

# IPREX implications for Thailand

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Thailand MOPH – US CDC Collaboration

US Centers for Disease Control and Prevention



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# IPREX implications for Thailand

Thailand MOPH - US CDC Collaboration

Silom Community Clinic

- 1) Research
- 2) Programmatic

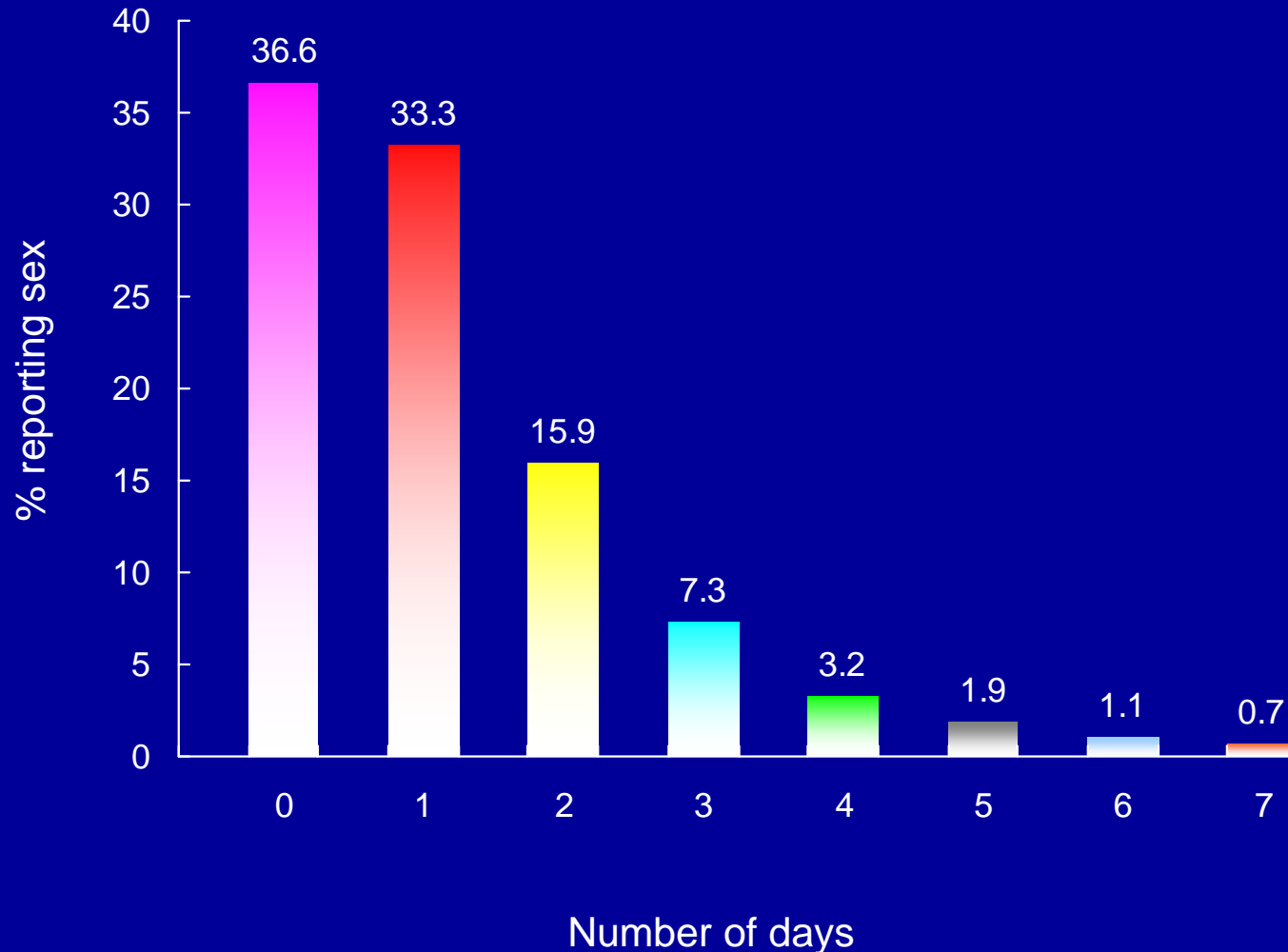
# IPREX implications for Thailand

## Silom Community Clinic

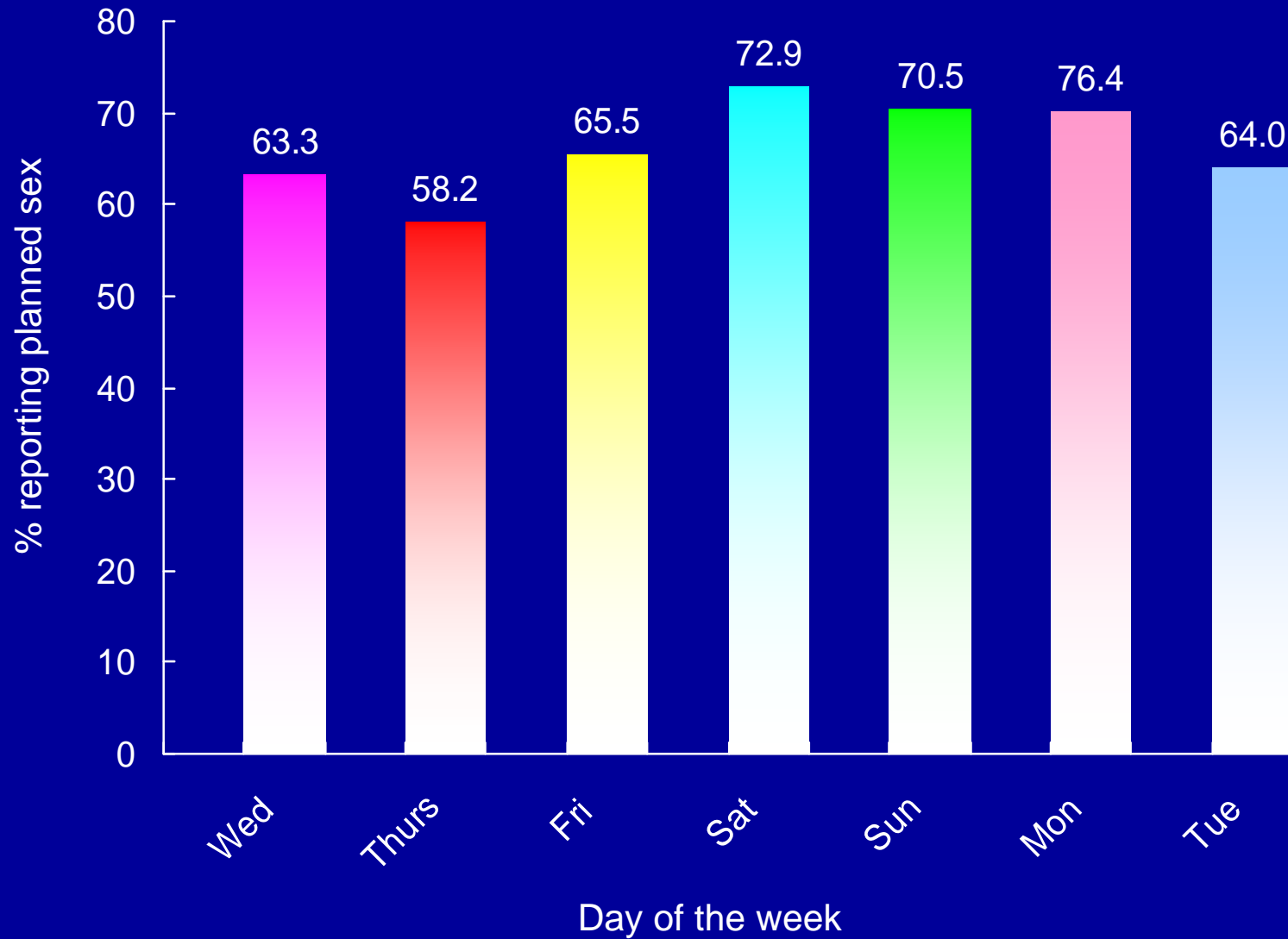
### 1) Research

- Willingness to participate in chemoprophylaxis trial
- Sex planning and sex spacing and intermittent chemoprophylaxis
- Pharmaco-economics

# Sex frequency among 823 HIV negative MSM in Bangkok Thailand ("On how many days in the past week did you have sex?")



# Sex planning among 823 HIV-negative MSM in Bangkok Thailand ("On the last day you had sex, was the first sex on that day planned?")



# Sex frequency and number of doses needed for different pre-exposure prophylaxis regimens among men who have sex with men (MSM) in Bangkok, Thailand

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From the Thailand Ministry of Public Health – US Centers for Disease Division of HIV/AIDS Prevention, Centers for Disease Control \*and Prevention, Atlanta, GA, USA



# Results

- Of 823 MSM (mean age 28.3 years, range 19-58 years) 33.3% reported to have had sex on one day in the past week, 15.9% on two days, 7.3% on three days, and 6.9% on four days or more
- No sex in the past week was reported by 36.6%
- The estimated number of PrEP doses for *event-driven* pre-post-exposure dosing in this cohort would be 1872 per week or 910 per 100 PPM
- The estimated number of PrEP doses for *time-event-driven* bi-weekly standing plus post-exposure dosing 2748 per week or 1,336 per 100 PPM
- The number of PrEP doses needed for *time-driven* daily dosing would be 5761 per week or 2,800 per 100 PPM





