

# ***Expanding Research Capacity & Accelerating HIV Vaccine Development in Asia***

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**WHO Satellite Meeting**

***Expanding Capacity and Promoting Regional Networking to  
accelerate HIV Vaccine Development in Developing Countries***

**AIDS Vaccine 07, 20 August 2007, Seattle, WA, USA**

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***Dr. Jean-Louis Excler  
Senior Medical Director  
International AIDS Vaccine Initiative, India***



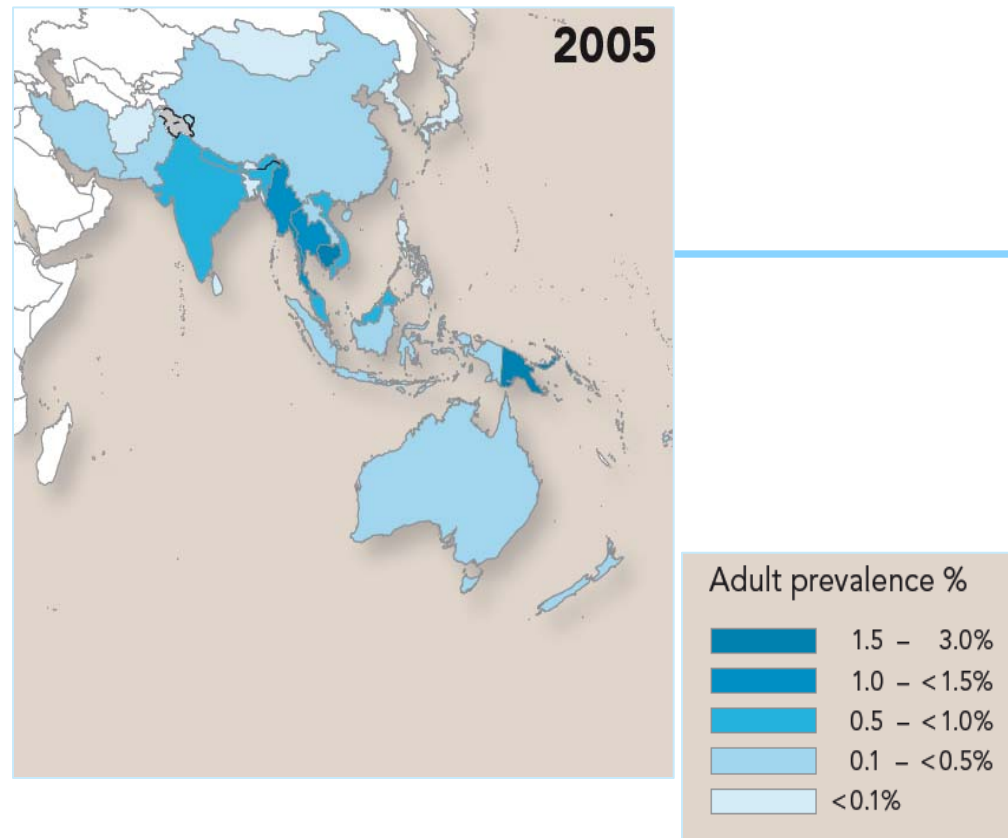
# Pathway

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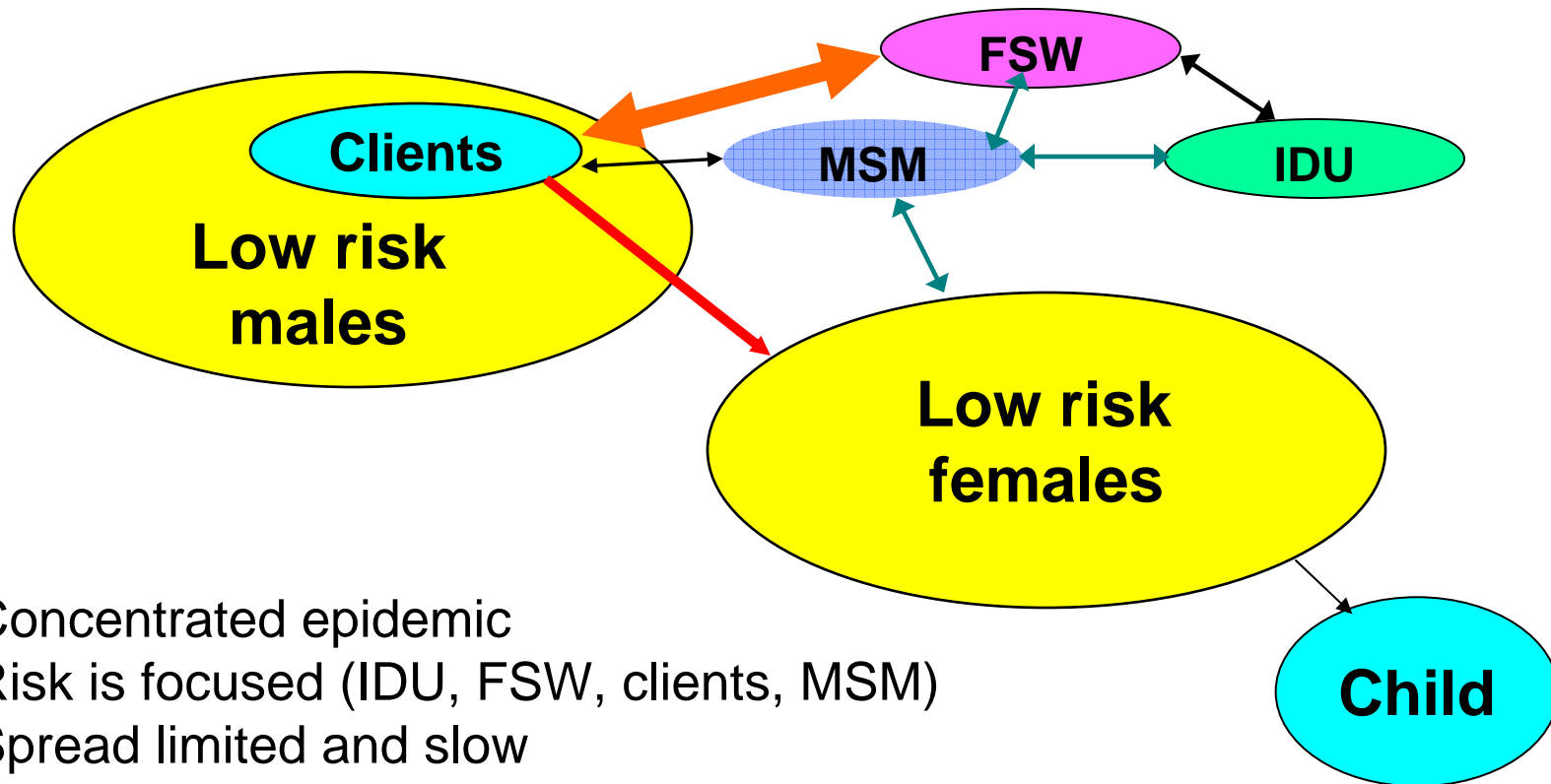
- ▶ Pattern and evolution of the epidemic in Asia
  - Implications for AIDS Vaccine Development
  
