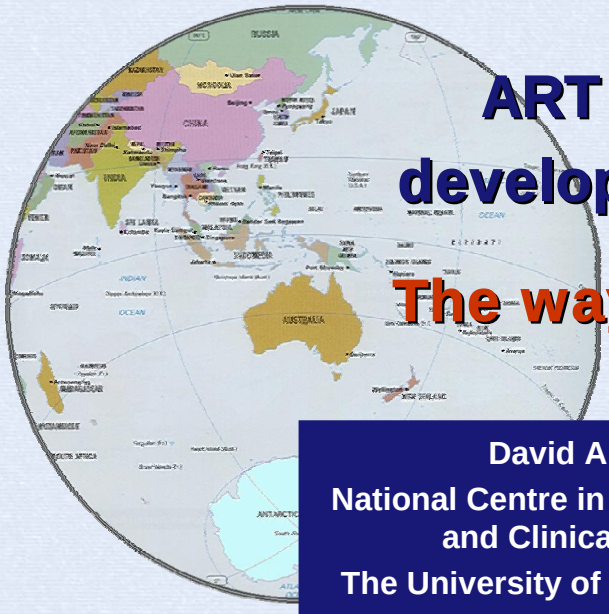

ART in the developing world

The way forward

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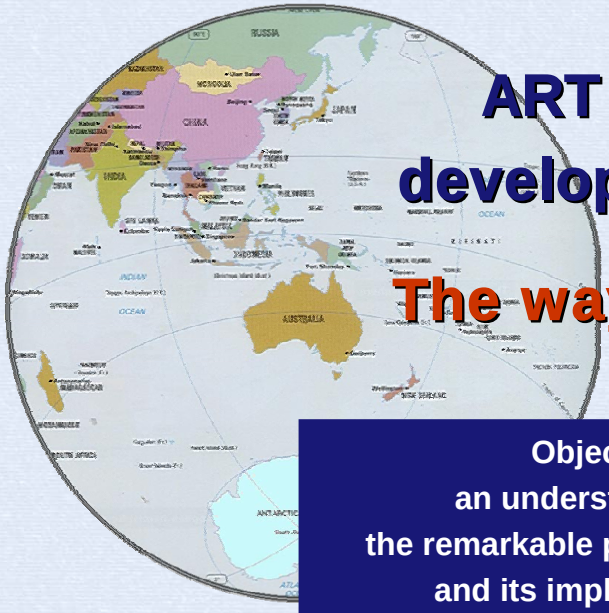


ART in the developing world

The way forward

Objective:
an understanding of
the remarkable progress in ART
and its implementation
in the developing world

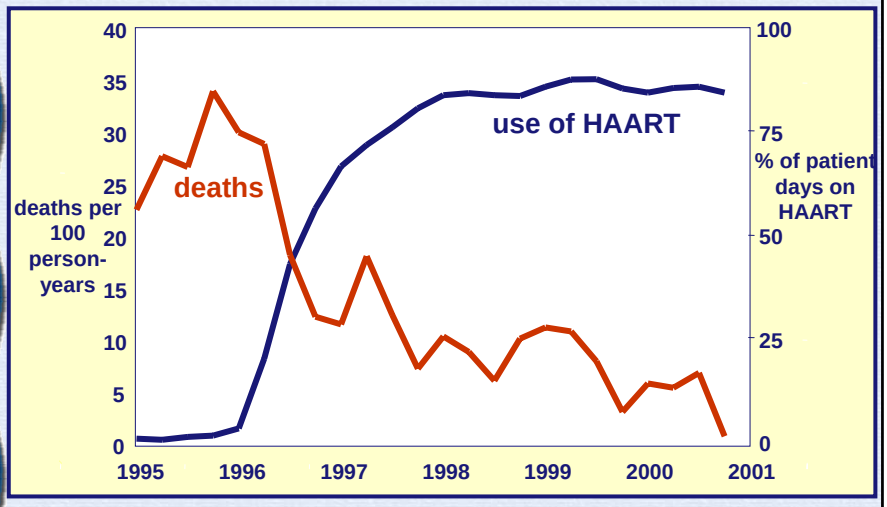
ART in the developing world

- Standard of care
- Treatment as prevention
- Access to ART
- Clinical and implementation research

