Trends of HIV-1 infection and AIDS in Asia

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Outlines

• Epidemiology Trends
• Care and ARV trends
• Coinfection: TB, HCV
• Researches highlights:
  • Asia-Pacific cohorts,
  • Implementing Research: PrEP, Same Day ART, and HIV cure
• Take home messages
HIV Epidemics
Since 1981 to 2017 (36 y)

The most affected region is in Sub-Saharan-Africa

77 M infected with HIV
35 M have died from AIDS
Adults and children newly infected with HIV | 1990–2017

From 3.4 M in past 22 yrs to 1.8 M
ALARMING RISE IN NEW INFECTIONS IN EASTERN EUROPE AND CENTRAL ASIA

- Eastern Europe and central Asia
- Asia-Pacific
- Western and central Africa
- Eastern and southern Africa
- Asia and the Pacific

Number of new HIV infections:
- 1990 to 2016

Graphs showing the rise in new HIV infections in different regions over time.
Adult and child deaths due to AIDS | 1990–2017

Adult and child deaths due to AIDS

Range of uncertainty

1.9 M

0.9 M
Adults and children estimated to be living with HIV | 2017

North America; western & central Europe
2.2 million
[1.9 million–2.4 million]

Caribbean
310 000
[260 000–420 000]

Middle East & North Africa
220 000
[150 000–300 000]

Western & central Africa
6.1 million
[4.4 million–8.1 million]

Latin America
1.8 million
[1.5 million–2.3 million]

Eastern Europe & central Asia
1.4 million
[1.3 million–1.6 million]

Asia and the Pacific
5.2 million
[4.1 million–6.7 million]

Eastern & southern Africa
19.6 million
[17.5 million–22.0 million]

Total: 36.9 million
[31.1–43.9 million]
UNAIDS Statistics 2017

Asia-Pacific

**Overall**
- PLWH: **5.2 Million**
- New HIV infection: **280,000**
- HIV-Death: **940,000**

**Children**
- LWH: **110,000**
- New infection: **10,000**
- Death: **64,000**
New infections in Asia-Pacific in 2017

Source: Dr Tim Brown, Population and Health Studies, East West Centre, Honolulu, USA
Increasing proportion of **New HIV infections** among MSM in Thailand

HIV-1 subtypes

www.hiv.lanl.gov/, as of 2015
Global Distribution of HIV-1 Subtypes
Available ART Regimens

All are available in High-income Countries, but only few ARVs are available in LIC. LMIC, MICs
Principle of ART combination

NRTI-1 + NRTI-2 + Integrase Inhibitor

- TAF
- TDF
- ABC*

- FTC
- 3TC*

Integrase Inhibitor

- Dolutegravir (DTG*)
- Elvitegravir (EVI)
- Raltegravir (RAL)
- Bictegravir (BIC*)

Protease Inhibitor

- Darunavir (DRV)
- Atazanavir (ATV) (both + a booster RTV or Cobi)

NNRTI

- Efavirenz (EFV)
- Rilpivirine (RPV)
- Doravirine (DOR*)

*ABC+3CT combined with DTG as a STR,

*a Newly approved (2018)
HIV Integrase Inhibitors

Chance to develop drug resistance

Subgroup meta-analysis from clinical trials


RAL vs DTG – DR rate 3.9% vs 0.1% (40-fold higher)
RAL, EGV/c: 10 major integrase mutations (N155H, Y143C/R, Q148H/R, Y143Y/H, L74L/M, E92Q, E138E/A, Y143C, Q148Q and Y143S)
For countries where **NNRTI-PDR rate >10%**

**WHO Recommends to plan transitioning from**

**TLE (EFV-based) to TLD (DTG-based)**

**Thailand 2016 data:** Overall DR 7.9 %, **NNRTI-DR 6%**, 3TC-DR 3%


**Thailand 2018 data:** Overall DR 8.1 %, **NNRTI DR 7.2 %**, 3TC-DR 0.1%

*Lertpiriyasuwat C et al. J Hum Virol Retrovirology 2018*
More challenges to be overcoming both globally and in our region
Global **90–90–90**