- ▶ AIDS Vaccine Development in Asia
  - Efforts
  - Challenges
  - Missed opportunities
  - AIDS Vaccine Asian Network

# Adults and children estimated to be living with HIV in Asia and Pacific, 2006

**Total: 8.6 (6 - 13) million**



# Dynamic of Asian HIV epidemics

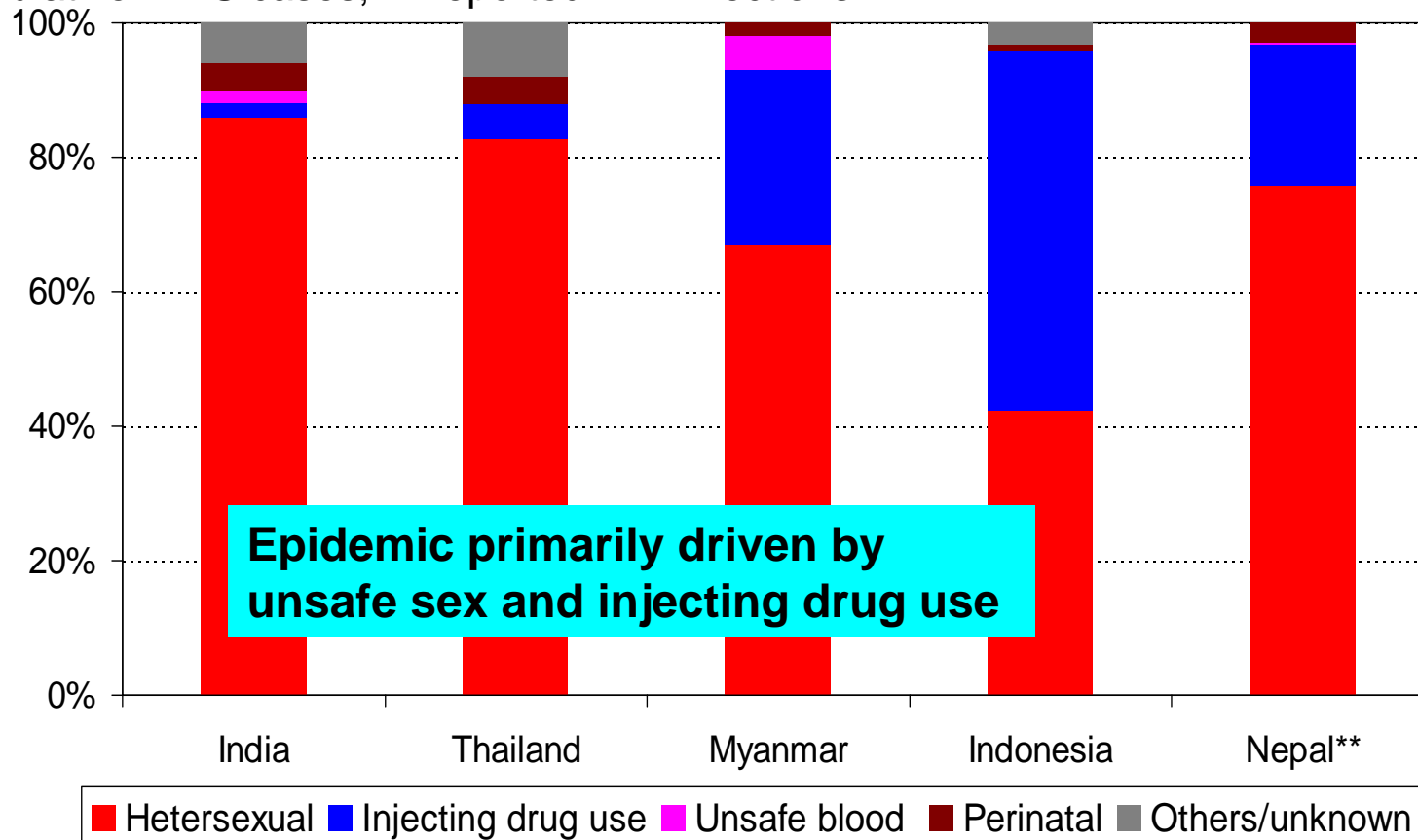


- Concentrated epidemic
- Risk is focused (IDU, FSW, clients, MSM)
- Spread limited and slow