**ADAPT**  
**HPPTN 067**  
**WE CAN CHANGE**

# Intermittent PrEP (iPrep)

- HPTN 067: the “ADAPT Study” at Silom Clinic
  - “Alternative Dosing to Augment Pill Taking Study”
  - Phase II, Randomized, Open-Label, Pharmacokinetic and Behavioral Study of the Use of Intermittent Truvada
  - 3-armed study:
    - 1) daily dosing (time driven)
    - 2) pre-post sexual exposure dosing (exposure driven)
    - 3) bi-weekly standing plus post exposure dosing (hybrid dosing)
  - N=360, High risk MSM n=180 Bangkok; high risk heterosexual women n=180, Capetown, South Africa
  - Primary endpoint: Adherence and coverage, by pharmacokinetics and self reports of risk behavior and pill taking (EDM device)
  - 6 weeks run in of DOT to set individual drug level in blood and hair
  - Sexual risk behavior, risk compensation, risk disinhibition, self-control, self-esteem
  - 6 weeks DOT, 24 weeks of f/u on therapy, post 4 week exit visit: total 36 weeks; enrollment 8 months
  - Start March 2011

# Safety and adherence to intermittent Truvada for HIV pre-exposure prophylaxis (PrEP) in Kenya and Uganda

		Kenya (MSM/FSW)	Uganda (DC)
<b>DAILY ADHERENCE RATE</b> Median [IQR]	Overall unadjusted	83% [63-92]	96% [93-100]
	Adjusted – Upper	92% [79-99]	97% [93-100]
	Adjusted – Lower	82% [63-92]	96% [93-100]
<b>INTERMITTENT ADHERENCE RATE</b> Median [IQR]	Overall unadjusted	68% [63-78]	80% [71-86]
	Fixed doses	55% [28-88]	91% [77-98]
	Post-coital doses	26% [14-50]	45% [20-63]
	Post-coital doses within 2hrs (self report and sexual events per SMS)	105% [57-175]	103% [62-133]

**Table 3.** Adherence rates for daily and intermittent groups. Adjusted upper accounts for extra openings and extra tablets taken out. Adjusted lower excludes curiosity openings.

# CAPRISA 004

Effectiveness & safety of vaginal  
microbicide 1% tenofovir gel for  
prevention of HIV infection in  
**women**

Quarraisha & Salim S Abdool Karim

**on behalf of the**

CAPRISA 004 Trial Group

# Methods

- Proof of concept double-blinded, randomized, placebo-controlled trial
- Enrolled high risk HIV uninfected women reporting two coital acts in past 30 days – known high risk populations from pre-trial feasibility studies
- Endpoint driven trial (92 HIV endpoints)
- HIV infection is primary safety & effectiveness endpoint:
  - HIV negative: 2 negative rapid HIV tests
  - HIV endpoint: PCR+ in 2 separate blood specimens  
Positive Western blot
- Intent-to-treat analysis except for adherence analysis

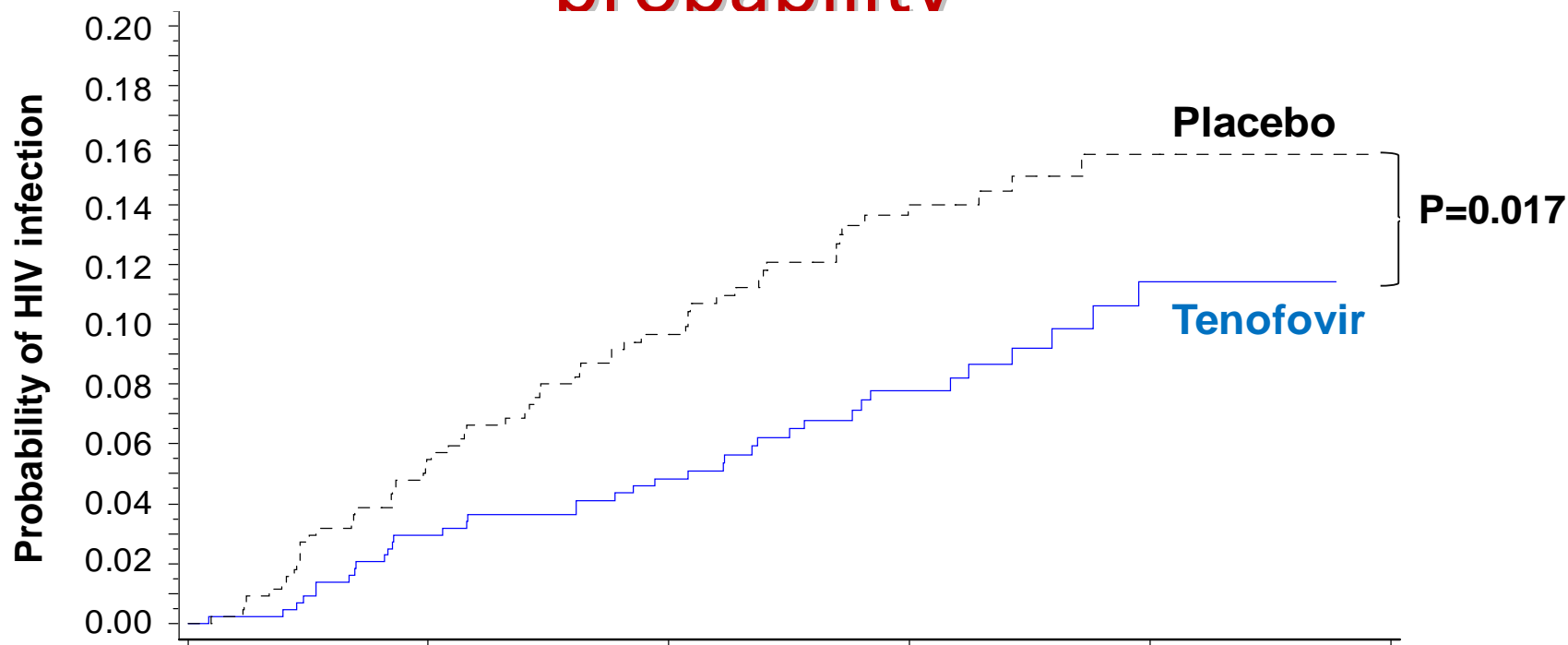
# Effectiveness of tenofovir gel in preventing HIV infection

