

# HIV, TB and Substance Use Triple Trouble

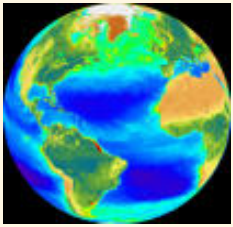
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# HIV, TB and Drug Use



- Epidemiology of HIV, TB and drug use
- “Perfect storm” of drug resistant TB
- Prevention and Treatment
  
- Historical and geographic examples



# Global TB/HIV Epidemics

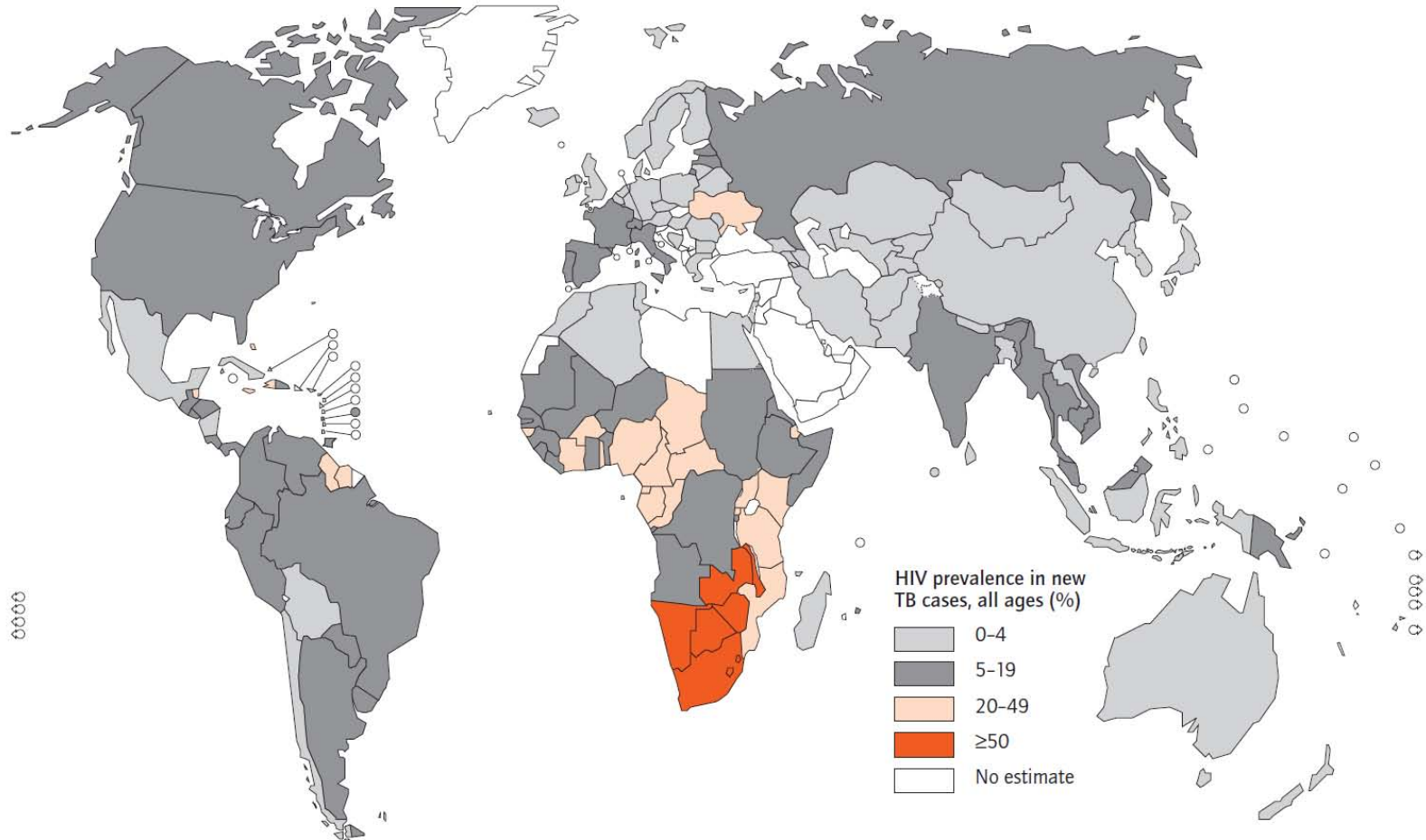
- **35 million persons infected with HIV**
  - 5 million new infections, 3 million deaths per year
  - >90% in resource limited countries
  - IDU major risk in many European countries
  - 2.5-3 million IDUs living with HIV
- **2 billion people are infected with *M.TB***
  - 8 - 9 million new active TB cases, ~2 million deaths per year
  - > 90 % in developing countries
  - >500,000 in Europe
- **12-14 million persons are TB/HIV co-infected**
- **TB epidemics have followed in wake of rising HIV rates**

# HIV Co Infection in New TB cases

■ **FIGURE 1.3**

Estimated HIV prevalence in new TB cases, 2007

5-20% HIV co infection rate in TB cases



# Recent Recognition of growing threat of drug resistant TB

- **MDR-TB multiple drug resistant TB**
  - resistance to at least **isoniazid and rifampin**
  - requires TB laboratory infrastructure for diagnosis
  - two most potent first line TB therapies
- **XDR-TB extensively drug resistant TB**
  - MDR+ resistance to **fluoroquinolones and at least one injectable**
  - requires TB laboratory infrastructure for diagnosis
  - two most potent second line therapies

