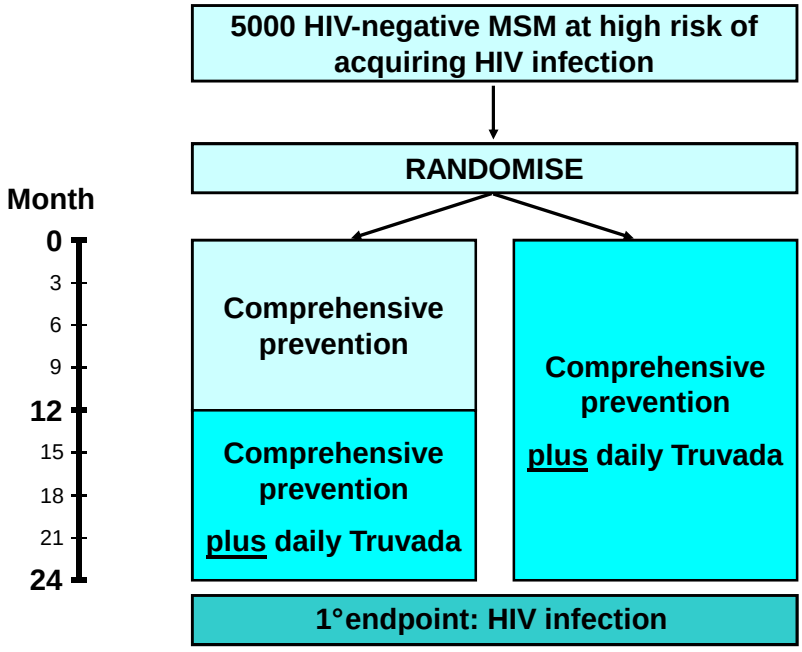

Key inclusion criteria

- Previously attended current GUM clinic at least once
- HIV negative test in previous 4 weeks
- Reported URAI (not counting HIV+ve partners on treatment) in previous 3 months
- Likely to have URAI (not counting HIV+ve partners on treatment) in next 3 months
- Willing/able to attend clinic every 3 months for next 24 months
- (Prepared not to seek PrEP elsewhere if randomised to deferred arm)

Endpoints

- Primary:
  - HIV infection acquired between trial entry and 12 months
- Secondary:
  - Proportion of acts of RAI protected by condom
  - Total number of different URAI partners
  - Anally-acquired STIs
  - HIV infection acquired between 12 and 24 months
  - Proportion of daily doses of Truvada taken
  - Presence of drug in cell/plasma samples at 6 and 18 months

Sample size

- 5000 participants (2500 per arm)
- 15% loss to follow-up
- Powered to detect a two-fold reduction in HIV incidence (2.5 per 100 person-years in deferred arm, 1.25 per 100 person-years in immediate arm)
- Anticipate 80 new HIV infections under these assumptions

Pilot study

- About to apply for regulatory approval to conduct a pilot study of **500** subjects
- Largely a dry run of main trial
- Funding from Gilead (including drug), HPA, MRC
- Hope to start Q3/2012
- ~12 sites (inside/outside London) in GUMNET network

Pilot Outcomes

- Who takes up offer of PrEP
- Acceptability of randomisation
- Rate of recruitment
- Retention in follow-up (especially deferred arm)
- Piloting of case record forms (especially on behavioural data)
- Early data on effect of PrEP on behavioural change
- Is HIV incidence broadly in line with assumptions?

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  - HPA colleagues: Noel Gill, Tony Nardone, Monika Desai and Sarika Desai
  - City/LSHTM/UCL colleagues: Jonathan Elford, Ford Hickson, Graham Hart, Anne Johnson, Rob Horne and Andrew Phillips
  - Clinical colleagues: Ann Sullivan, Brian Gazzard, Martin Fisher, Sarah Fidler
  - CTU colleagues: Sheena McCormack, David Dolling, Kholoud Porter, David Dunn

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