	Tenofovir	Placebo
# HIV infections	38	60
<b>Women-years (# women)</b>	<b>680.6 (445)</b>	<b>660.7 (444)</b>
HIV incidence (per 100 women-years)	5.6	9.1

**39% lower HIV incidence in tenofovir gel group**

**Incidence rate ratio: 0.61 (CI: 0.4 to 0.94); p = 0.017**

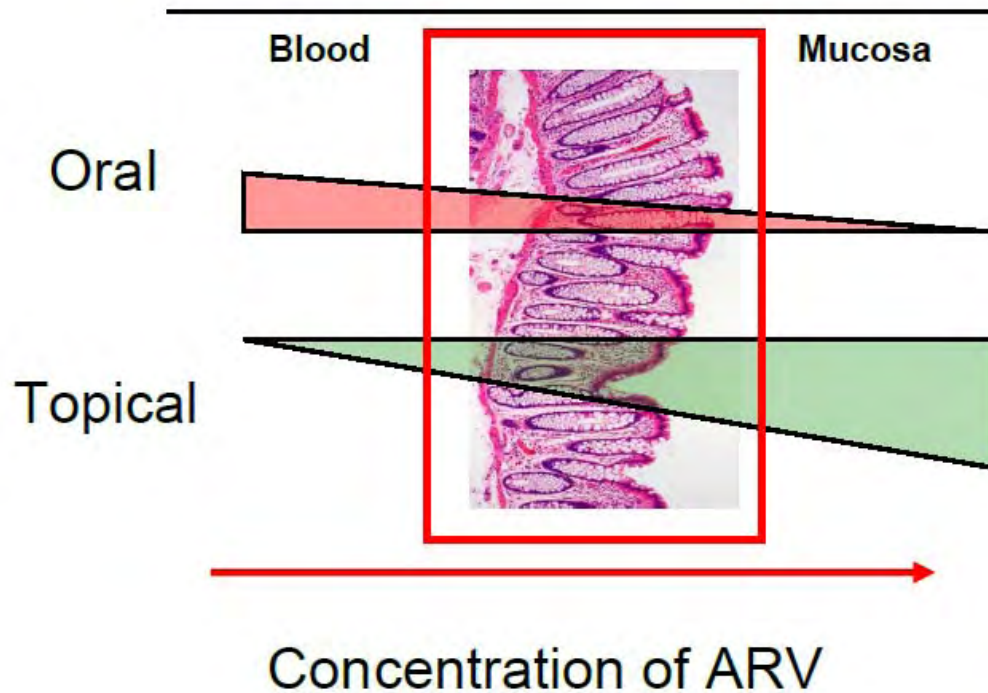
# HIV infection rates in the tenofovir and placebo gel groups: Kaplan-Meier survival probability



Months of follow-up	6	12	18	24	30
Cumulative HIV endpoints	37	65	88	97	98
Cumulative women-years	432	833	1143	1305	1341
HIV incidence rates (Tenofovir vs Placebo)	6.0 vs 11.2	5.2 vs 10.5	5.3 vs 10.2	5.6 vs 9.4	5.6 vs 9.1
Effectiveness (p-value)	47% (0.069)	50% (0.007)	47% (0.004)	40% (0.013)	39% (0.017)

# In the shadow of Caprisa

## Oral or Topical ARV PrEP?



Strong push for evaluation of rectal microbicides, e.g., TDF gel, possibly in combination with oral formulations



# IPREX implications for Thailand

## Silom Community Clinic








### 1) Research

- Sub-study of rectal cleansing
- Willingness to participate trial of rectal gel
- Study of lubricant use
  
- Feed into phase II/III studies of dosing, acceptability, feasibility and efficacy of
  - rectal 1% tenofovir gel
  - Combination use of rectal and topical formulations of tenofovir

# MTN 017 (Microbicide Trial Network)

- Phase II, multi-site, randomized, six sequence, three period, open label crossover study of adherence and pharmacokinetics of oral and rectal formulations of tenofovir
- Arms: 1) oral; 2) rectal; 3) both
- 120 MSM
- Bangkok, Thailand; Lima, Peru; 2 US Sites
- Possibly roll-over into Phase IIB, III efficacy trial