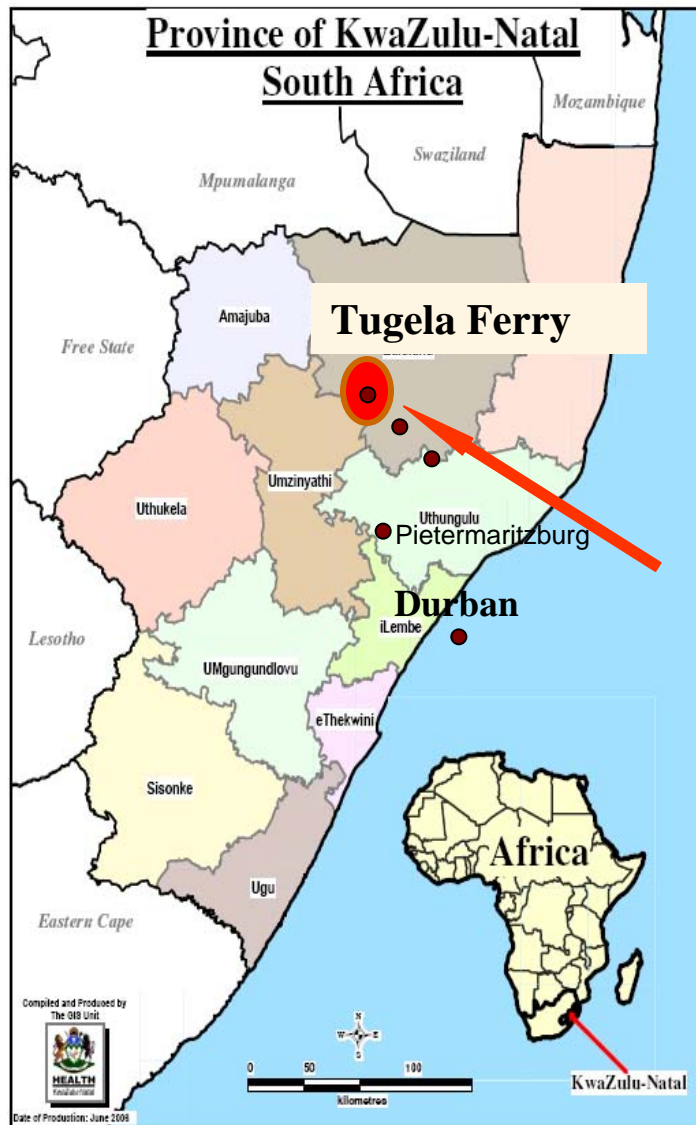
# M/XDR TB Definitions

- **Acquired resistance**
  - Resistance as a result of treatment failure
    - The predominant mechanism in past and many areas
    - A consequence of program and/or patient limitations
- **Primary resistance**
  - Resistance resulting from transmission of resistant organisms
    - The predominant mechanism in areas of high HIV prevalence
    - A consequence of increased susceptibility, rapid progression to disease and absence of infection control

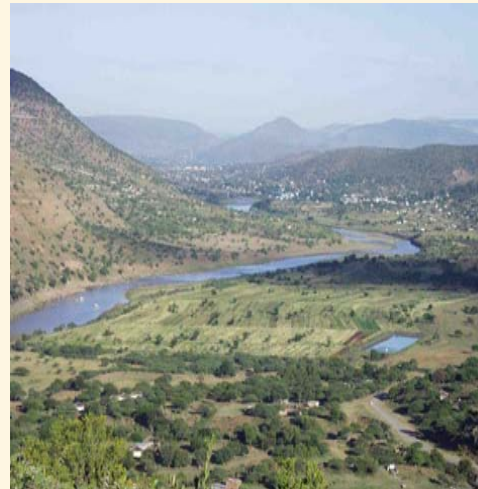
# HIV-related MDR-TB Outbreaks in Industrialized Countries, 1988-1995

Location	Total cases	% HIV infected	% Death	Median time to death (weeks)
Hospital, New York City, USA, 1989-1990	51	100	89	16
Hospital, New York City, USA, 1990-1991	70	95	77	4
Hospital, New York City, USA, 1991-1992	32	91	83	4
Hospital, Florida, USA, 1988-1990	65	93	72	7
2 Hospitals, Italy, 1991-1995	116	98	95	6-8
Hospital, Madrid, Spain, 1991-1995	48	100	98	7
Hospital, Buenos Aires, Argentina, 1994-1995	68	100	93	5
Prison system, New York State, USA 1990-1991	42	98	79	4

# Tugela Ferry KwaZuluNatal Province Rural South Africa



- 1800 sq km rural district
- Population 200,000 traditional Zulu people
- **TB case rate**  
1,100/100,000/yr  
>1200 new cases/yr, ~50% completion rate
- **TB laboratory/Durban**  
culture and 1st and 2nd line DST



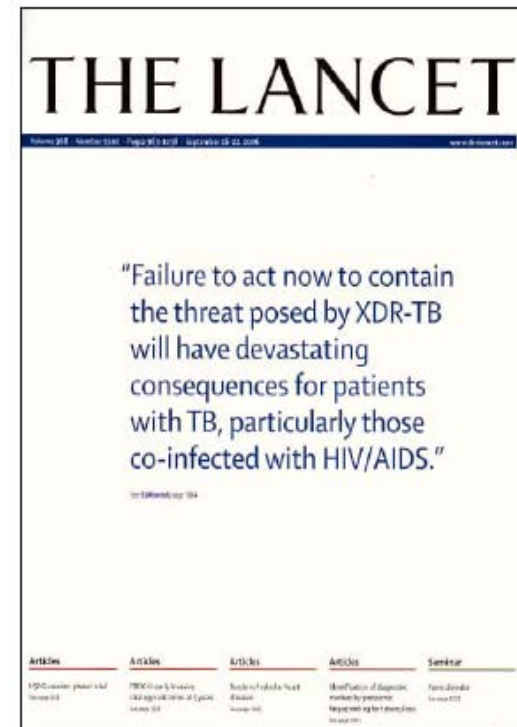


# TB/HIV Integration

## MDR/XDR TB in Tugela Ferry

### 2005 – 2006

- MDR/XDR TB – major cause of death
- 53 cases XDR TB
  - All tested HIV+
  - 98% rapid mortality
    - Median 16 days
  - Strong evidence for nosocomial transmission
    - >50% no previous Rx
    - 83% single strain
    - HCW deaths