ART in the developing world

Standard of care

Mortality and HAART utilisation



Palella et al, CROI 2002

ART in the developing world

Standard of care

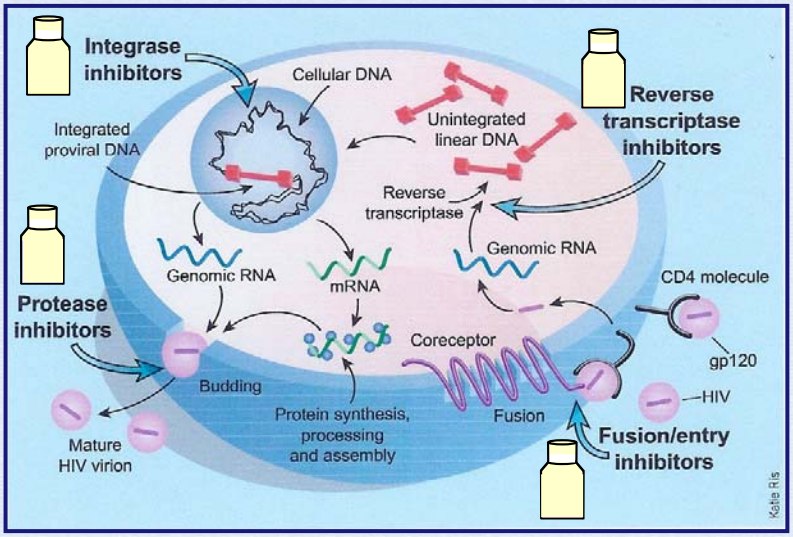
Current drugs and classes

NRTI	NtRTI	NNRTI	PI	FEI
AZT	TFV	NVP	SQV	ENF
ddI		DLV	RTV	
ddC		EFV	IDV	
d4T			NFV	
3TC			APV	
ABV			LPV/r	
FTC			ATV	
			fAPV	

