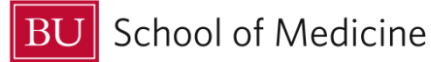




EXCEPTIONAL CARE. WITHOUT EXCEPTION.



Clinical Addiction Research and Education

Illicit Drugs, Alcohol, and Addiction in HIV

Jeffrey H. Samet, MD, MA, MPH

Chief, Section General Internal Medicine

Boston Medical Center

Professor of Medicine and Public Health

Boston University Schools of Medicine and Public Health



FIT 2012



Topics

Substance Use and HIV

- HIV epidemiology
- HIV risk behaviors
- HIV testing
- Engagement and retention in care
- Access to clean needles
- HIV disease progression
- ART adherence
- Addiction treatment



Topics

Substance Use and HIV

■ **HIV epidemiology**

- HIV risk behaviors
- HIV testing
- Engagement and retention in care
- Access to clean needles
- HIV disease progression
- ART adherence
- Addiction treatment

Drug Use as a Risk Factor for HIV

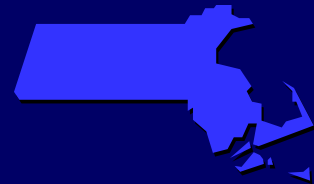
- IDU: Typically heroin
 - Other drugs (e.g. cocaine, amphetamines)
 - Estimated 3 million HIV infected via IDU worldwide*
- HIV prevalence elevated among non-injecting drug users
 - IDU (past 6-month) vs. never injecting, heroin/cocaine users†
 - 13% (CI 12-15%) vs. 12% (CI 9-16%)
 - Addiction treatment center (n=2121)
 - 15% (CI 11-19%) vs. 17% (CI 12-21%)
 - Respondent-driven store-front sampling (n=448)

* Mathers, Degenhardt, Phillips, et al. *Lancet*. 2008;372:1733-1745.

† Des Jarlais, Arasteh, Perlis, et al. *AIDS*. 2007;21:2311-2312

IDU and HIV in USA

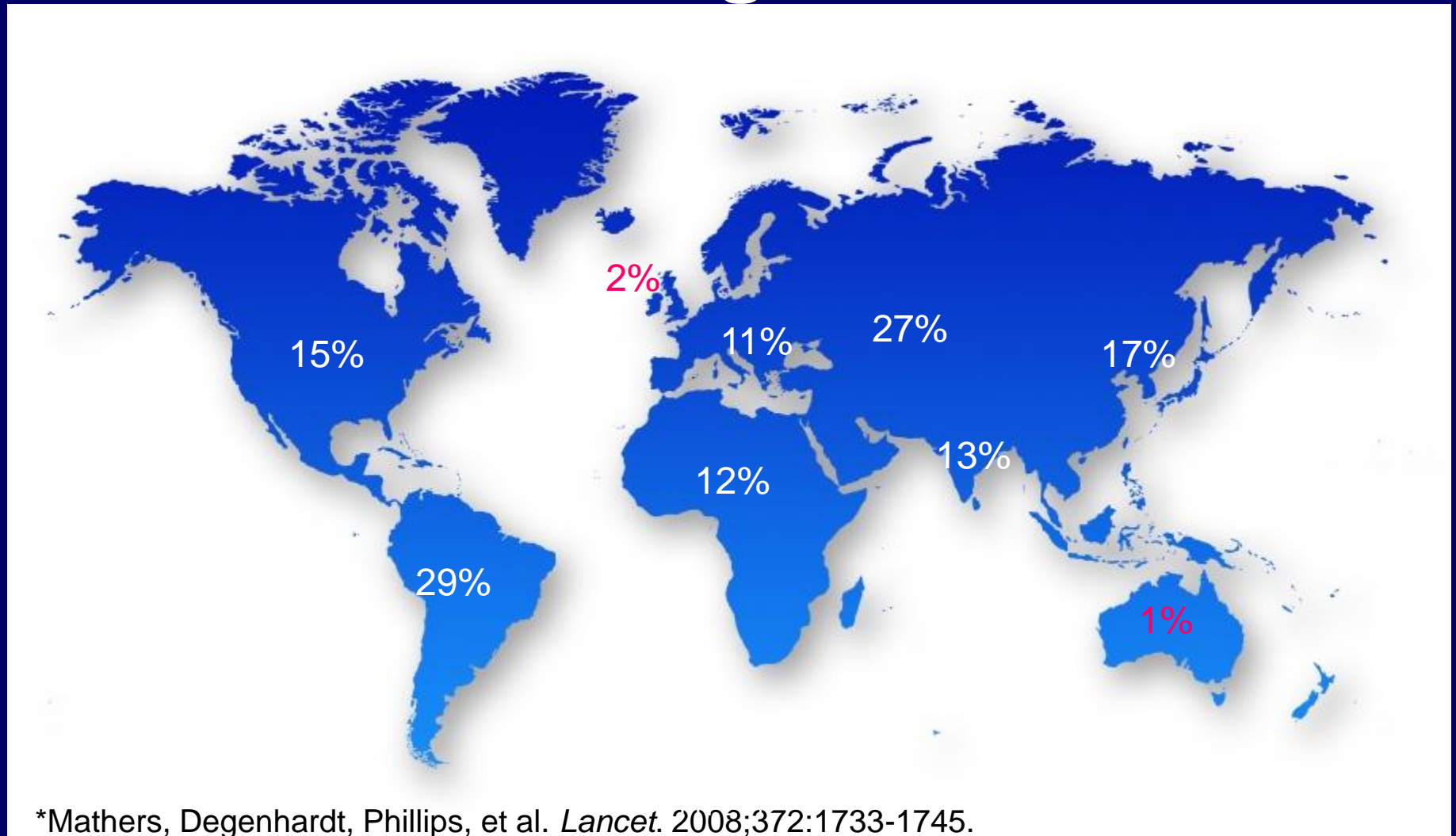
- In USA, IDU accounted for*
 - 8% of new HIV infections (2010)
 - 17% of people living with HIV (2010)
- In Massachusetts, IDU accounted for†
 - 24% of adult HIV/AIDS cases in Massachusetts (2009)