*Gandhi, Moll, Sturm, Pawinski, Govender, Lalloo, Zeller, Andrews, Friedland Nov 2006*

# Recognition that MDR/XDR TB are Widespread in South Africa and Beyond

- > 600 cases M and XDR TB Tugela Ferry
- XDR TB from ~60 KZN facilities in KZN
- Mortality XDR TB 85%, MDR TB 65%
- XDR TB cases in all 9 South African provinces and neighboring countries
  - Botswana, Mozambique, Lesotho, Swaziland, Namibia, ? Zimbabwe
- Full extent unknown; no denominator, culture and DST limited

# Etiology of M and XDR-TB Epidemic in KwaZuluNatal

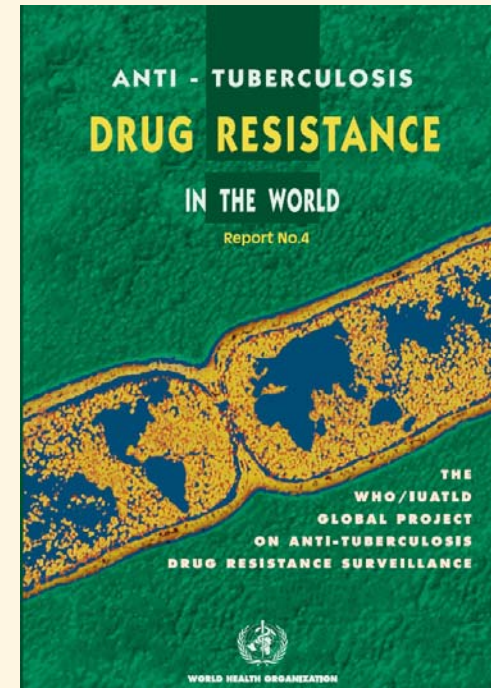
- High prevalence *M. tb*; weak TB control program
  - Low cure and completion rates
  - Acquired, previously treated drug resistance
- Arrival and progression of the HIV epidemic
  - Massive increase in TB cases
  - Increasing population and individual immuno-compromise
  - Rapid progression to disease
  - New, transmitted drug resistance
- Absent/limited infection control
  - Nosocomial transmission
  - Community transmission in congregate settings (prisons)

# WHO February 2008

- Global surveillance indicates substantial and rising numbers of M and XDR TB

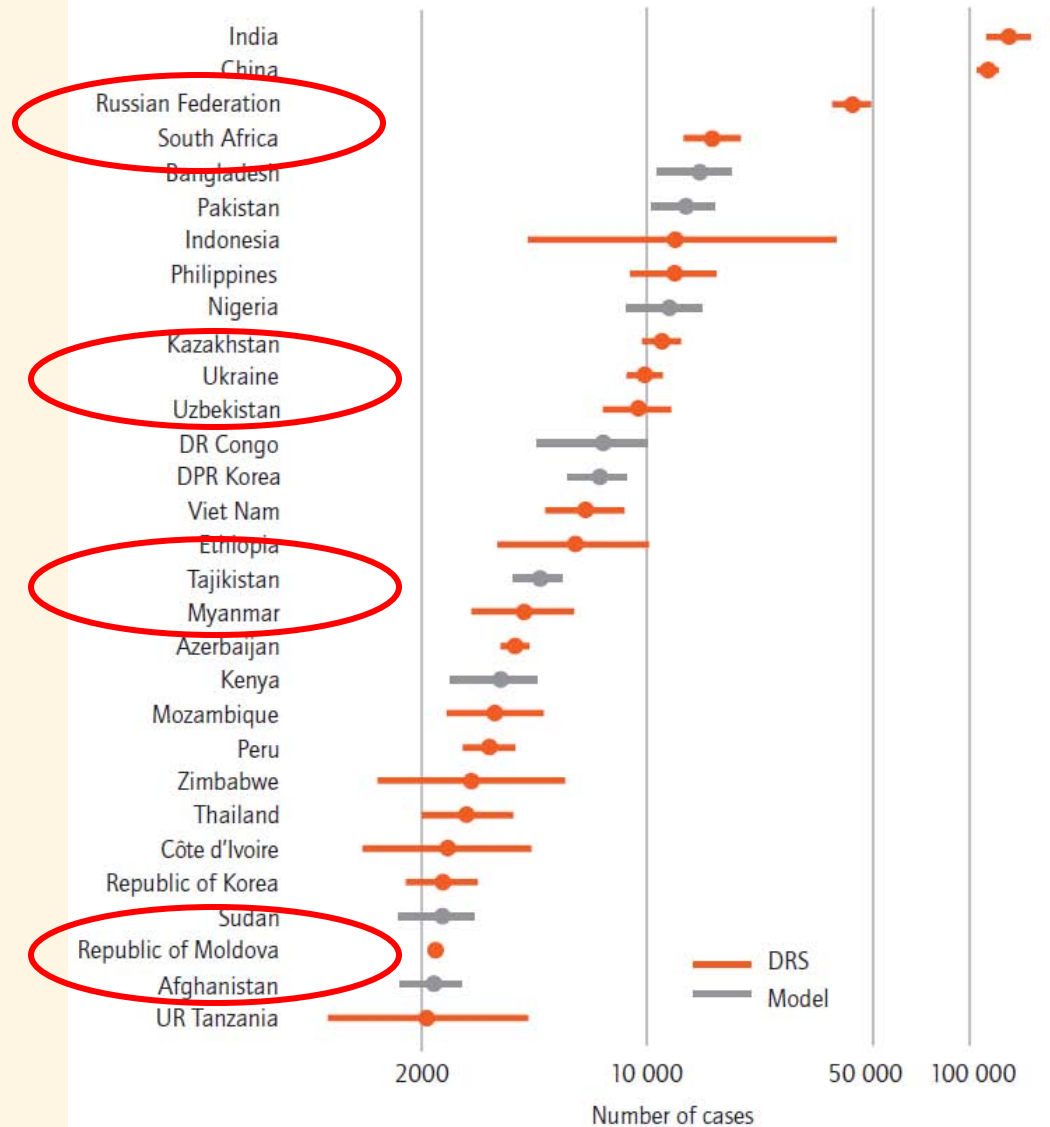
- **MDR 489,000 (5%)**  
(95% CI 455,000-614,000)