*Adapted from T. Brown, UNAIDS Collaborating Centre at the East-West Centre*

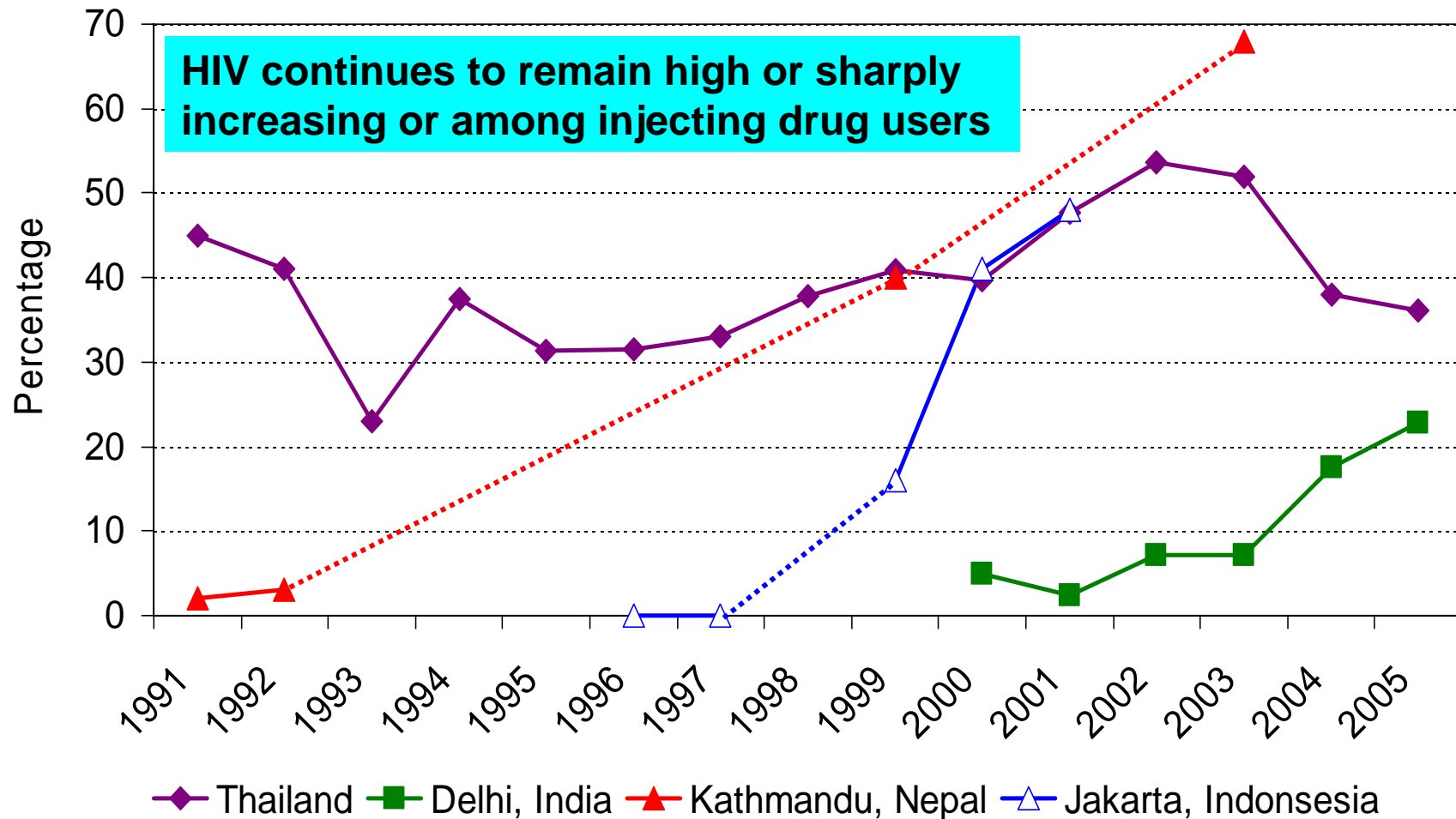
## Mode of Transmission Among Reported AIDS Cases\* in Selected South-East Asian Countries, 2005

\*Cumulative AIDS cases; \*\*Reported HIV infections



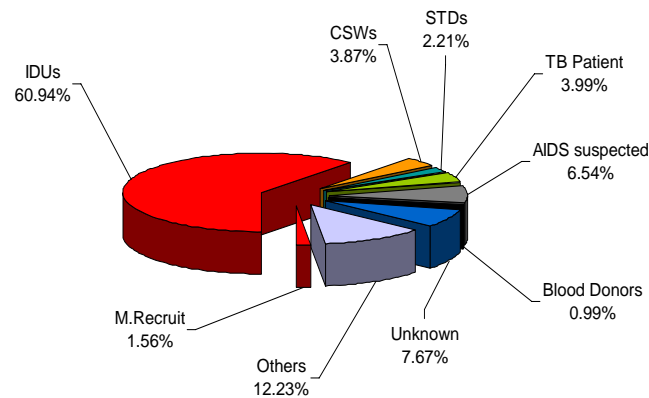
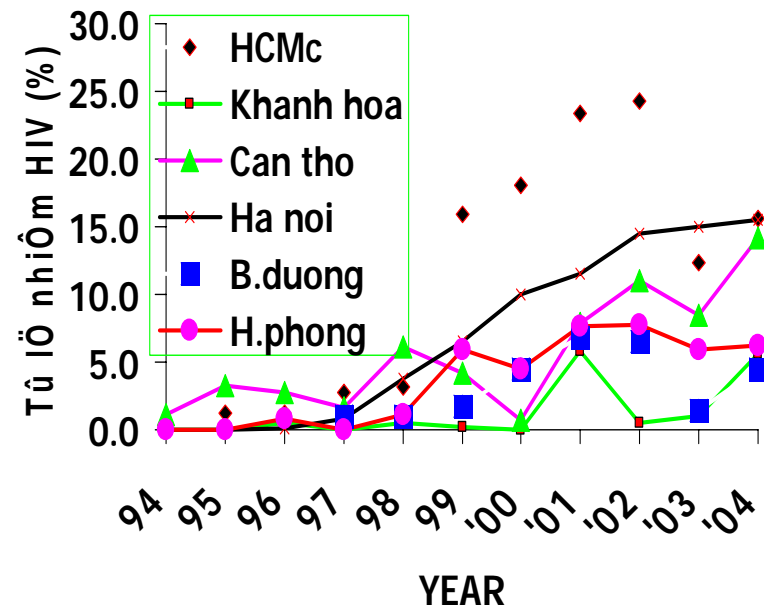
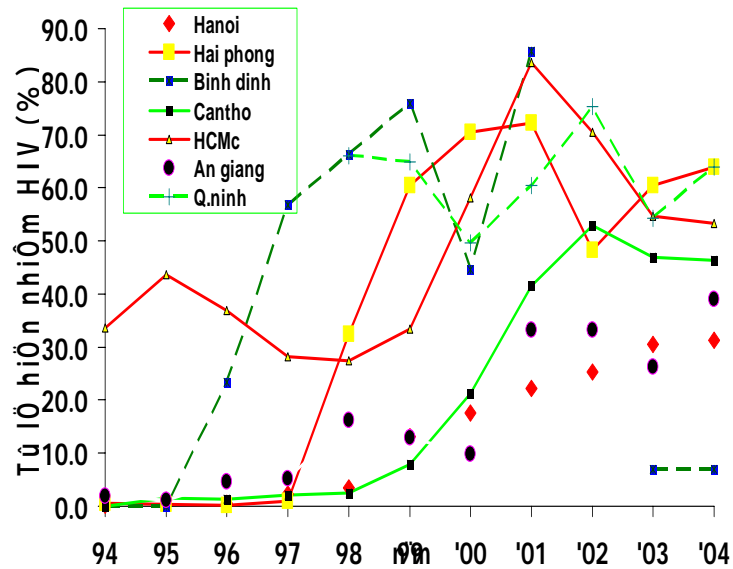
Source: National AIDS Programme, 2005