HIV treatment and care cascade

<table>
<thead>
<tr>
<th>Stage</th>
<th>Percentage</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Know HIV Status</td>
<td>75%</td>
<td>5.7 M</td>
</tr>
<tr>
<td>On Treatment</td>
<td>59%</td>
<td>8.2 M</td>
</tr>
<tr>
<td>Virally suppressed</td>
<td>47%</td>
<td>9.4 M</td>
</tr>
</tbody>
</table>

Source: UNAIDS special analysis, 2018;
Asia-Pacific 90–90–90 (estimated PLWHA 5.2 M)

**ASIA AND THE PACIFIC**

- **74%** of PLWHA are aware of their HIV status
- **53%** of PLWHA are on HIV treatment
- **45%** of PLWHA are virally suppressed

- **71%** of those aware of their status
- **85%** of those on treatment

Source: UNAIDS Data 2018
Only 59% of Total 36.9 million
NNRTIs ~80%

PIs <20%

TREAT Asia data as of Oct 2018
Use of ART at ACC in 2017, Tokyo

**All Patients**

- N=2,308
- STR: 35.7%

**Naïve Patients**

- N=211
- STR: 35.1%

- **Japan 84% INIs**
  - 49% TAF/FTC + DTG
  - 24% ABC/3TC/DTG
  - 11% TAF/FTC/EFV/c

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Prof. Shinichi Oka, ACC, Tokyo
Commonly used First-line ART

**NNRTI**
- **EFV > NVP > RPV**
  - Indonesia
  - Vietnam
- **EFV > RPV**
  - Thailand
- **EFV > DTG**
  - Malaysia, Singapore

**INI: DTG**
- Japan
- Taiwan
Twelve-month retention on ART - % by country

**ART Retention Rate in Asia-Pacific**

Source: Global AIDS Monitoring 2018
Thailand: National UC AIDs Programs (2000-2014)
N= 309,313m age >15, mean = 37, mean FU 3.7 yrs
ART first-line: 93% NNRIIs (NVP 66%, EFV 24%); bPI 6%
Additional year of Life (yrs)

ARV started from age 20

<table>
<thead>
<tr>
<th>Baseline CD4 counts</th>
<th>50</th>
<th>150</th>
<th>200</th>
<th>250</th>
<th>350</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equal/more</td>
<td>39</td>
<td>46</td>
<td>49</td>
<td>51</td>
<td>61</td>
</tr>
</tbody>
</table>

Life-expectancy: 20 + 61 = 81 yo

Sirinya Teeraananchai et al. Antiviral Therapy 2016
HIV and Co-infections

Tuberculosis and HCV
Double disease burden of TB-HIV in Asia and the Pacific:

Globally, Asia and the Pacific accounts for:

- 2/3 of estimated new TB cases
- 3/5 of multidrug-resistant/ rifampicin-resistant TB
- 1/5 of estimated TB-HIV co-infections
- 1/2 of estimated TB mortality
Scaling Up Strategies to Control TB in HIV-TB

Scale UP ART

- Test and Treat
- Universal ART for all HIV-infected TB patients

The 3 I's for TB/HIV

- **Intensified** case finding (ICF)
- **Isoniazid** preventive therapy (IPT)
- **Infection control** for tuberculosis (IC)
IPT in PLWH in Myanmar: a five-fold decrease in incidence of TB disease and all-cause mortality

• N= 7177 patients; 1278 (18%) patients received IPT.
• Among patients receiving IPT, 855 (67%) completed 6 or 9 months of INH.
  • a significantly lower risk of incident TB than those who never received IPT (aHR \(0.21\), 95%CI 0.12–0.34).
  • a significantly lower risk of death than those who never received IPT (PLHIV who completed IPT, aHR \(0.25\), 95%CI 0.16–0.37)

HIV and HCV Co-infection

General Population

MSM 15-50% in N. America

Heterosexual Pregnant Women ≤5-15%

People who inject drugs PWID ≥50%

Prevalence (anti-HCV)
- No data
- ≤5%
- 5-15%
- 15-50%
- 50-75%
- >75%

Figure 2: Best estimates of prevalence of hepatitis C virus (HCV) co-infection in four population samples

Hepatitis C virus infection among people who inject drugs in Bangkok, Thailand, 2005-2010.

