PROUD

Background to PrEP research

November 2010: iPrEX trial shows Truvada almost halves the risk of HIV among gay and other men who have sex with men (GMSM) and transgender women (TGW)[1].

April 2011: FemPrEP trial among women in east & southern Africa shows no benefit of daily Truvada - largely explained by low levels of adherence.

July 2011: Truvada shown to reduce the risk of HIV infection among heterosexual sero-discordant couples in Kenya (Partners PrEP) and heterosexual women and men in Botswana (TDF2).

July 2011: HPTN052 trial shows that ART use by HIV positive individual reduces the risk of onward HIV transmission by 96%.

January 2012: British HIV Association & British Association for Sexual Health and HIV release joint statement recommending that in the UK, ad hoc prescribing of PrEP be avoided and PrEP be prescribed in the context of a clinical research study in order to collect UK specific information as quickly as possible.

July 2012: The Food and Drug Administration approve Truvada for HIV prevention in the USA.

November 2012: PROUD pilot study launched to assess feasibility of a larger clinical trial that would be necessary to assess Truvada effectiveness in the UK[2].

March 2013: VOICE trial among women in east & southern Africa shows no benefit of tenofovir or Truvada – again this seems mainly related to low adherence.

June 2013: Bangkok CDC study shows tenofovir halves the risk of HIV among injecting drug users.

September 2013: A survey among about half of all prescribers in the USA shows slow uptake of PrEP outside of clinical studies with around 2000 individuals prescribed Truvada as PrEP from 2011 to early 2013. About a third of prescribers had no prior experience of prescribing ARVs.

October 2013: Microbicides Trial Network launch first trial of tenofovir rectal microbicide.

March 2014 PrEP research update:

Truvada in USA	Approx. a dozen demonstration studies: not evaluating the effect of Truvada on HIV reduction - the main questions are about Truvada use among marginalized groups such as black or adolescent GMSM/TGW and women, as well as evaluating the best ways to support regular use of PrEP and include PrEP in broader HIV prevention packages.
Truvada in Africa, Austral-Asia, southeast Asia, Asia, South America	Approx. a dozen demonstration studies: again not evaluating the effectiveness of Truvada but addressing questions such as uptake of PrEP including among adolescents, service delivery models for PrEP, and using PrEP as a bridge to ARV treatment for sero-discordant couples.
IPERGAY in France, Canada, Germany	Comparing use of Truvada before and after sex to placebo.
ADAPT in South Africa, Thailand, USA	Comparing Truvada when used before and after sex, twice per week plus after sex, to daily.
NEXT-PrEP in USA	Comparing: Maraviroc, Maraviroc + FTC, Maroviroc + tenofovir, to Truvada (which is FTC + tenofovir).

[1]Effectiveness results for each trial provided in table on page 3

[2]There is an update on the PROUD pilot study at http://www.proud.mrc.ac.uk/news.aspx

PROUD

Participant Involvement Meeting on 19th March 2014

Discussion topic: **Future HIV prevention research priorities: a discussion about research priorities in the event that PROUD demonstrates benefits of PrEP in the UK**

In break out groups, we would like you to discuss the following three questions:

1) **What are the next priorities for clinical trials in the UK?**

   Should we be testing different ways of using Truvada or new HIV prevention drugs? For example should we test Truvada with alternative dosing, Truvada with new ways to support adherence, different PrEP pills, monthly injectable PrEP, comparing pre to post exposure options, rectal microbicide gels, etc.

2) **How acceptable would various clinical trial designs be to test the priority clinical trial questions?**

   All clinical trial designs require a control group in order to compare the test product. Based on the clinical trial priorities discussed in the last question, would it be acceptable for the next clinical trial to have the following as control groups:

   - Placebo
   - Deferred start (as in PROUD)
   - Daily Truvada

3) **What are the next priorities for clinical research around Truvada in the UK?**

   If PROUD shows Truvada to be effective in the UK, what are the other clinical research questions that we need to prioritise? For example evaluating the ways that Truvada is prescribed, evaluating ways to support adherence such as peer support, understanding more about how sero-discordant couples use PrEP and treatment as prevention, etc.

PROUD

Effectiveness of PrEP in clinical trials

Study	Drug	Population	Effect (95%CI)	Effect with detectable drug
Partners PrEP	Truvada	Discordant	75% (55, 87)	86% (57,95)
Partners PrEP	Tenofovir	Discordant	67% (44, 81)	90% (56, 98)
CDC TDF2	Truvada	Hetero	62% (22, 83)	78%
iPrEX	Truvada	G&MSM	44% (15, 63)	92% (40, 99)*
CDC Bangkok	Tenofovir	IDU	49% (10, 72)	74% (17, 94)
FemPrEP	Truvada	Women	0%	
VOICE	Tenofovir	Women	0%	
VOICE	Truvada	Women	0%	

*Subsequent mathematical modelling based on drug levels observed in iPrEX estimate that daily Truvada use could reduce the risk of HIV infection by as much as 99%.