- **XDR 40,000 (8%)**  
(95% CI 4.6-6.0%)

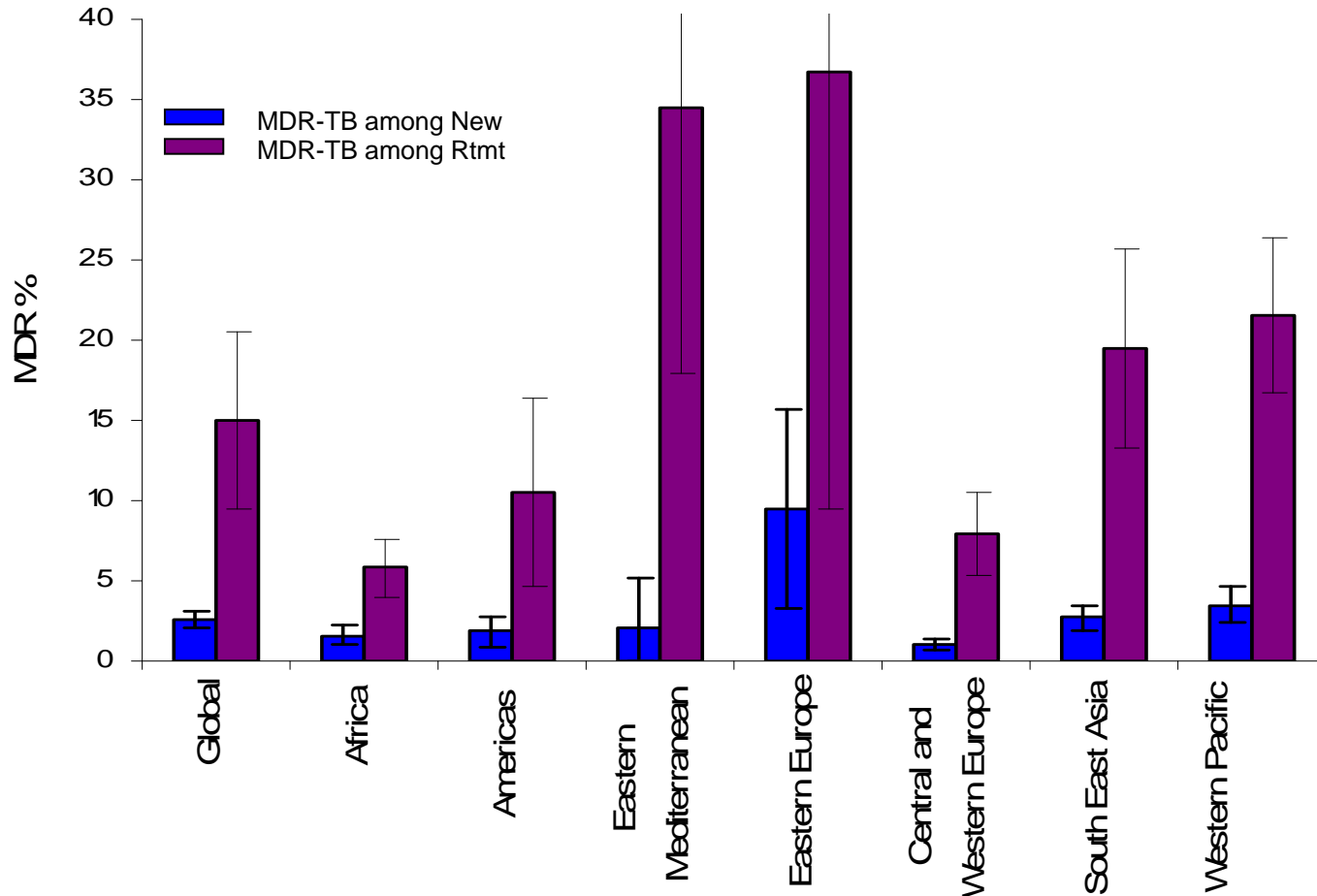


### ■ FIGURE 1.6

Countries with the highest numbers of estimated MDR-TB cases, 2007. Horizontal lines denote 95% confidence intervals. The source of estimates is drug resistance surveillance or surveys (DRS, in red) or modelling (in grey).