• The Bangkok Tenofovir Study (BTS) was a pre-exposure prophylaxis trial conducted among PWID, 2005-2013.

• N = 3679
  • 12% HIV positive
  • 44% Anti-HCV positive,
  • 36% HCV RNA positive

• the most common HCV subtypes were 1a (30.3%), 1b (12.8%), 3a (35.8%), 3b (6.9%) and 6n (8.7%).

Huge global treatment gap for hepatitis C

Cascade of care for people living with hepatitis C virus infection, by WHO region, 2016

2030 target:
- 90% of infected are diagnosed
- 80% of diagnosed are treated

Only 10% are treated

<3% Cured
Researches Highlights in Asia

- Cohort analyses: TreatAsia cohort
- Implementing Researches
- Acute HIV infection and Cure Researches
Trends in mortality among ART-treated HIV-infected adults in the Asia-Pacific region from 1999-2017:

Results from TAHOD and AHOD of IeDEA Asia-Pacific.

10,386 patients

Asian + Australian Cohorts

187 AIDS-related Death

2003-2007: 0.51 \rightarrow 0.09 /100 PYS

2013-2017: 0.78 \rightarrow 0.37 /100 PYS

80% ↓

53% ↓

335 Non-AIDS-related Death

Cardiovascular disease incidence projections in the TREAT Asia HIV Observational Database (TAHOD)

Rimke Bijker, Nagalingeswaran Kumasamy, Sasisopin Kiertiburanakul, Sanjay Pujari, Wilson Lam, Romanee Chaiwarith, Wing W Wong, Adeeba Kamarulzaman, Pacharee Kantipong, Anchalee Avihingsanon, Kinh V Nguyen, Junko Tanuma, Oon Tek Ng, Benedict LH Sim, Tuti P Merati, Jun Y Choi, Rossana Ditangco, Evy Yunihastuti, Ly P Sun, Cuong D Do, Jeremy Ross, Matthew Law, the TREAT Asia HIV Observational Database (TAHOD) of IeDEA Asia-Pacific

CVD prediction = **Double** in next 10 yrs

- **3703** Patients in 2019
- **730** per 100,000 pys
- **1432** per 100,000 pys in 2028
CVD-related mortality and factors associated with CVD events in the TREAT Asia HIV Observational Database (TAHOD)

- 8069 patients with a median follow-up of 7.3 years

Factors associated with any CVD event (IR 2.2 per 1000 PY):

- Older age: sub-hazard ratio (sHR)
  - 2.21 (95% CI 1.36-3.58) for age 41-50 years;
  - 5.52; 95% CI 3.43-8.91 for ≥ 51 years, compared with < 40 years

- High blood pressure (sHR 1.62; 95% CI 1.04-2.52),
- High total cholesterol (sHR 1.89; 95% CI 1.27-2.82),
- High triglycerides (sHR 1.55; 95% CI 1.02-2.37) and
- High body mass index (BMI) (sHR 1.66; 95% CI 1.12-2.46)

A longitudinal study of behavioral risk, adherence and virologic control in adolescents living with HIV in Asia

Ross, Jeremy L, MBBS, MSc\textsuperscript{1}; Teeraananchai, Sirinya, PhD, MS\textsuperscript{2}; Lumbiganon, Pagakrong, MD, MSc\textsuperscript{3}; Hansudewechakul, Rawiwan, MD\textsuperscript{4}; Chokephaibulkit, Kulkanya, MD\textsuperscript{5}; Khanh, Truong Huu, MD\textsuperscript{6}; Van Nguyen, Lam, MD, MSc\textsuperscript{7}; Jamal Mohamed, Thahira A, MBBS, M. Med\textsuperscript{8}; Nik Yusoff, Nik Khairulddin, MBBS\textsuperscript{9}; Fong, Moy Siew, MBBS\textsuperscript{10}; Prasitsuebsai, Wasana, MD\textsuperscript{2}; Sohn, Annette H, MD\textsuperscript{1}; Kerr, Stephen J, PhD, MIPH, BPharm\textsuperscript{2,11}


• N=250

• 19% had \textbf{virologic failure} at 144 weeks

• Self-reported adherence ≥95% was \textbf{60%} at week 144.