# HIV Prevalence Among Injecting Drug Users in Jakarta and Kathmandu, 1992–2005



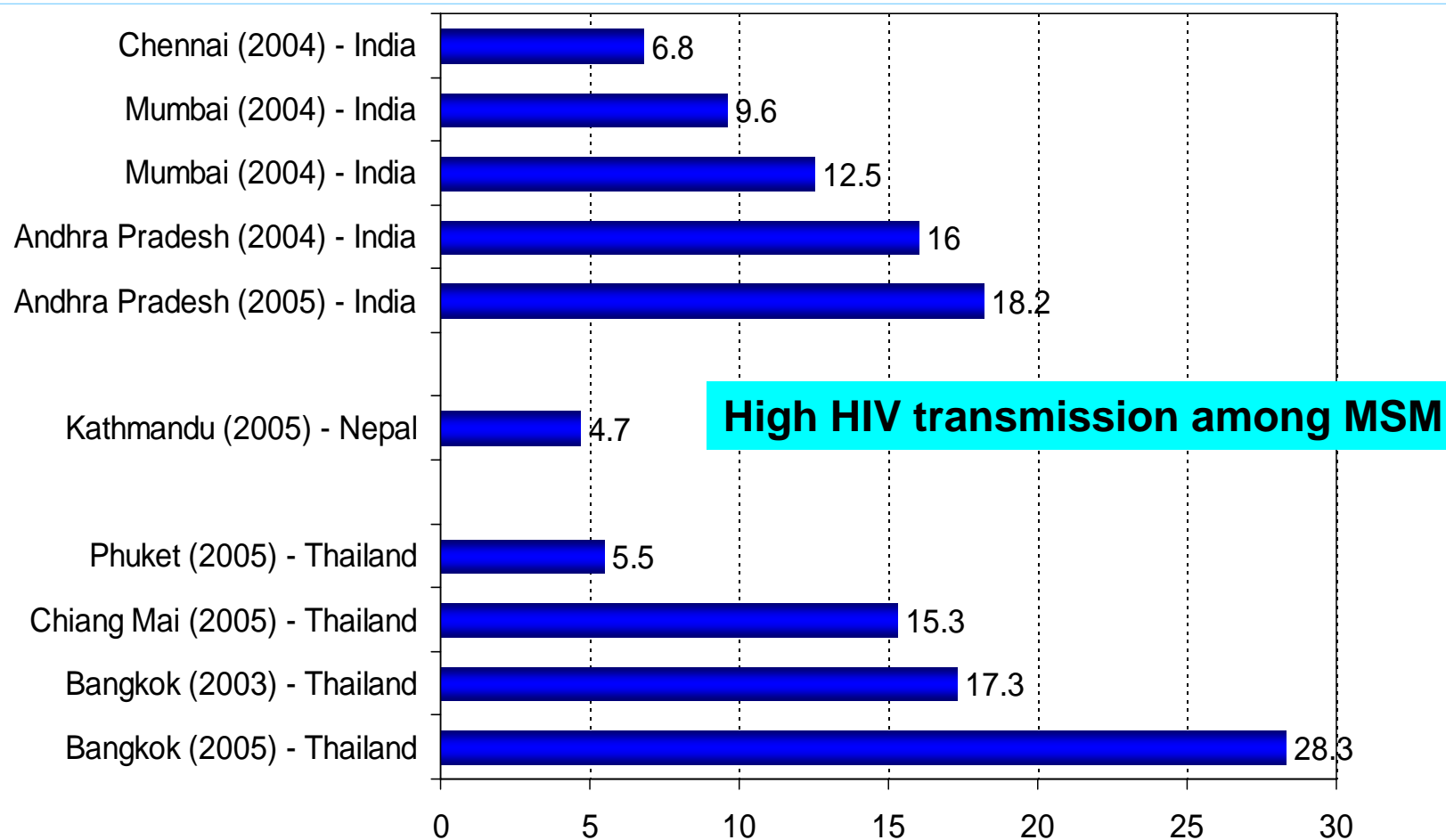
Source: WHO-SEARO and National AIDS Programme, 2005