# % MDR TB among new and previously treated patients by region



- Multidrug resistance (MDR) more frequent in the Baltic States (combined MDR: 10–21%) than in the other countries

# MDR-TB and HIV in Ukraine

	Civilian sector		Penitentiary sector	
	New cases n=924	Previously treated cases n=369	New cases n=78	Previously treated cases n=125
MDR rates (95% CLs)	15.5 (13.1 to 17.8)	41.5 (36.4 to 46.5)	21.8 (12.4 to 31.2)	52.8 (43.9 to 61.7)

- Independent predictors for MDR-TB

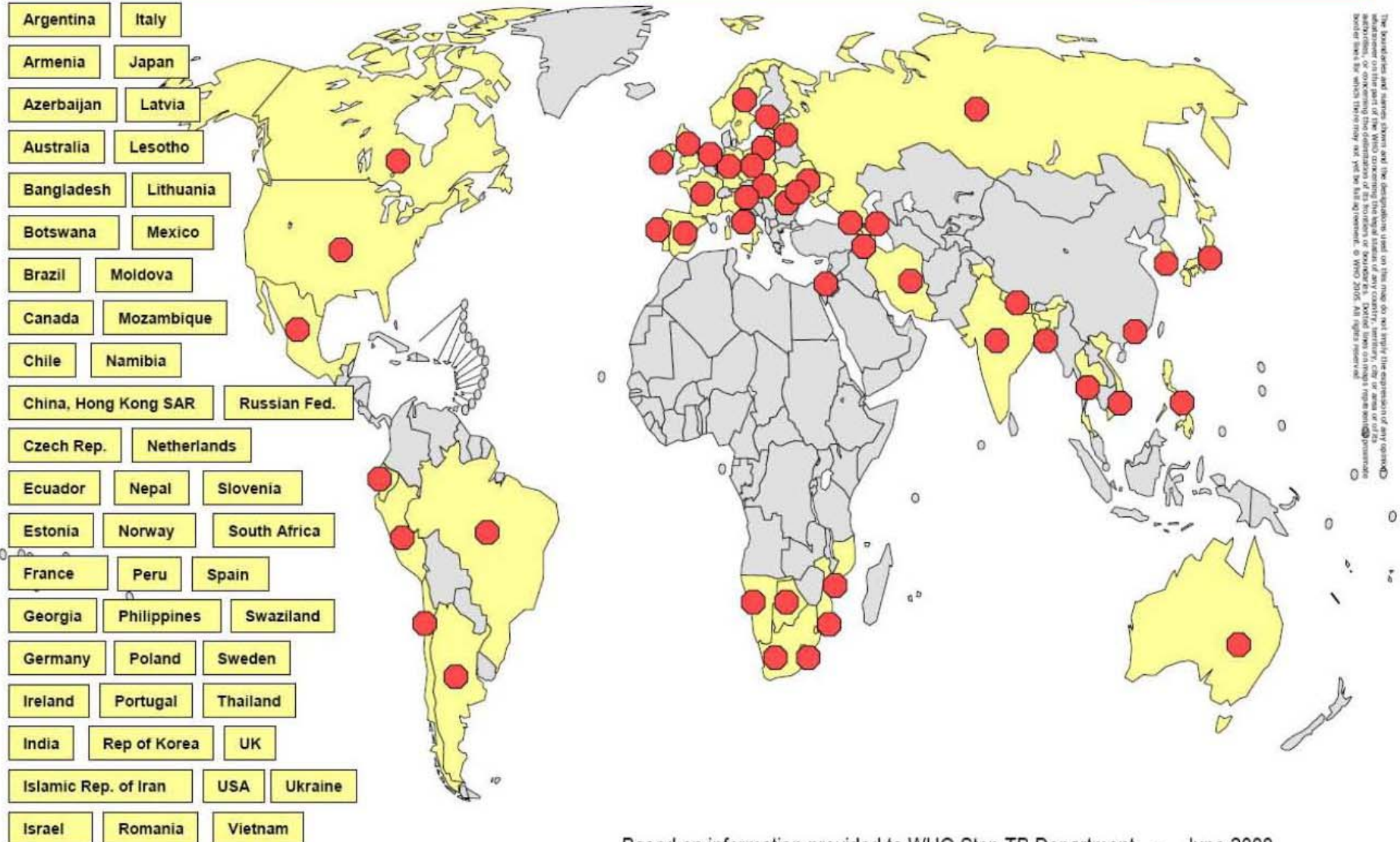
History of previous treatment: OR: 4.0 (95%CLs 3.1-5.1)

Imprisonment: OR: 1.5 (95%CLs 1.1-2.0)