* CDC. *HIV Surveillance – Epidemiology of HIV Infection (through 2010)*. Published March 2012. http://www.cdc.gov/hiv/topics/surveillance/resources/slides/general/index.htm?utm_source=At-a-Glance&utm_medium=e-mail&utm_campaign=Epidemiology%2Bof%2BHIV%2BInfection. Accessed March 20, 2012.

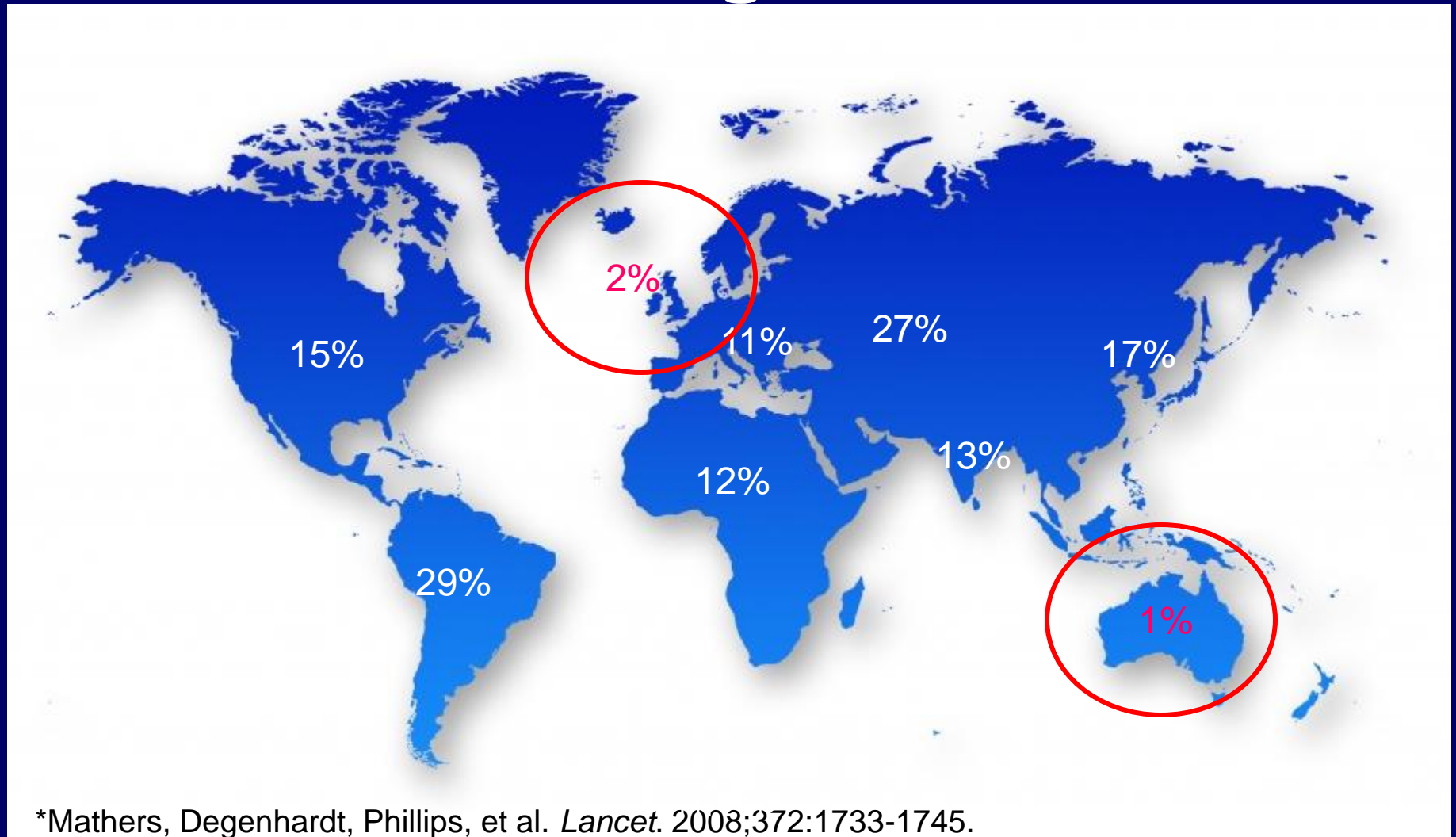
† http://www.mass.gov/Eeohhs2/docs/dph/aids/2009_profiles/epidemic_glance.pdf. Accessed January 18, 2012.

