SuPS3:Recent Progress in Basic and Clinical HIV Research:Outcomes from Asia and The Pacific

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SuPS3-04: From the Laboratory to the Field-Advances in Prevention Sciences

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Outline of Presentation

- Introduction
- Rationale for use of ARVs as prevention
- Prevention for negatives
- Topical PrEP
- Oral PrEP
- Prevention for Positives
- ART as prevention
- Strategic use of antiretrovirals and combination prevention

New HIV infections continue to occur

At the end of 2009

- 33 million people living with HIV
- 2.6 million annual new infections
- 6.6 million are on antiretroviral treatment (ART)

- for every person starting ART two people are newly infected
- Need to sustain current prevention programmes at sufficient intensity and scale (condoms, harm reduction)
- Need for more effective new prevention tools and a vaccine

Recent events

- CAPRISA 004, 23 july 2010
- iPrEx, 15 November 2010
- FEM-PrEP study stopped for futility, 18 April 2011
- HPTN-052 delayed treatment arm stopped for efficacy, 12 May 2011
- Partners PrEP placebo arm stopped for efficacy, 13 July 2011
- CDC announces positive TDF2 results, 13 July 2011

Why the interest in use of ARVs for Prevention?

- Biological plausibility-effect of ARVs on viral replication
- Numerous animal models since 1995 show protection
- Success of post-exposure prophylaxis for needle stick exposure in observational data
- PMTCT: Proof of concept
- Observational studies-effect of ART on community viral load and prevention of transmission in sero-discordant couples

Considerations regarding TDF & TDF/FTC for PrEP

Potent

- Broad antiviral activity (HIV-1 subtypes, HIV-18-2)
- Active against virus types found both in early and late HIV infection
- Act early in the life cycle of HIV (Pre-integration) so it can block initial infection
- Rapidly active (suggesting evern intermittent use might be possible)

Safe

- Favorable safety and tolerability
- Hight bareier to resistance, and limited cross-resistance

Easy

- Relative easy to use (low pill burden, nofood restrictions, no drug interactions with contraception /TB meds/antibiotics)

CAPRISA 004

- 889 women randomized to receive tenofovir 1% gel(n=445)or placebo)n=444)with coitally dependent regimen
- South Africa

	Tenofovir	Placebo
#HIV infections	38	60
HIV incidence (per 100 women-years)	5.6	9.1
95% Cl	(6-60%)	
p-value	0.017	

39% lower HIV incidence in tenofovir gel group

FEM-PrEP

- 1,951 women randomized to receive TDF/FTC or placebo
- Kenya, South Africa, and Tanzania
- Study stopped because of futility
  - 56 HIV endpoints
    - Truvada: n = 28
    - Placebo: n = 28
- Possible explanations for lack of efficacy
  - Poor adherence of drug sharing
  - Differential compartmental PK

Partners PrEP

- 4,758 HIV serodiscordant couples randomized to receive TDF (n= 1584), TDF/FTC (n = 1579) or placebo (n =1584)
- Kenya and Uganda

	TDF	FTC/TDF	Placebo
Number of HIV infections	18	13	47
HIV incidence, per 100 person-years	0.74	0.53	1.92
HIV protection eddicacy, vs placebo	62%	73%	
95% Cl	(34-78%)	(49-85%)	
p-value	0.0003	<0.0001	

Both PrEP strategies associated with significant reduction in HIV transmission vs placebo in both men and women

TDF2

-1,200 men and women randomized to TDF/FTC (n = 601) or placebo (n = 599) -Botswana		
	TDF/FTC	Placebo
#HIV infections	9	24
HIV protection efficacy	63	
Cl 95%	22-83	
P-vale	0.0133	
63% lower HIV incidence in TDF/FTC group		