- HIV status: OR: 1.7 (95%CLs 1.3-2.3)**



# Countries with confirmed cases of XDR-TB as of November 2008



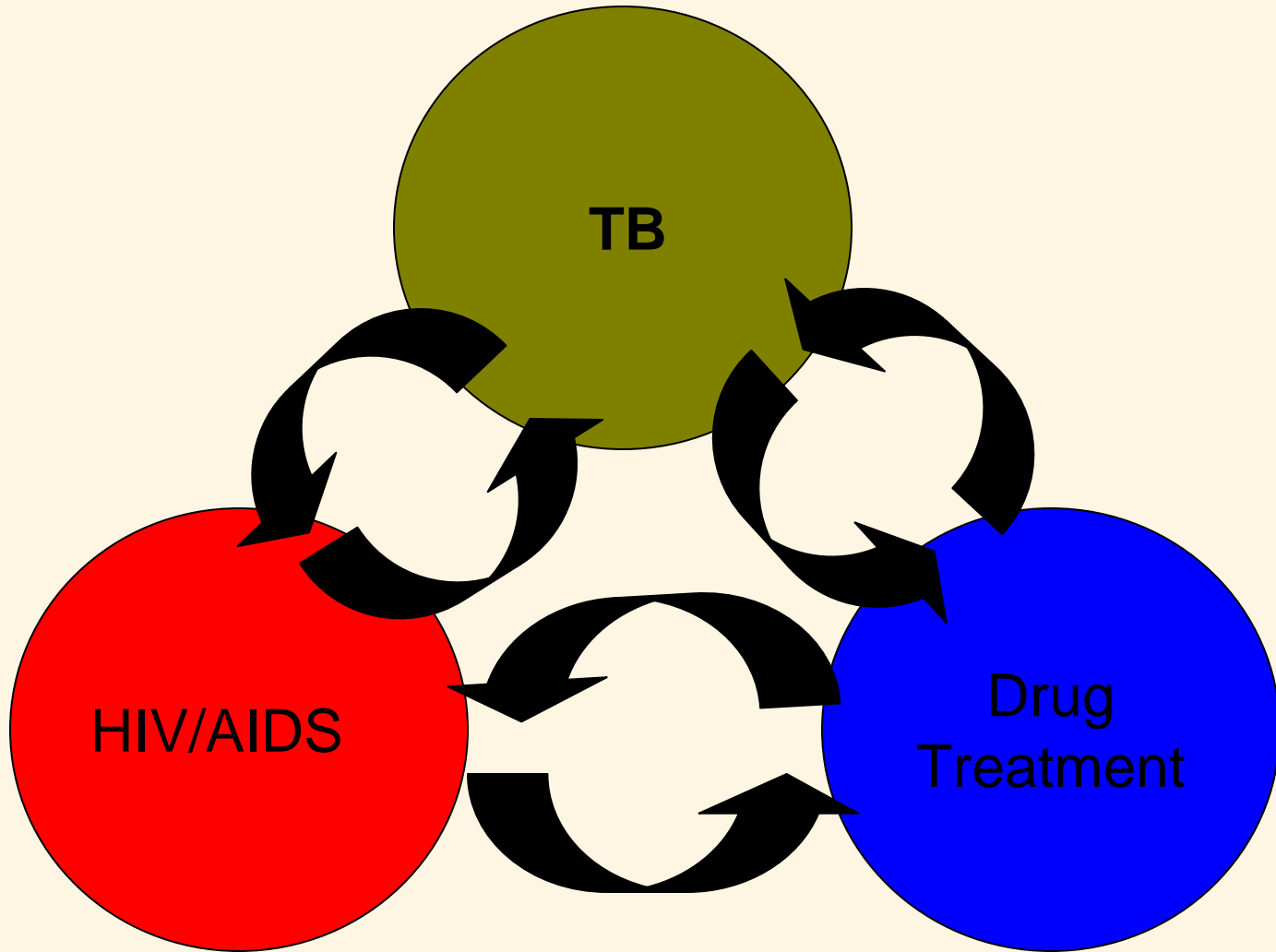
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# Treatment and Prevention Challenges and Opportunities in HIV, TB and Substance Use

- Triple stigma
- Access to prevention, care and treatment
- Organization of services
- Integration and co location of services-best strategy to reduce morbidity and mortality from HIV and TB in drug users
  - Three I's
  - Medication Adherence
  - Drug-drug interactions
  - M/XDR TB treatment

# Current Approaches to Treatment



# Treatment and Prevention Challenges and Opportunities in HIV, TB and Substance Use

- Hidden population, avoidance of traditional health care system
  - Community outreach
  - Non-traditional care sites
  - Prison health
- 3 I's
  - Intensive case finding
    - HIV C and T of all TB cases
    - TB screening of all HIV+ pts
  - Infection control
  - Isoniazid prophylaxis therapy (IPT)

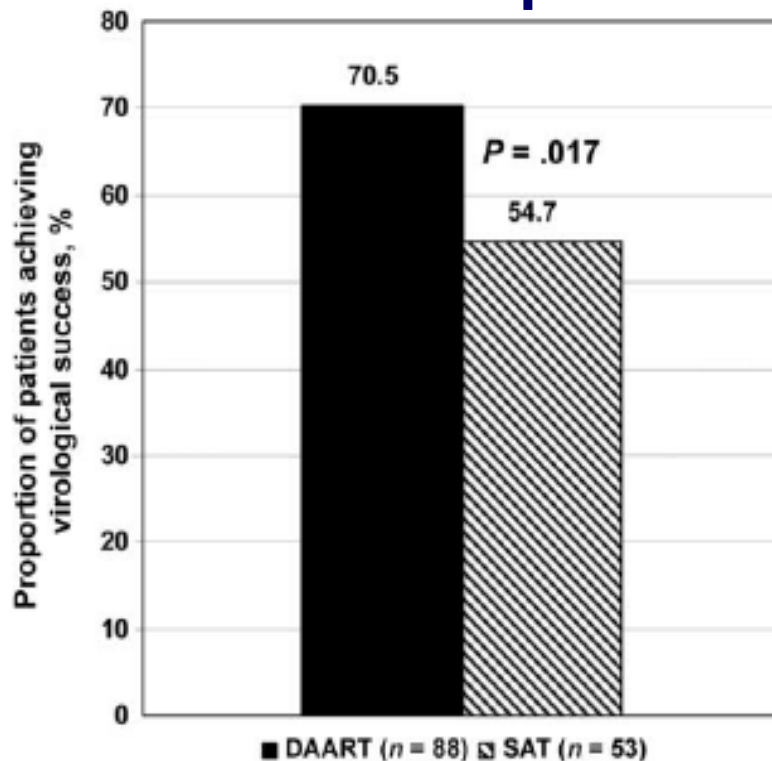


# Superiority of Directly Administered Antiretroviral Therapy over Self-Administered Therapy among HIV-Infected Drug Users: A Prospective, Randomized, Controlled Trial