# Trends of HIV Prevalence among IDUs and FSWs Vietnam, 2005



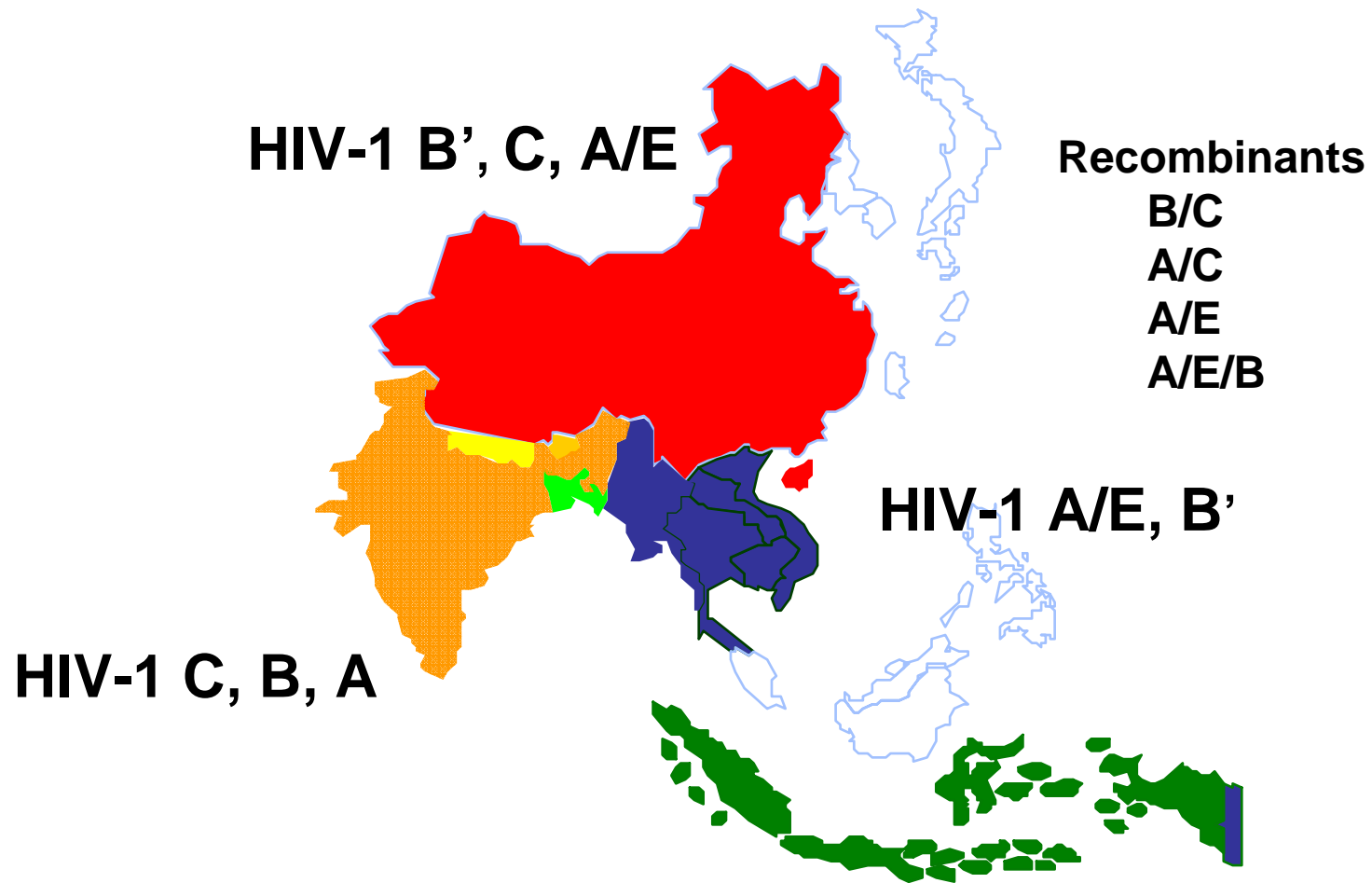
Source: Ministry of Health

## HIV Prevalence Among Men Who Have Sex With Men in Selected Countries in South-East Asia, 2003–5



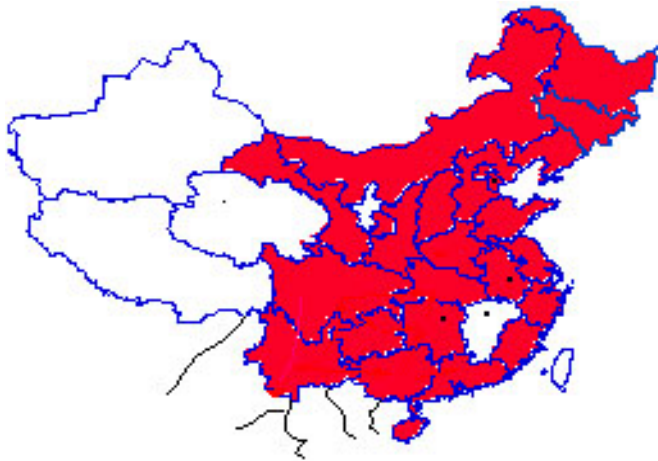
Source: National AIDS Programme, 2005 % HIV prevalence