ART in the developing world

Standard of care

Targets for anti-HIV drugs



Fauci Nature Medicine 2003

ART in the developing world

Standard of care

When to start therapy

Strong evidence base

- symptomatic disease
- CD4+ cell count < 200/μL

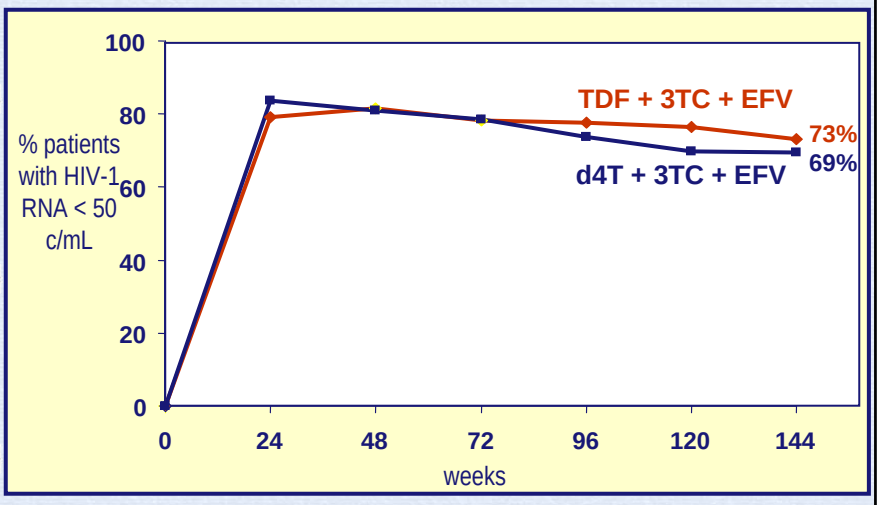
Guidelines driven

- 200/μL < CD4+ cell count < 350/μL
- high VL

ART in the developing world

Standard of care

Gilead 903: week 144 efficacy intent to treat

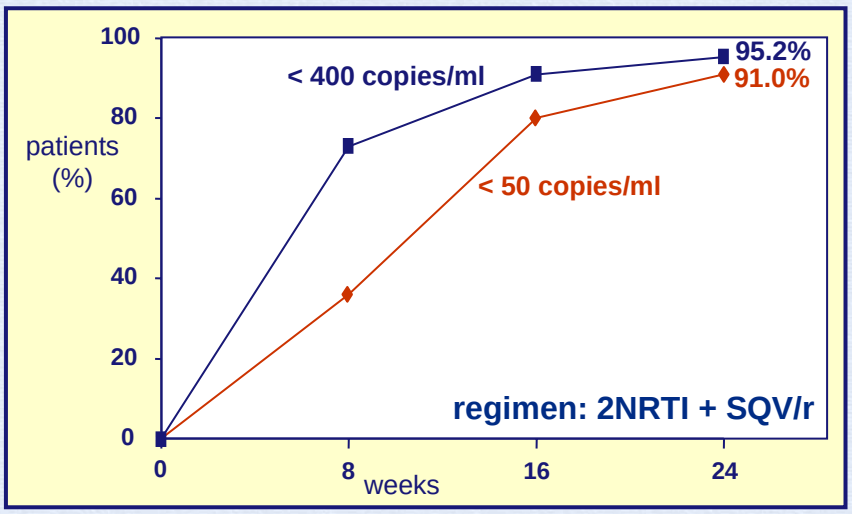


Gallant et al. 2004

ART in the developing world

Standard of care

Staccato: viral load response during induction period

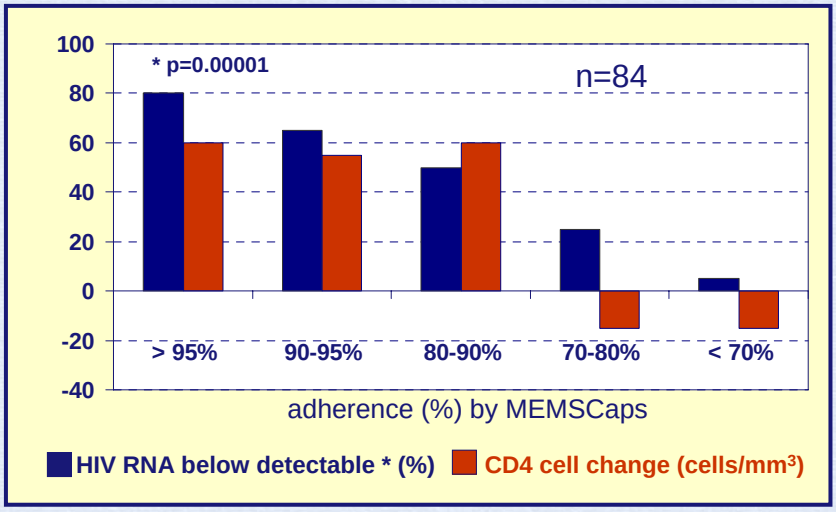


Ananworanich et al, WAC 2004

ART in the developing world

Standard of care

Level of adherence determines response



Paterson et al, Retroviruses 1999

ART in the developing world

Standard of care

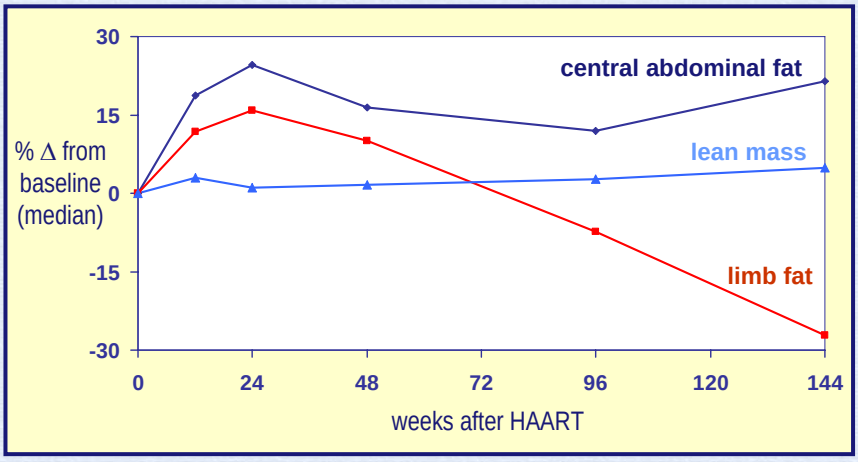
Fixed dose combinations

advantages	disadvantages
adherence	toxicity management
pill burden	dose escalation