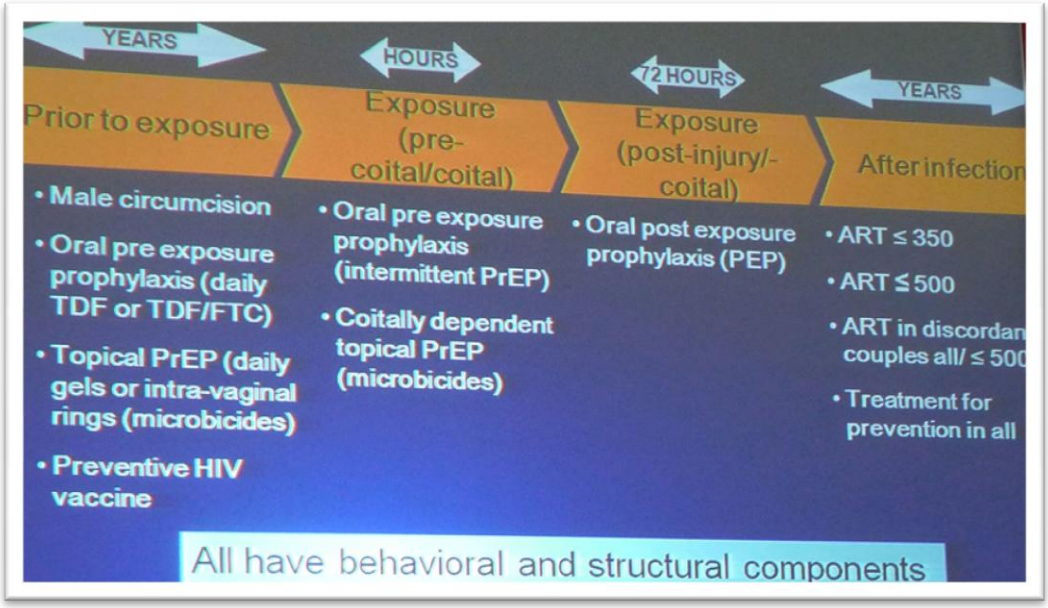
Ongoing PrEP studies

- VOICE Phase III
  - 5 arm study: TDF/FTC/TDF, Vaginal TFV gel including oral and vaginal placebo groups
  - 5000 women in Uganda and Zimbabwe
- The Bangkok Tenofovir Study, CDC Thailand Phase III
  - TDF vs placebo
  - Bangkok, Thailand
  - Enrollment completed, 2413 IDU
- IAVI intermittent PrEP Phase I/II E001 and E002(publication in preparation)
  - Small, exploratory studies to provide preliminary data on an intermittent PrEP regimen in African FSW,MSM and discordant couples
  - Intermittent FTC/TDF vc daily FTC/TDF vs intermittent and daily placebo
  - Adherence, sexual activity, drug levels

Rectal microbicides

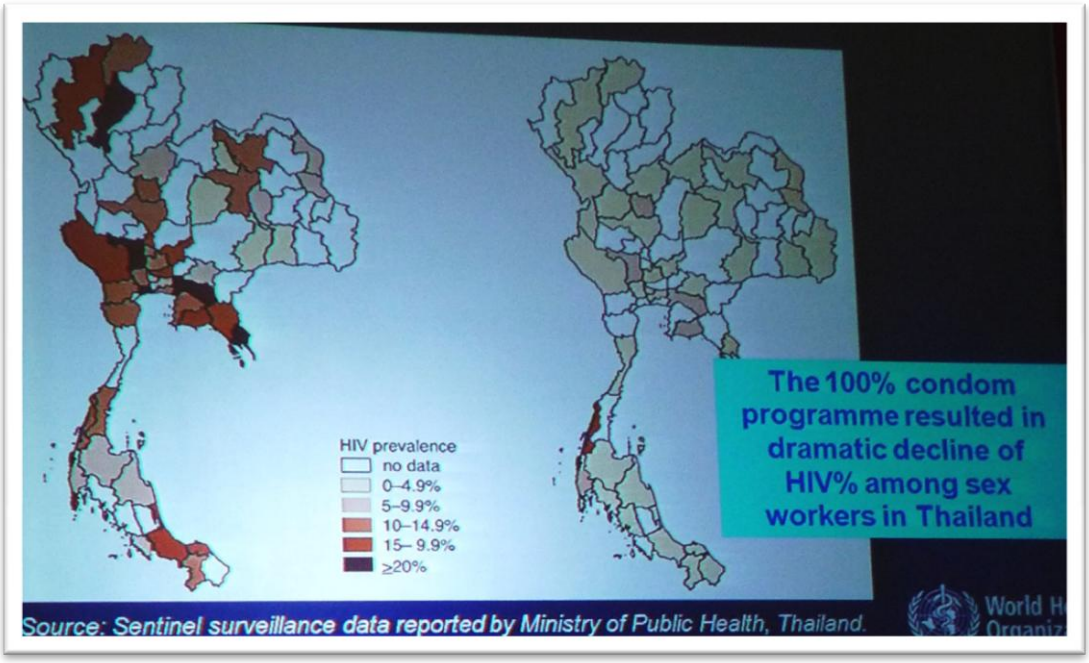
- Receptive anal sex common proactice in MSM and heterosexuals
- Proof of concept in NHP SIV/SHIV model
- Phase 1 evaluation includes safety, acceptability, PK, and PD of different formulations