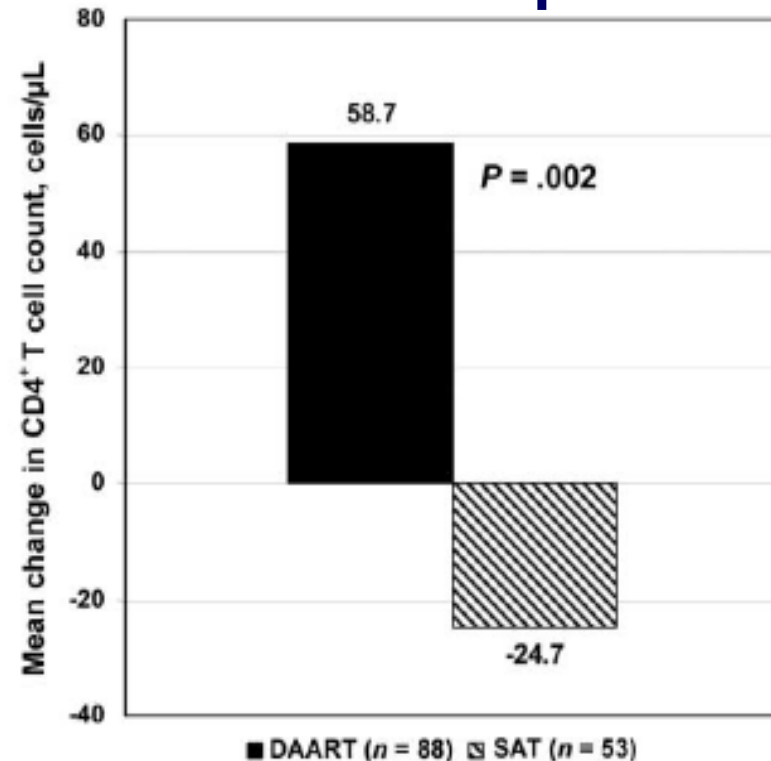
Frederick L. Altice,<sup>1</sup> Duncan Smith-Rohrberg Maru,<sup>1,2</sup> R. Douglas Bruce,<sup>1</sup> Sandra A. Springer,<sup>1</sup> and Gerald H. Friedland,<sup>1,2</sup>