ART in the developing world

Standard of care

Changes in body composition following HAART



Mallon et al, AIDS 2002

ART in the developing world

Standard of care

Clinical lipodystrophy




ART in the developing world

Standard of care

Clinical lipoatrophy in a child

ART in the developing world

Standard of care

Choosing first-line regimens

- use fixed dose combinations first line
- implement adherence strategies
- select NNRTI-based regimens
- choose HAART regimens on basis of established efficacy, safety, ease of administration, and tolerability
- suboptimal treatments must not be used
- track development of ART resistance
- plan second line regimens for failure
- integrate TB management

ART in the developing world

Standard of care

Failure of first line regimens

- design regimens for failure of 2NRTI and NNRTI
- will require PI-based therapy
- NRTI backbone will be impaired
- subsequent regimens following PI failure will be problematic
- substitutions for toxicity will be limited

ART in the developing world

Standard of care

Treatment as prevention

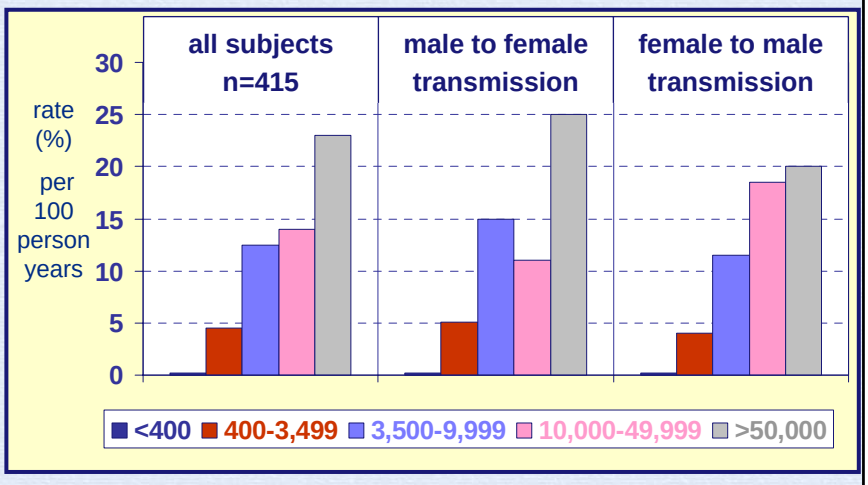
Access to ART

Clinical and implementation research

ART in the developing world

Treatment as prevention

Heterosexual transmission by HIV-1 viral load



Quinn et al, NEJM 2000

ART in the developing world

Treatment as prevention

Infected person

treat infected person to reduce transmission

- examples
  - serodiscordant couple (+ve partner)
  - mother
- will benefit infected person
- requires combination ART

ART in the developing world

Treatment as prevention

Uninfected person

treat uninfected person to prevent transmission

- examples
  - serodiscordant couple (-ve partner)
  - baby of HIV +ve mother
  - high risk HIV -ve
- population-based chemoprophylaxis
- monotherapy may be sufficient