# Rectal Microbicide Timeline\*

	2010	2011	2012	2013	2014	2015	2016	2017	2018
Phase 1									
Phase 2									
Phase 2B									
Review									
Available									
Vaginal microbicides									

\*An approximation based on 1% tenofovir

Slide: courtesy of Dr Ian McGowan

# IPREX implications for Thailand

- PrEP
  - No roll out
    - Continuing concerns
      - Viral resistance
      - Safety
      - Costs
      - Behavioral disinhibition or compensation
      - Dependency
      - Access : controlled/market/programmatic
      - Grey and black markets

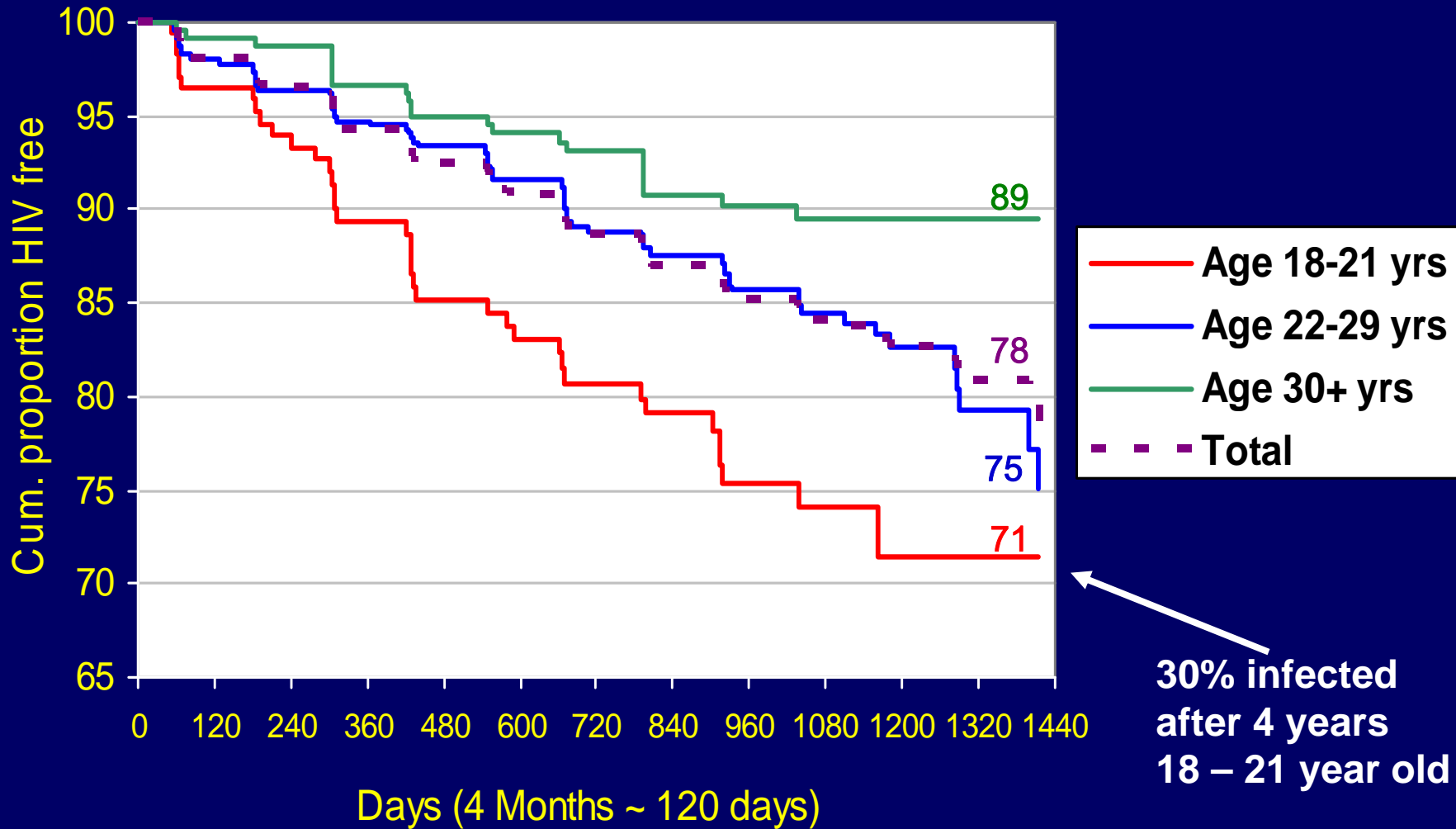
# IPREX implications for Thailand

- PrEP
  - Adherence is poor
    - MSM don't like to take pills to avoid negative consequences
    - MSM like to take pills to experience positive consequences
    - MSM don't like to use condoms and gel because they interfere with sexual excitement, decrease sexual sensation and feelings of intimacy and unity