# HIV Subtypes in Asia

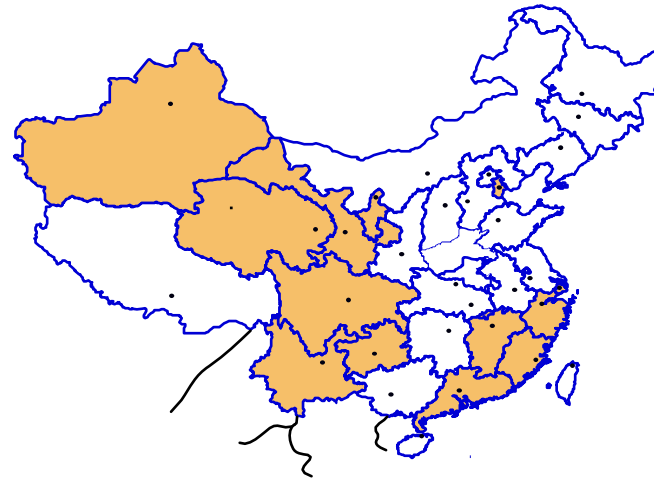


# Geographic Distribution of HIV Subtypes in China

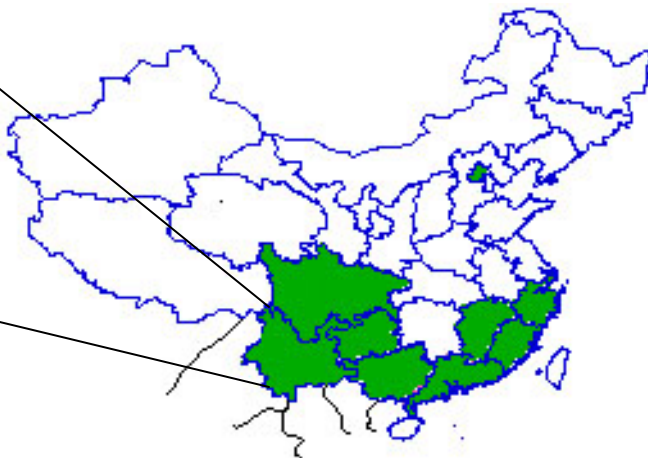
Subtype B and B' HIV-1



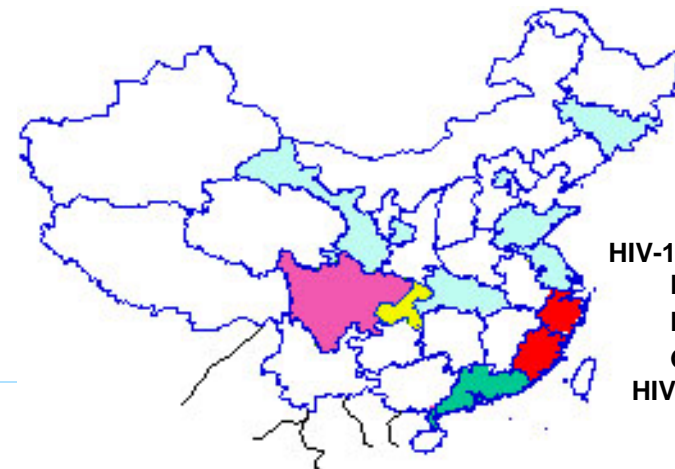
Subtype C and B'/C recombinant HIV-1



Subtype A/E HIV-1

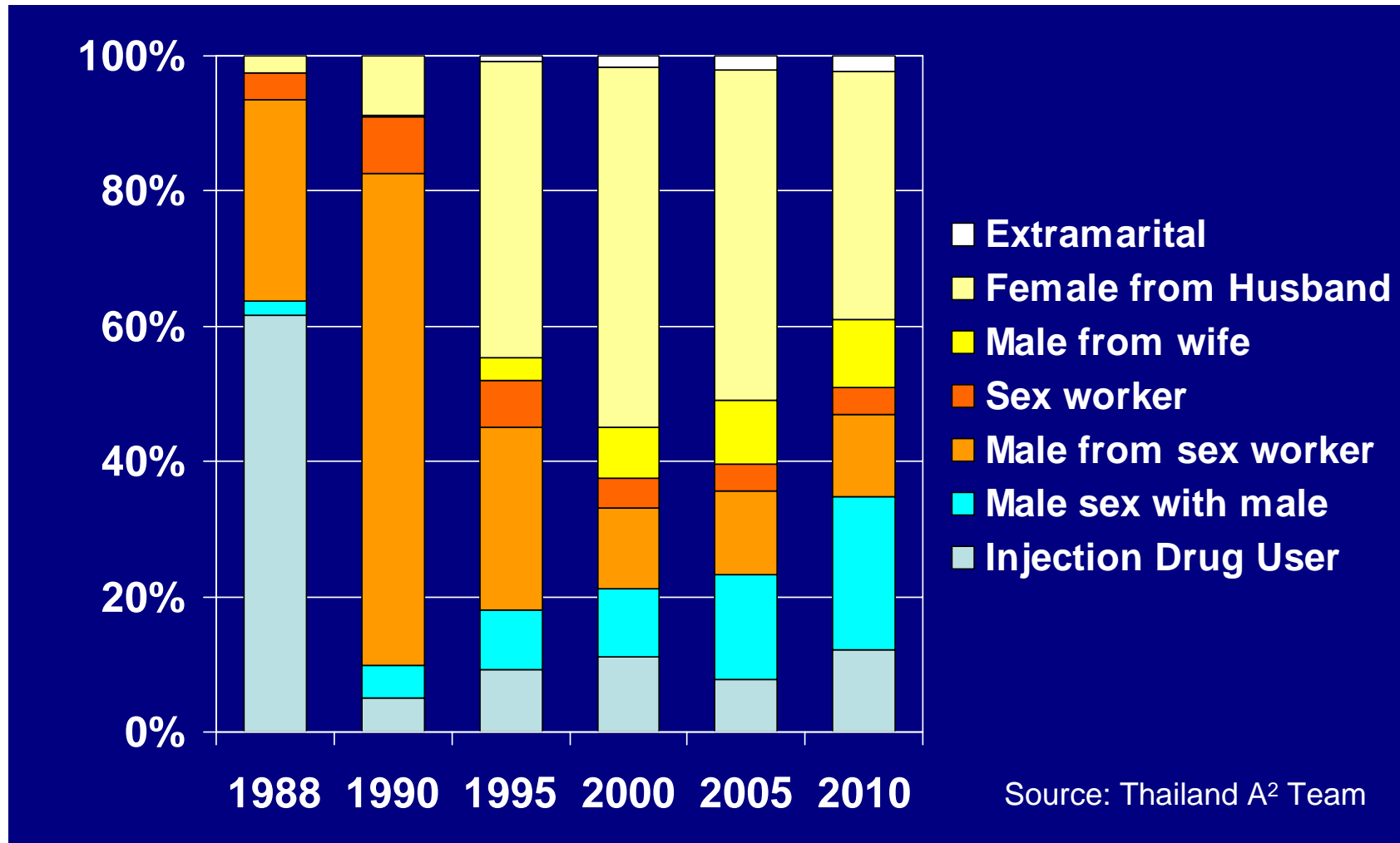


Subtype A D F and G HIV-1 and HIV-2 in China

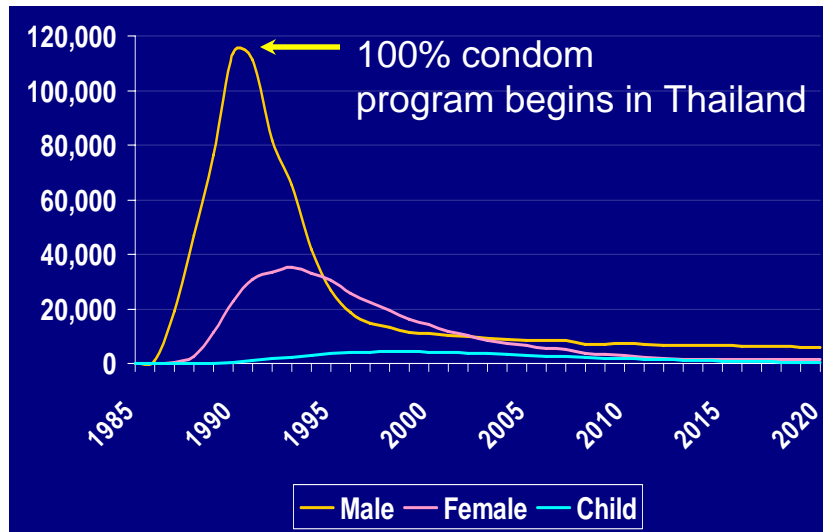


- HIV-1 A ■
- D ■
- F ■
- G ■
- HIV-2 ■

## Responses adapt over time as the epidemic evolves

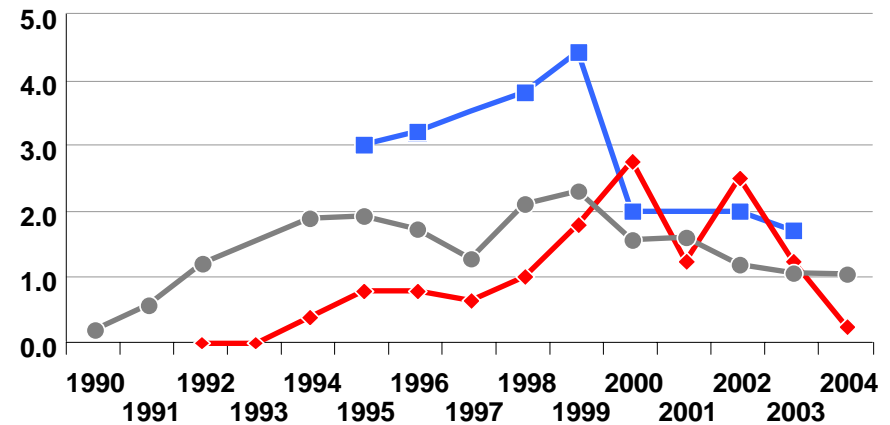


# Responses do correlate with prevalence



## HIV prevalence trends among pregnant women in major cities in Cambodia, Myanmar and Thailand, 1990–2004

% HIV prevalence



Sources: Cambodia National Center for HIV/AIDS, Dermatology and STDs (Phnom Penh); Myanmar Ministry of Health (Mandalay and Yangon); Thailand Ministry of Public Health (Bangkok), 2005.

■ Phnom Penh    ◆ Mandalay and Yangon    ● Bangkok

## Examples of HIV incidence in Asian countries

Country	IDU	CSW	STD patients	MSM	General Pop
<b>China</b> Yunnan 1994 2005  Guangxi 1999 2005  Sichuan 2002  Xinjiang	0 - 25% 4% 3.8% (spouses)  2.38 - 6.86% 3.1%  3.17%  7-8.8%	NA	NA	NA	NA
<b>India</b> Pune 1993-04 Pune 2000-02	NA	3.7% 3.6%	F 16.6 – M 6.8 F 5.6 – M 2.5	NA	NA
<b>Thailand</b> 1994 2002-04	5.8 - 7.3%	12.8% NA	4.92 -5.2 % NA	Pending	<1%
<b>Cambodia</b> 1999 2002	NA	13.9% 6.45%	NA	NA	<1%

# Summary of the HIV Epidemic Patterns in Asia

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- ▶ Higher risk groups are mostly represented by IDU, FSW, MSM and Transgender populations