ART in the developing world

Standard of care

Treatment as prevention

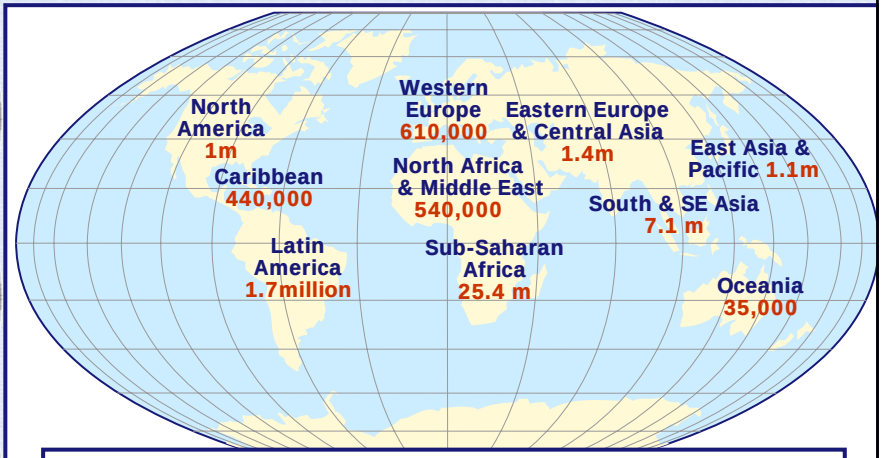
Access to ART

Clinical and implementation research

ART in the developing world

Access to ART

Adults and children estimated to be living with HIV/AIDS



total 38.6 million living with HIV

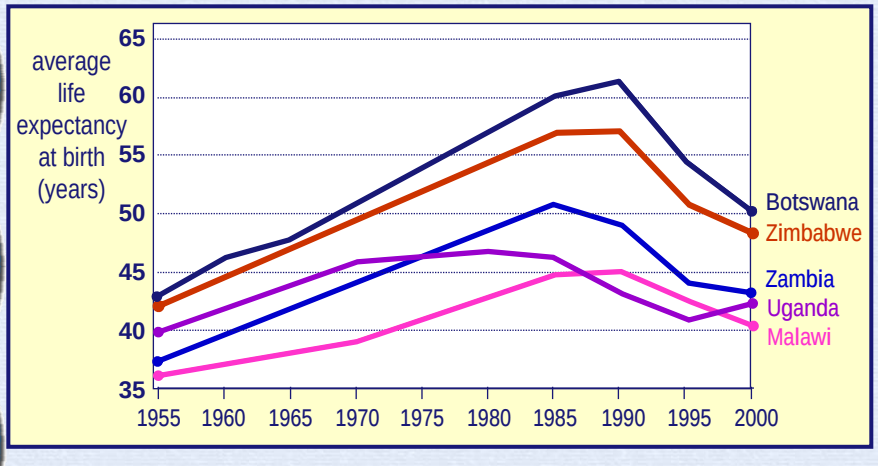
8,500 die each day

WHO/UNAIDS 2004

ART in the developing world

Access to ART

Projected changes in life expectancy in selected African countries with high HIV prevalence

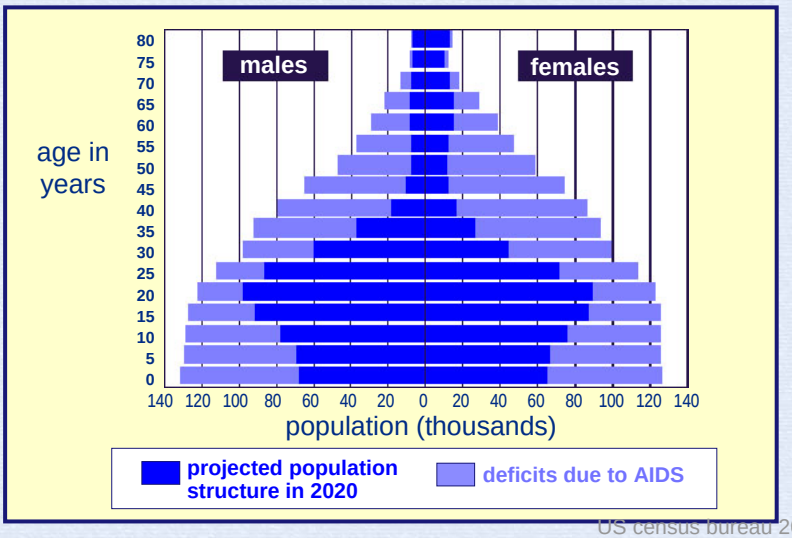


United Nations Population Division, 1996

ART in the developing world

Access to ART

Projected population structure with and without the AIDS epidemic: Botswana 2020



US census bureau 2000

ART in the developing world

Access to ART

What should we do?

- we cannot afford not to treat those who need to be treated with antiretrovirals (HAART)
- we should avoid the false dichotomy between prevention and treatment

Treat those who need to be treated with antiretrovirals (HAART)

ART in the developing world

Access to ART

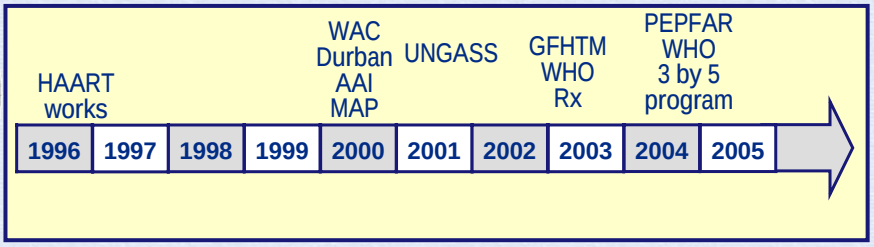
Reasons to make the fight against HIV, including access to HIV medicines, a global priority