Opportunities for biomedical interventions

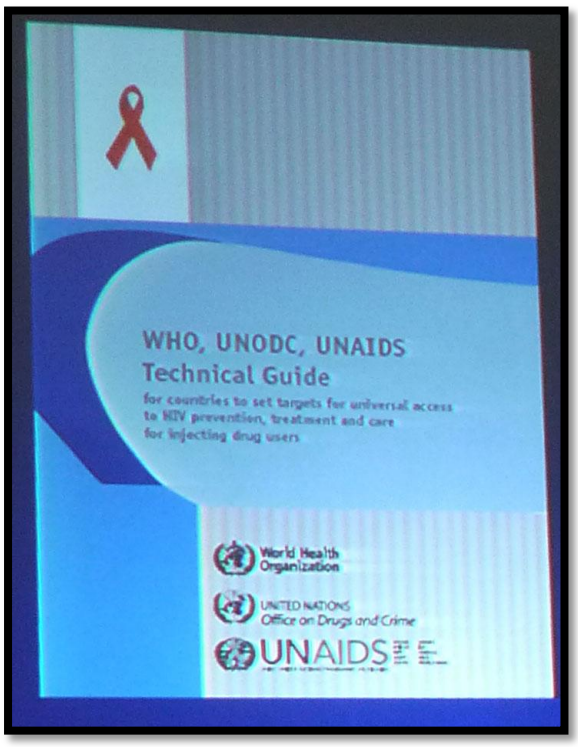


Existing prevention methods are highly effective if implemented at large scale

Comparison of HIV prevalence among female sex workers,by district, Thailand



Comprehensive package of nine harm reduction

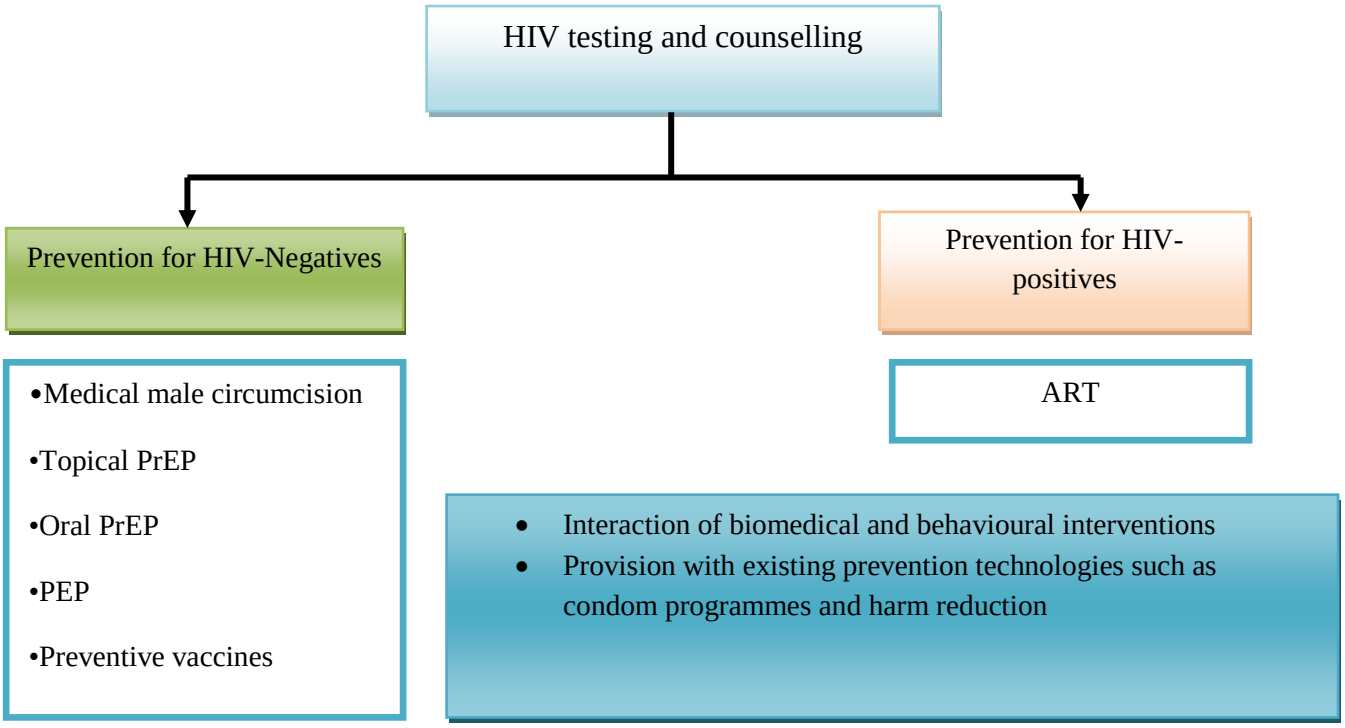


- Needle and syringe programmes (NSP)
- Opioid substitution therapy (OST)
- Voluntary counseling and testing(VCT)
- Anti-retroviral treatment(ART)
- STI prevention and treatment
- Condom programming
- Targeted Information, Education and Communication(IEC)
- Vaccination, diagnosis and treatment of viral hepatitis
- Diagnosis and treatment of TB

ARVs for prevention – key issues

- Topical and oral PrEP
  - Complex intervention requiring exclusion of acute HIV infection and monthly HIV re-testing
  - Call for demonstration projects
  - Microbicides will need to be manufactured (obtain licensure for tenofovir 1% gel)
  - Who is going to pay?
- ART for prevention
  - How to prioritize and who is going to pay?
  - Prioritize pregnant women and/or discordant couples?

New Prevention approaches are based on knowledge of HIV



What is WHO doing?

serodiscordant couples (being developed)

- Rapaid advice for daily oral PrEP for MSM and serodiscordant couples for use in demonstration projects
- Explore the strategic us of ARVs for prevention and treatment
- Review implications of use of ARVs for prevention for programmes and research

Conclusions

- Exiting success in HIV prevention sciences
- How to integrate new interventions in combination prevention approaches for specific populations and settings
- Hope for virtual elimination of HIV
- Global economic crisis – who will pay