# IPREX implications for Thailand

- PrEP
  - Programmatic implementation (ignoring possible emergence of grey and black markets, prescribers etc.)
    - Only for those at the highest behavioral risk for whom condoms, behavioral modification and partner reduction are no feasible options
      - Young MSM experimenting and exploring their sensuality, sexuality and sexual behavior (15 years and up)
      - Young entering male sex workers (15 years and up)

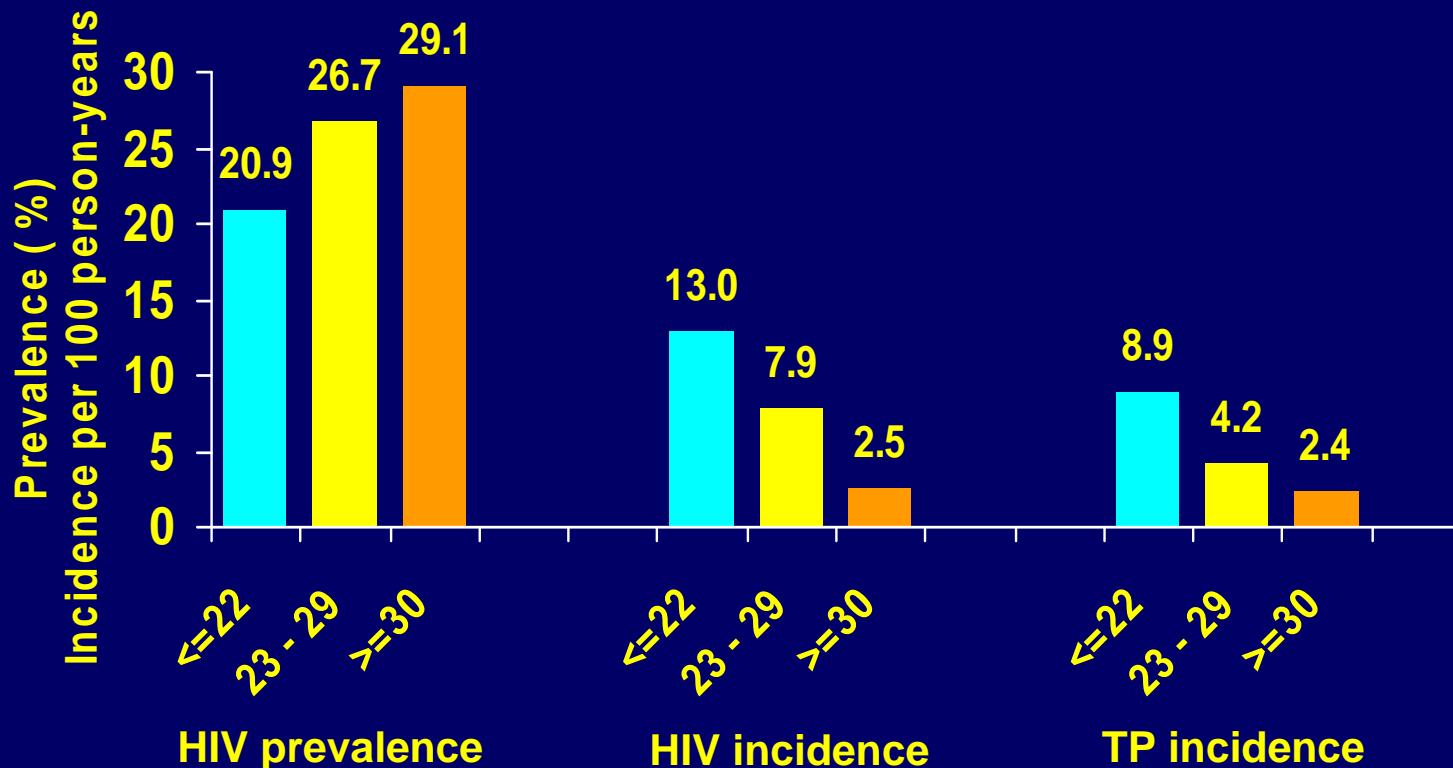
# Proportion HIV uninfected in the Bangkok MSM Cohort Study, 2006-2010



# Silom Community Clinic: since 2005

HIV and TP prevalence and incidence among VCT clients  
September 30, 2005 – June 16, 2009

- HIV prevalence significantly increased by age
- HIV and TP incidence significantly decreased by age