• Associated with VF at any time:
  • Smoking cigarettes, >1 sexual partner, and
  • living with non-parent relatives, a partner or alone,
**Same-Day ART**: Time to ART initiation

**Population (n=2,867)**

- **MSM**: 91.3% (N=1,949)
  - 91.3% YES
  - 8.7% NO
- **TGW**: 96.4% (N=137)
  - 96.4% YES
  - 3.6% NO
- **Gen. Population**: 83.4% (N=781)
  - 16.6% YES
  - 83.4% NO

**Same day**: 74% (1-7 days: 22%)

**At 12 months**

- 90% Retention
- 90% undetectable VL

**Retention**

- Same day: 74%
- 1-7 days: 22%
- 8-30 days: 3%
- >30 days: 1%

**Source**: Same-Day ART database, Thai Red Cross Anonymous Clinic (July 2017-December 2018).
Thailand’s **PrEP** Programs

*Princess Prevention Fund*

**UNAIDS Goodwill Ambassador for HIV Prevention in Asia-Pacific (2019-2020)**

Trained KP lay providers dispense free PrEP from the Princess Soamsawali Prevention Fund, covering half of all current PrEP users.

**Estimated PrEP target 250,000**

- **Only 2%** receiving PrEP
- **5,613**
- **55%** of Thai PrEP users accessed PrEP through key population lay providers


Thailand’s Achievements in Cure research

315,354 samples screened in real time

730 cases identified with acute HIV infection

579 cases enrolled into the study

574 cases Immediate ART

RV254/SEARCH010
Acute HIV cohort with early ART

95% MALE
91% MSM
81% CRF01_AE
26 YEARS-OLD
19 DAYS OF INFECTION

81 Fiebig I
131 Fiebig II
259 Fiebig III
68 Fiebig IV
32 Fiebig V

SEARCH, TRC-ARC

December 2018
Small HIV **Reservoir Size** with Early ART

- Low levels of total HIV DNA in treated acute vs. chronic infection
- Total HIV DNA is barely detected in Fiebig I, treated participants

However, **treatment interruption trials** to date have shown rapid viral load rebound

**RV254/SEARCH010 data**

Louise Leyre, Amelie Pagliuzza, Nicolas Chomont (University of Montreal)
Benefits of **Early Treatment:** RV254

**BRAIN**
- Normal cognition and MRI brain
- No CSF viremia

**GUT**
- CD4 reconstitution
- Resolution of inflammation

**LYMPH NODE**
- Preservation of B and CD8
  - vRNA+ cells are detected as early as Fiebig I and persists in LN after 24 months of viral suppression

**IMMUNE PRESERVATION**
- High immune function and memory potential

**IMMUNE ACTIVATION**
- Normal levels of most cellular and soluble markers

**HIV**
- Low viral diversity

*Colby, Nat Med 2018; Ananworanich, JIAS 2017, Ebiomedicine 2016; Peluso, AIDS 2017; Takata, Sci Transl Med 2017; Muir, Plos Pathog 2016; Deleage, JCI Insight 2016; Valcour, Plos One 2015; Schuetz, Plos Pathogens 2014*
Conclusions

• Although overall trends in last decades HIV epidemics has been improving significantly, in Asia-Pacific
  • >5 million PLWH,
  • up to 300,000 newly-infected and
  • up to 1 million died from AIDS each year

• While the quest for an efficacy vaccine and cure are still challenging, strategies to reach 90-90-90 in combination with PrEP, Same day ART will help us ending this epidemic in the next decade
Acknowledgements

- Prof. Praphan Phanuphak
- Dr. Nittaya Phanuphak
- Ms. Krittaporn Termvanich
- Professor Elaine Abrams
- Professor Jintanat Ananworanich
- Dr. Annette Sohn
- HIV-NAT, SEARCH, the Anonymous Clinic, the Tangerine Clinic, and the Thai Red Cross AIDS Research Centre
- Community partners and networks of people living with HIV across Thailand