- ▶ Prevention interventions and HIV care & treatment are scaled up with growing success
- ▶ HIV incidence data are scarce and may decrease
- ▶ HIV genetic subtypes are still relatively homogeneous by geographic region, with however more and more recombinant viruses observed

# AIDS Vaccine Development in Asia

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**1993-2007**

*Thailand*

*China*

*India*

*Japan*

*Australia*

# AIDS Vaccine Development in Asia

<b>Country</b>	<b>Vaccine</b>	<b>Sponsor</b>	<b>Subtype</b>	<b>Phase</b>
<b>Thailand</b>	<i>V3 peptides</i>	<i>UBI</i>	<i>Multiclade</i>	<i>I</i>
	<i>DNA</i>	<i>US DoD</i>	<i>B</i>	<i>I</i>
	<b>gp120</b>	<i>Vaxgen, Chiron</i>	<i>E, B, B'/E</i>	<i>I/II, III</i>
	<i>gp160</i>	<i>DoD</i>	<i>E</i>	<i>I/II</i>
	<i>Canarypox + gp140 vs 120</i>	<i>US NIH/DoD</i>	<i>B/E</i>	<i>I/II</i>
	<b>Canarypox + gp120</b>	<i>US NIH/DoD</i>	<i>B/E</i>	<i>III</i>
	<i>Adenovirus type 5</i>	<i>Merck</i>	<i>B</i>	<i>I/II</i>
	<i>MVA</i>	<i>US NIH/DoD</i>	<i>A/E</i>	<i>I</i>
	<i>DNA + fowlpox</i>	<i>Australia</i>	<i>A/E</i>	<i>I</i>
<b>China</b>	<i>DNA + MVA China</i>	<i>China</i>	<i>B'/C</i>	<i>I</i>
	<i>DNA + MVA</i>	<i>China/ADARC</i>	<i>C</i>	<i>In discussion</i>
	<i>DNA + Tiantan replicative</i>	<i>China/NIH</i>	<i>B'/C</i>	<i>I</i>
	<i>DNA + Tiantan attenuated</i>	<i>China/NIH</i>	<i>B''/C</i>	<i>Preclinical</i>
	<i>Anthrax-derived fusion protein</i>	<i>China/NIH</i>	<i>B'/C</i>	<i>Preclinical</i>
	<i>DC with inactivated HIV (therapeutic)</i>	<i>China/France</i>	<i>C</i>	<i>In discussion</i>