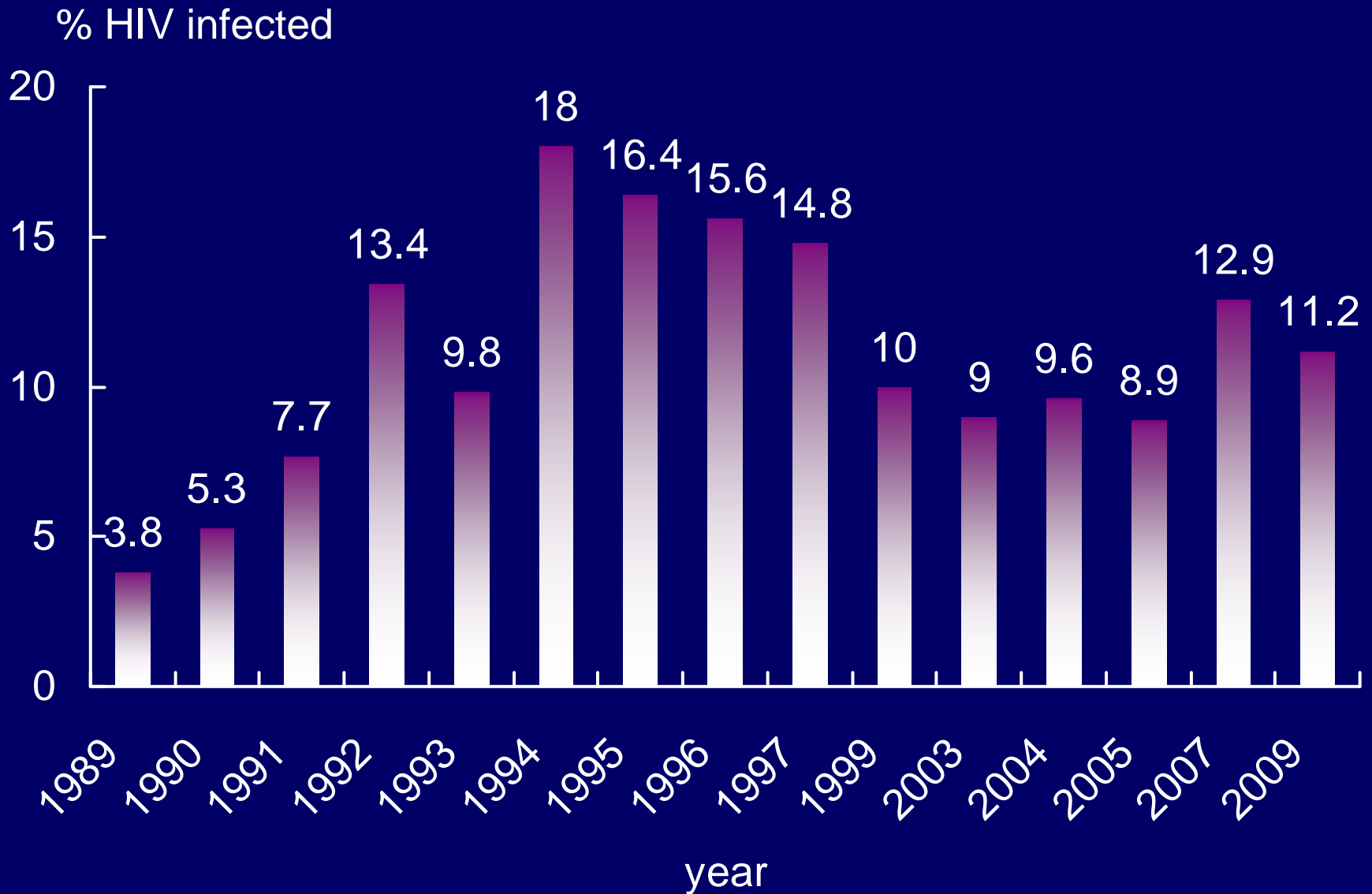




# IPREX implications for Thailand

- PrEP
  - Young MSM experimenting and exploring their sensuality, sexuality and sexual behavior
    - Limited knowledge and awareness
    - Limited perception of risk
    - Limited negotiation skills
    - Physically inexperienced
    - Challenging youth culture demanding performance and rewarding sexual pleasure and delectation
    - High background HIV prevalence and incidence (acute infection)