*CID, 2007*

## VL Response

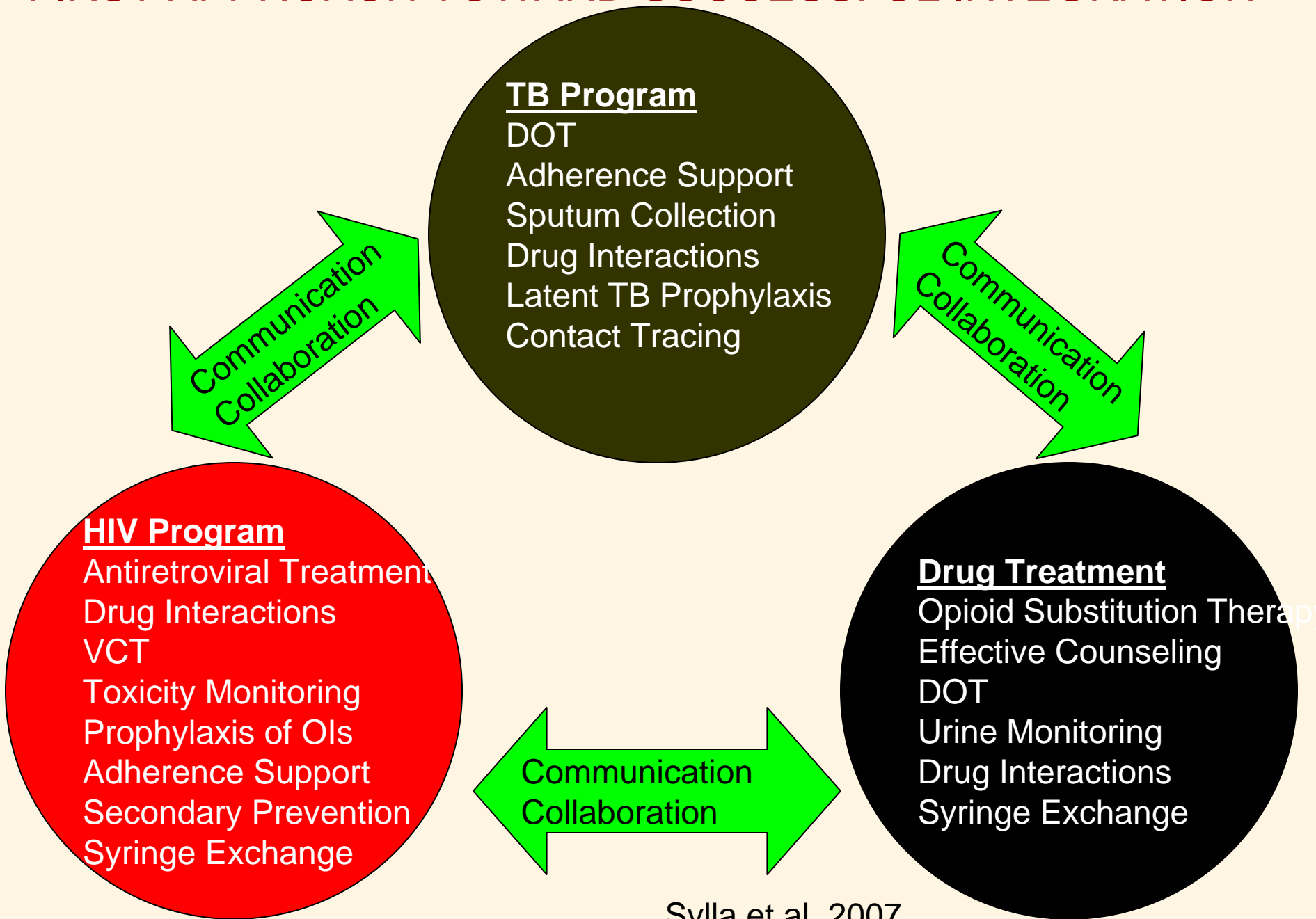


## CD4 Response

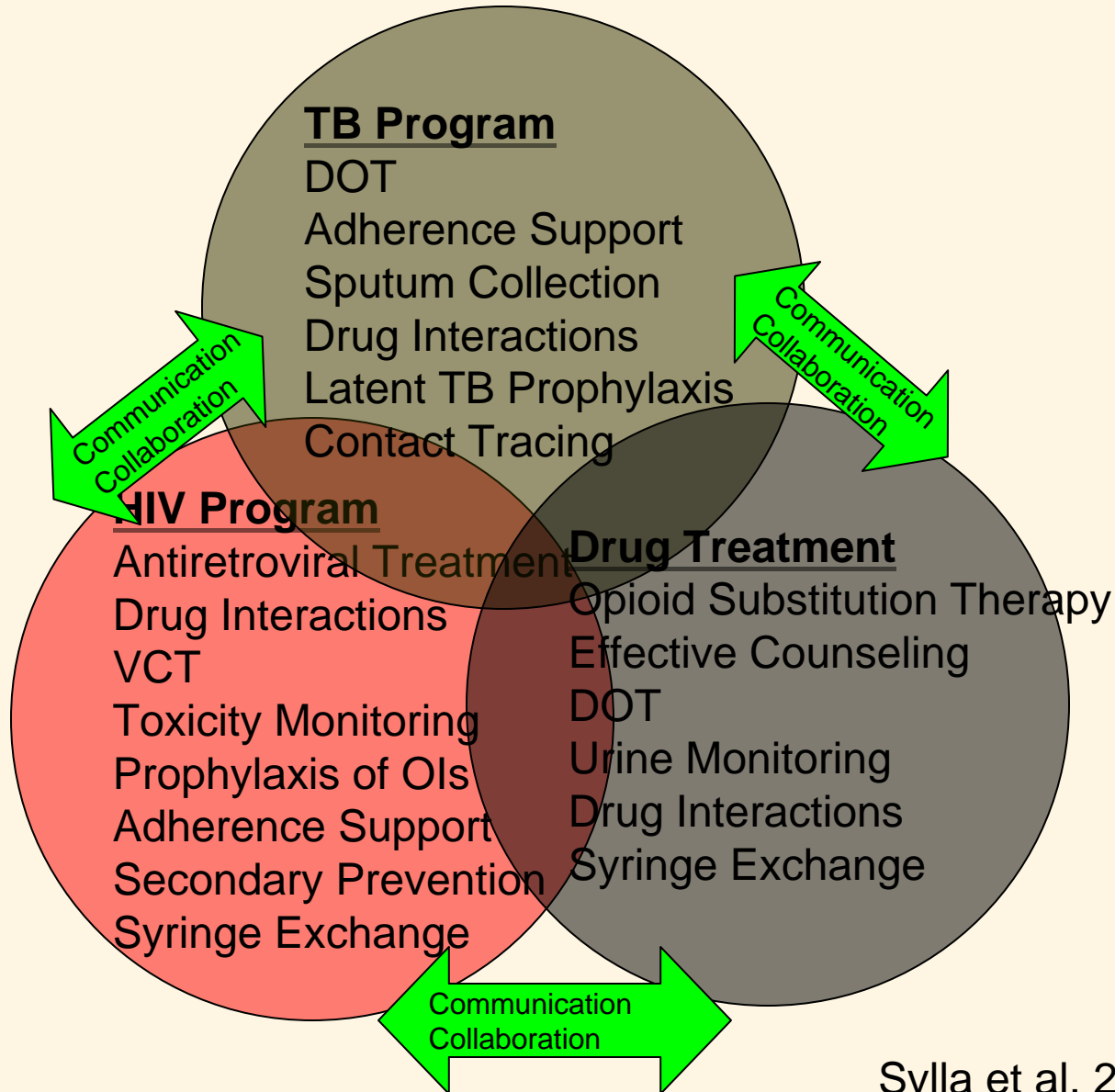


# Antiretroviral Agents, TB and Substance Use Therapies' Drug Interactions

- Antiretroviral and methadone/buprenorphine interactions
  - Marked induction of methadone metabolism by efavirenz and nevirapine with severe opiate withdrawal
  - Milder but unpredictable induction methadone metabolism by some protease inhibitors
  - Milder reduction in buprenorphine levels
  - Decreased methadone levels with raltegravir
- TB and methadone and antiretroviral interactions
  - Rifampin induces methadone, protease inhibitor and NNRTI metabolism



# LATER APPROACH TOWARD SUCCESSFUL INTEGRATION





**World Health  
Organization**



UNITED NATIONS  
*Office on Drugs and Crime*



**UNAIDS**  
UNITED NATIONS PROGRAMME ON HIV/AIDS

UNEP  
UNEP  
UNEP  
UNEP  
UNEP  
UNEP  
UNEP  
UNEP

Evidence for action on HIV/AIDS  
and injecting drug use

**POLICY BRIEF: POLICY GUIDELINES  
FOR COLLABORATIVE TB AND HIV  
SERVICES FOR INJECTING  
AND OTHER DRUG USERS**

The aim is to provide a strategic approach to reducing TB- and HIV-related morbidity and mortality among drug users and their communities in a way that promotes holistic and person-centered services.

Thirteen recommendations covering issues of joint planning, prevention and treatment of TB and HIV in drug users and service delivery



*“TB claims 1.7 million lives each year, and eliminating it will be a global challenge - but it's a challenge we must take on....”*

*Barack Obama,*

*October 3,2008*