# AIDS Vaccine Development in Asia

<b>Country</b>	<b>Vaccine</b>	<b>Sponsor</b>	<b>Subtype</b>	<b>Phase</b>
<b>India</b>	<i>Adeno-associated virus</i>	<i>IAVI</i>	<i>C</i>	<i>I</i>
	<i>MVA</i>	<i>IAVI</i>	<i>C</i>	<i>I</i>
<b>Australia</b>	<i>DNA + fowlpox</i>	<i>NIH</i>	<i>B</i>	<i>I</i>
	<i>DNA + fowlpox</i>	<i>Australia</i>	<i>A/E</i>	<i>I</i>
<b>Japan</b>	<i>DNA + DI (attenuated vaccinia)</i>	<i>Japan</i>	<i>A/E</i>	<i>Preclinical</i>
	<i>BCG</i>	<i>Japan</i>	<i>A/E</i>	<i>Preclinical</i>
	<i>Replicative Sendai</i>	<i>DNAVEC/IAVI</i>	<i>A</i>	<i>Preclinical</i>

# Challenges of efficacy trials in Asia

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- ▶ HIV incidence in general population is low
- ▶ HIV incidence may lower in higher risk groups
  - More targeted interventions
  - Access to Care and Treatment will increase

# Challenges of efficacy trials in Asia

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- ▶ Sample size needs will also balloon as 1st partially-effective vaccine or other prevention method sets new bar & becomes comparison group or additional intervention
- ▶ Vaccine efficacy trials may compete for access to volunteers with efficacy trials of non-vaccine HIV prevention technologies

# Are efficacy trials in Asia still feasible?

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- ▶ **China:** *likely if stable HIV incidence*
  - *Yunnan, Guangxi, Sichuan, Xinjiang*
- ▶ **India:** *Still unknown*
  - *Recent estimates less than half of previous ones*
  - *Feasibility studies needed in high risk groups*
  - *Investment and time*
- ▶ **Thailand:** *Yes - MSMs and IDUs*
- ▶ **Vietnam, Indonesia, Cambodia, Myanmar, others?**
  - *Possibly - Need thorough assessment*

*This situation 'snapshot' will likely evolve over time*

## Implications for AIDS Vaccine Development in Asia

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- ▶ Bring and develop new vaccines for Asia
- ▶ Prioritize AIDS vaccines for efficacy trials
  - Design test of concept trials to screen vaccine candidates
- ▶ Prioritize prevention interventions for efficacy trials
- ▶ Expand capacity to conduct clinical trials
  - Tremendous capacity and (missed) opportunities
  - Document HIV incidence in different settings
  - Develop new sites for clinical trials

# South East Asia Assets 1

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- ▶ Thailand has developed a wonderful and efficient technical platform for AIDS vaccine clinical development and has now high risk cohorts necessary for advanced clinical development.
- ▶ Subtype E or A vaccines in early human trials (MVA), monkey trials (Ad35, Japanese BCG, Sendai).
- ▶ The relative homogeneity of subtype E in SEA facilitates both genetically matched and mismatched trials.
- ▶ Post-infection Viral Load and CD4 count are extremely well defined for subtype E and will therefore be most useful in planning for surrogate endpoints (without much confounding by the presence of other subtype effects on progression).
- ▶ The availability of ARV and adherence to standardized guidelines for initiation will enhance data precision around clinical surrogate endpoints.

# South East Asia Assets 2

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- ▶ Major sponsors already present in Thailand have unfortunately not expressed a renewed interest in SEA as a site for short-term HIV vaccine development (next 3 years).
- ▶ Finally the relatively strong public health infrastructure means that uptake and utilization of an effective vaccine will be greater in SEA than other regions.
- ❖ **Dressed up to dance... Desperately needs partners and funding to advance vaccines to trials in SEA.**

# AIDS Vaccine Development Capacity in selected Asian countries

	Advocacy	Applied Research	Feasibility studies	Clinical Trials	Manufacturing
China	Yes	Yes	Yes	Ph I to III	Yes
India	Yes	Possibly	Possibly	Phase I	Yes
Thailand	Yes	Possibly	Yes	Ph I to III	Limited
Indonesia	Yes	Assess	Assess	Ph I to ?	Yes
Vietnam	Yes	Assess	Assess	Ph I to ?	Limited
Japan	No	Yes	No	No	Yes
Australia	Yes	Yes	No	Phase I	Yes

# What should be done for and in Asia?

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- ▶ *Engage other Asian countries*
- ▶ *Engage sponsors and donors for and in Asia*
- ▶ *Bring and develop new AIDS vaccines*
- ▶ *Different countries: different capacity and skills*
- ▶ *Think regional*
  - Multi site
  - Multi country
- ▶ *Foster and facilitate alliances and networks*

# First and next steps

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- ▶ **AIDS vaccine research in Asia: needs and opportunities;** Report from a UNAIDS/WHO/NIID meeting Tokyo, 28-30 October 1998. AIDS 1999; 13:1-13.
- ▶ **Expanding Research Capacity and Accelerating HIV Vaccine Development in Asia** - WHO-UNAIDS regional consultation in Sapporo, Japan, 30 October – 1 November 2006
  - *Rationale and recommendation for an AIDS Vaccine Asian Network at the WHO VAC Meeting – March 19, Milano*
  - *Publication of the Proceedings (in preparation)*
  - *Constitution of the **Asian AIDS Vaccine Network***
- ▶ **Regional visits:** *advocacy, gathering information on willingness, epidemiological situation, capacity, gaps and needs, approval process*

# Acknowledgements

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*UNAIDS*

*Initiative for Vaccine Research, WHO Geneva*

*WHO Regional Office for South East Asia*

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*HIV Vaccine Trial Network*

*IAVI Team*



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Buitenlandse Zaken



NORWEGIAN MINISTRY OF FOREIGN AFFAIRS



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- Basque Autonomous Government
- Becton, Dickinson and Company (BD)
- Bill & Melinda Gates Foundation
- Broadway Cares/Equity Fights AIDS
- Canadian International Development Agency
- Continental Airlines
- Crusaid
- Deutsche AIDS-Stiftung
- European Union
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- The Haas Trusts
- Irish Aid
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- The New York Community Trust
- Norwegian Royal Ministry of Foreign Affairs
- Pfizer Inc
- The Rockefeller Foundation
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- The Starr Foundation
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- Swedish Ministry of Foreign Affairs
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\* As of 11/06