# HIV prevalence among male sex workers, Thailand 1989 - 2009

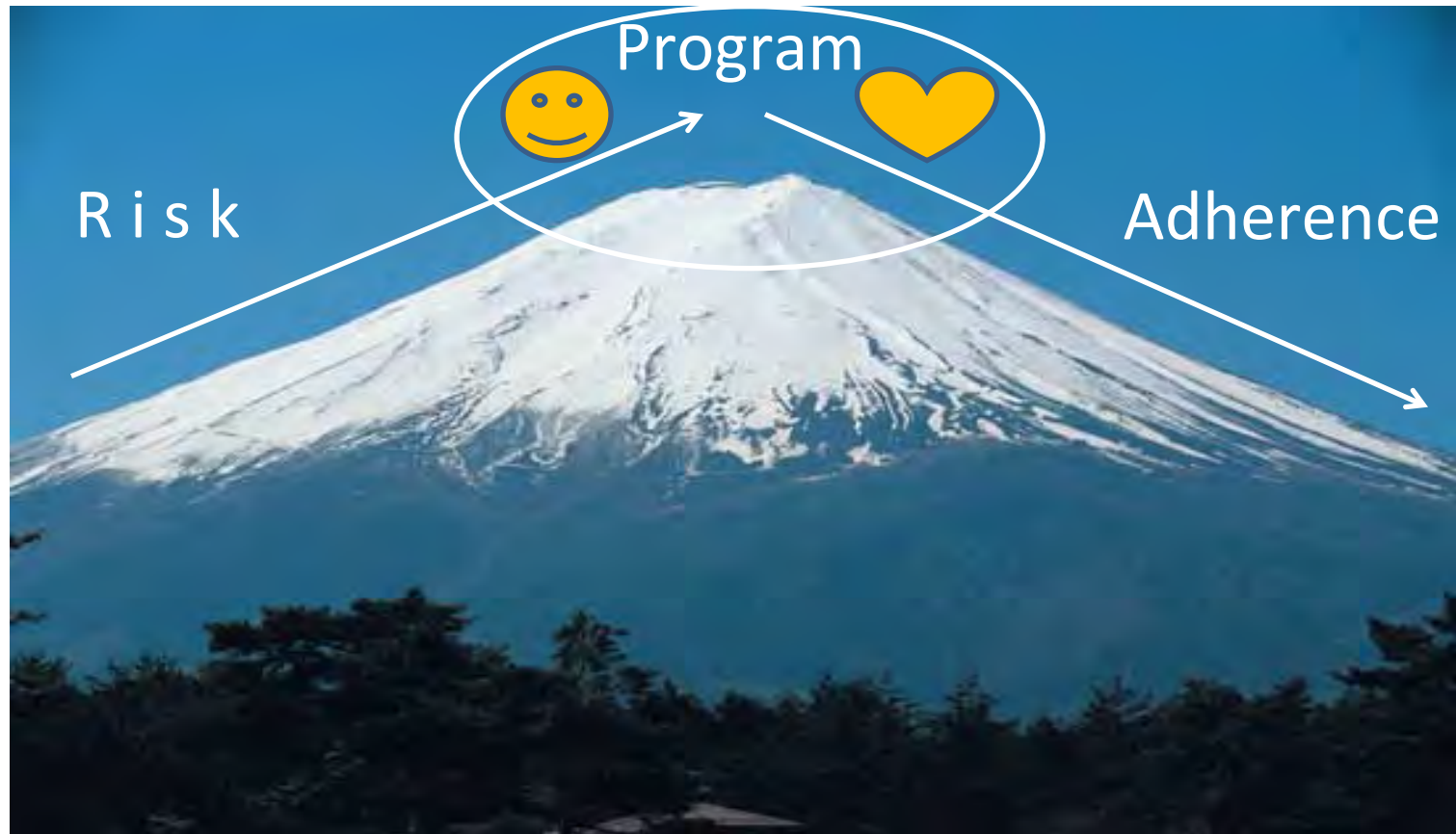


Source: Bureau of Epidemiology, Ministry of Public Health, Thailand

# IPREX implications for Thailand

- PrEP
  - Young entering male sex workers
    - May have more or less overlap with young MSM by geographic region, e.g., Chiang Mai versus Pataya
    - Limited knowledge and awareness
    - Limited perception of risk
    - Limited negotiation skills
    - Physically inexperienced
    - Social pressure: need to deliver/achieve, family, social environment, social self and lifestyle
    - Drug use: stimulant, mind-altering and erectile drugs
    - High turnover rate, relatively short duration of exposure
    - High HIV prevalence equivalent to high HIV incidence

# Bridging risk and adherence



# IPREX implications for Thailand

- PrEP Program

- Two six months (short) demonstration pilot projects of daily PrEP to prevent HIV infection among young MSM and young entering male sex workers
  - Daily Truvada PrEP
  - Intensive adherence training for self-therapy (condition 1)
  - Intensive adherence training for dyads, buddy observed therapy (BOTPREP) (condition 2)
    - » Weekly for 1 month
    - » Monthly for 4 months
  - Intensive educational, motivational, empowering sexual and drug use risk reduction training program
    - » Weekly for 2 months
    - » Monthly for 4 months

# IPREX implications for Thailand

- PrEP Program

- Demonstration pilot projects of daily PrEP
  - Weekly visits for HIV infection evaluation
    - » Drug resistance
  - Monthly KAP behavioral and adherence assessments
    - » Comprehension
    - » Motivation
    - » Sexual and drug use behavior
    - » Risk compensation
    - » Pill burden
  - Monthly pill count, adherence evaluation
  - Assessment of drug burden en side effects
  - Pre-post study bone density evaluation

# IPREX implications for Thailand

- PrEP Program

- Demonstration pilot projects of daily PrEP

- n = 500 per group (250 dyads ;Total = 1000 (500 MSM and 500 MSW)
    - 2 condition comparative design or cross-over 2x2 design
    - Compare to historical HIV incidence
    - Location Bangkok and Chiang Mai (Pata ya....?)
    - Partnerships
      - » WHO, UNAIDS, USAID, AVAC, Gates, GAP, EU
      - CDC, FHI, MOPH, BMA, SWING, RSAT, Pee Man, SCC, M Plus
    - Costs: 180.000 truvada pills a 1 US\$ = 180000
      - » Total ~ 1 million US\$