- humanitarian
- economic and social development
- tuberculosis
- “security”

ART in the developing world

Access to ART

Forces for change



- global treatments activism
- generic competition
- funding mechanisms
- technical programs

ART in the developing world

Access to ART

The reality

- in quite a few countries there is currently (some) government commitment to facilitate access to ART
- a number of NGOs and CBOs are providing HIV treatment and care
- there is also an increase in employer schemes including comprehensive HIV-care, incuding HAART
- however, out of the millions of people that need to be treated TODAY in the developing world, only 5% of the population in immediate need are receiving it

ART in the developing world

Access to ART

Challenges of ART in resource poor settings

1. insufficient political commitment
2. cost of care (including antiretrovirals)
3. lack of infrastructure
4. lack of expertise
5. lack of a common agenda and leadership in implementation
6. planning for the future

ART in the developing world

Access to ART

Challenges of ART in resource poor settings

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6. planning for the future

ART in the developing world

Access to ART

Challenges of ART: 2. cost of care

- predominance of cheapest fixed dose HAART regimens in developing country ART scale up (d4T/3TC/NVP)
- the long-term costs of this choice should not be ignored
- while the choice for d4T/3TC/NVP is understandable in the light of emergency, we need to move to less toxic regimens as soon as possible, even if the cost is higher

ART in the developing world

Access to ART

Challenges of ART: 2. cost of care

Lipodystrophy associated with d4T/3TC/NVP FDC

ART in the developing world

Access to ART

Challenges of ART: 2. cost of care

- health care budgets of most countries are limited; in poor developing countries per capita spending is often less than $10 per year
- so HAART scale up is dependent on the international donor community
- but… governments also make choices…

ART in the developing world

Access to ART

Challenges of ART: 4. lack of expertise

There simply are not enough expert doctors to cope with the scale up; the situation is most extreme in sub-Saharan Africa, but Asia also has a problem (Treat Asia Report).

- massive training effort needed
- involvement in delivery of care by non-physicians may be necessary (DOT?)
- retention of health care workers is a priority

ART in the developing world

Access to ART

Challenges of ART: 4. lack of expertise

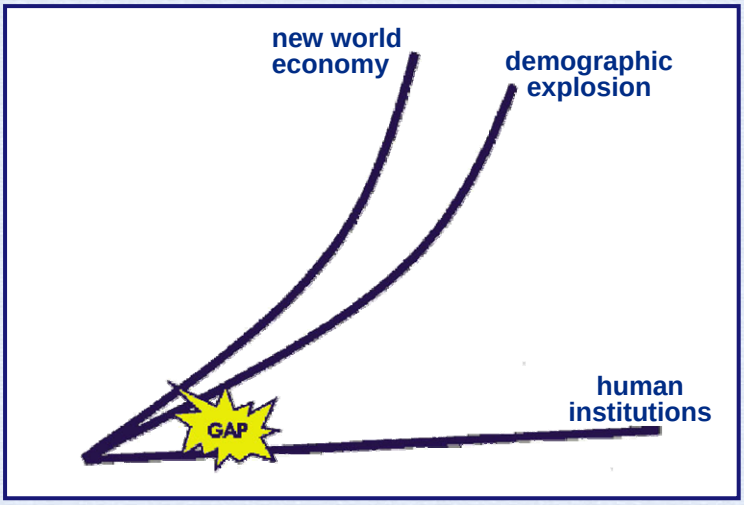
- recognise economic realities on the ground

Like people in developed countries, people in developing countries need to be able to make a decent living out of their activities even if they involve laudable goals like providing HIV therapy to the millions.

ART in the developing world

Access to ART

Challenges of ART: bridging the leadership gap?



Rischard, High Noon: 20 global issues, 20 years to solve them

ART in the developing world

Access to ART

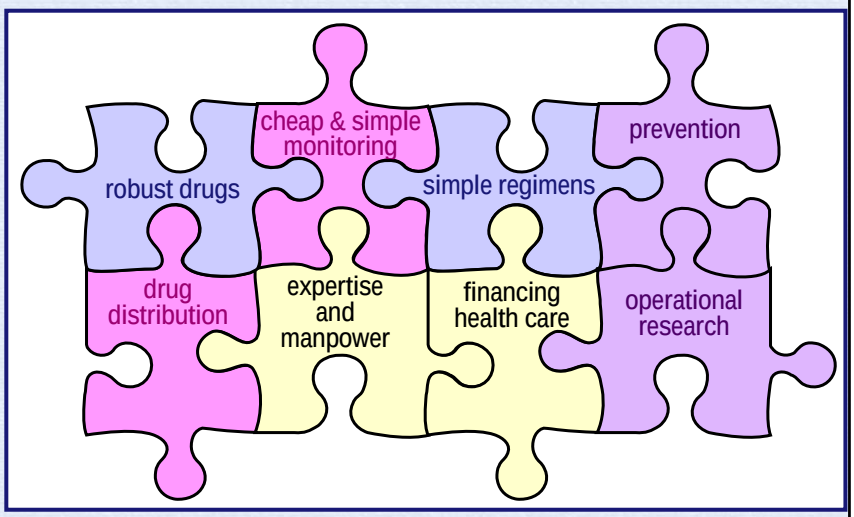
Challenges of ART: 5. lack of a common agenda and leadership in implementation

- a sense of urgency and funding may be there with regard to the antiretroviral scale up, but there is still no undisputed global leadership and common agenda with a clear division of tasks
- majority of funding delivered through the public sector
- in countries, donors and technical assistance agencies are often in clear competition with each other

ART in the developing world

Access to ART

Challenges: 6. planning from thousands to millions?



ART in the developing world

Access to ART

Challenges: 6. planning for independence

- technology transfer to manufacture generic antiretrovirals
- models of free comprehensive ART, using manufacture of generics followed by pressure on pharma to cut price
- national generic manufacturing programs
- regional agreements with pharma on price cuts
- cheap, robust assays for CD4 and viral load

ART in the developing world

Access to ART

Challenges: summary

The wide-scale introduction of adequate antiretroviral therapy in developing countries requires

- a concerted global effort
- of a broad coalition of
  - the public sector
  - the private sector
  - civil society
  - academia
- with clear divisions of tasks and accountability

ART in the developing world

Access to ART

Cambodia meeting the challenge in 2005

- **PLWHA: 123,000**
- **eligible for treatment: 20,000**
- **currently on treatment: 6,100 at 15 sites**
- **end 2005 on treatment: 10,000 at 26 sites**

ART in the developing world

Standard of care

Treatment as prevention

Access to ART

Clinical and implementation research

ART in the developing world

Clinical and implementation research

Treat Asia: background

- the use of combination antiretroviral therapy has led to reduced morbidity and mortality caused by HIV infection in western countries
- relatively little is known regarding HIV disease natural history and response to antiretroviral treatments among Asian people infected with HIV
- information from observational studies is important for developing treatment and care guidelines, and planning resources for health services

ART in the developing world

Clinical and implementation research

Treat Asia: what is it?

A cooperative network of clinicians throughout Asia and the Pacific that aims to expand capacity for the broader introduction of HIV/AIDS treatments in the region.

ART in the developing world

Clinical and implementation research

TAHOD: what is it?

- first collaborative study by the TREAT Asia network
- a multi-centre, observational study of patients with HIV

ART in the developing world

Clinical and implementation research

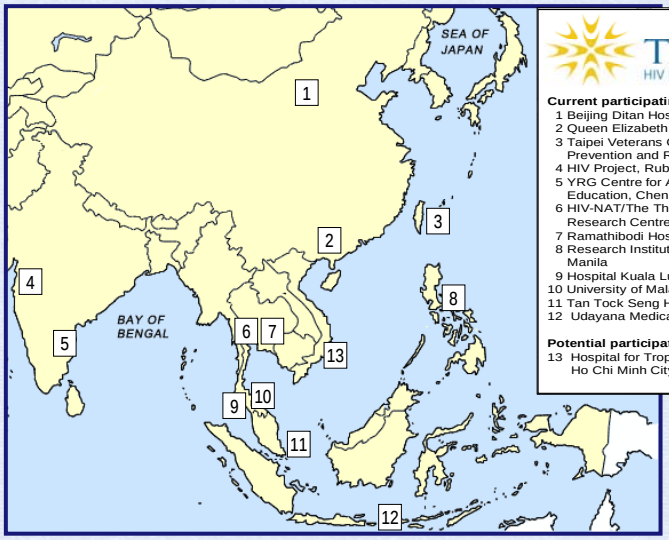
TAHOD: primary objectives

- develop capacity in HIV clinical data collection in countries of the Asia-Pacific region
- assist in evaluation of new HIV treatments for the Asia-Pacific region
- monitor anti-retroviral and prophylactic treatment as related to demographics and markers of HIV disease stage
- monitor toxicity to anti-retroviral therapy
- examine HIV natural history, including relationship between access to antiretroviral therapy and disease progression

ART in the developing world

Clinical and implementation research

TAHOD: participating sites



TAHOD HIV Observational Database

Current participating sites:

1 Beijing Ditan Hospital, Beijing
2 Queen Elizabeth Hospital, Hong Kong,
3 Taipei Veterans General Hospital and AIDS Prevention and Research Centre, Taipei
4 HIV Project, Ruby Hall Clinic, Pune
5 YRG Centre for AIDS Research and Education, Chennai
6 HIV-NAT/The Thai Red Cross AIDS Research Centre, Bangkok
7 Ramathibodi Hospital, Bangkok
8 Research Institute for Tropical Medicine, Manila
9 Hospital Kuala Lumpur, Kuala Lumpur
10 University of Malaya, Kuala Lumpur,
11 Tan Tock Seng Hospital, Singapore
12 Udayana Medical School, Bali

Potential participating sites:

13 Hospital for Tropical Medicine, Ho Chi Minh City

ART in the developing world

Clinical and implementation research

TAHOD: patient recruitment

TAHOD HIV Observational Database

	n=	with follow-up	follow-up rate
Nov 2003	1,282		
Mar 2004	1,887	1174	92%
Sep 2004	2,089	1710	91%

ART in the developing world

Clinical and implementation research

TAHOD: patient characteristics

n=	2089
gender	male=72%
median age (IQR)	37
ethnicity	
Chinese	44%
Indian	21%
Thai	21%
exposure	
heterosexual contact	75%
homosexual contact	14%
injecting drug use only	2%

ART in the developing world

Clinical and implementation research

TAHOD: patient characteristics

	at baseline	
median baseline CD4 count (IQR)	291 (158-435) cells/µl	
baseline HIV viral load	<400 copies/ml	64%
median (IQR)	<400 (<400-11000) copies/ml	
ARV at entry to TAHOD	no ARV	28%
	mono/ dual ARV	5%
	HAART	67%

ART in the developing world

Clinical and implementation research

TAHOD: prior AIDS at entry (42%)

prior AIDS defining illness %			
TB	37.1	cryptosporidiosis	1.0
Pneumocystis carinii pneumonia	21.5	cytomegalovirus	0.9
oesophageal candidiasis	7.3	recurrent pneumonia	0.9
cryptococcosis/ extrapulmonary	4.5	histoplasmosis	0.4
toxoplasmosis	4.5	Kaposi's sarcoma	0.4
herpes simplex	4.2	leukoenephalopathy	0.3
cytomegalovirus retinitis	4.2	HIV encephalopathy	0.2
Salmonella septicemia	3.0	lymphoma/ Burkitt	0.2
non-TB mycobacterial diseases	2.9	lymphoma/ brain	0.2
candidiasis/ bronchi,trachea,lung	2.6	isosporiasis	0.1
HIV wasting syndrome	2.4	lymphoma/ immunoblastic	0.1
penicilliosis	1.5		

ART in the developing world

Clinical and implementation research

TAHOD: rates of AIDS or death

number of patients	1710
number with AIDS or death	91
years of follow-up	1199
event rates	7.6 per 100 person-years

by treatment	rate
yes	5.6
no	17.0

ART in the developing world

Clinical and implementation research

TAHOD: summary

- overall response to HAART in terms of CD4 and HIV viral load in Asian patient populations is similar to that seen in western countries
- higher rates of clinical progression (new AIDS and/or death) among TAHOD patients compared to that seen in western countries
- similar predictors related to clinical progression
  - baseline CD4 count the most important predictor
  - other markers (e.g. hemoglobin) provide useful prognostic models when CD4 count unavailable

ART in the developing world

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