Global HIV Prevalence Among IDUs



*Mathers, Degenhardt, Phillips, et al. *Lancet*. 2008;372:1733-1745.

Global HIV Prevalence Among IDUs



*Mathers, Degenhardt, Phillips, et al. *Lancet*. 2008;372:1733-1745.

Alcohol Problems among HIV-Infected Persons

- HIV Cost and Services Utilization Study (n=2864)^{*}
 - 8% current hazardous drinkers
- HIV Research Network (14 sites, n=951)[†]
 - 11% current hazardous drinkers
- Women's Interagency HIV Study (WIHS, 6 sites, n=2770)[‡]
 - 14-24% past-year hazardous drinkers (11-year period)
- Veterans Aging Cohort Study (VACS, n=881)^{1**}
 - 36% past-year hazardous drinkers (AUDIT ≥ 8)

¹ >7000 HIV-infected veterans and non-infected controls, 8 sites, 98% men

^{*} Galvan, Bing, Fleishman, et al. *J Stud Alcohol*. 2002;63:179-186.

[†] Chander, Josephs, Fleishman, et al. *HIV Med*. 2008;9:196-202.

[‡] Cook, Zhu, Belnap, et al. *Am J Epidemiol*. 2009;169:1025-1032.

^{**} Conigliaro, Gordon, McGinnis, Rabeneck, Justice. *JAMA*. 2003;289:521-525.



Topics

Substance Use and HIV

- HIV epidemiology
- **HIV risk behaviors**
- HIV testing
- Engagement and retention in care
- Access to clean needles
- HIV disease progression
- ART adherence
- Addiction treatment

Drug Use and Sex Risk

- Crystal meth among HIV-infected MSM (n=398)*:
 - Greater sex risk- unprotected anal sex with possible serodiscordant partner - past 6 months (OR 2.6, CI 1.4-4.8)
- HIV-infected crack cocaine users, binge vs non-binge users (n=303)[†]
 - Greater mean # of sex partners - past 6 months (12 vs. 4)
 - More likely never use a condom - past 30 days (OR 2.5, CI 1.1-5.5)
- Sexually active, HIV-infected IDU men (n=469)[‡]:
 - 32% reported unprotected sex with HIV negative or status unknown main partner – past 3 months

* Mayer, O'Ceirigh, Skeer, et al. *Sexually Transmitted Infec.* 2010;86:66-70.

[†] Harzke, Williams, Bowen. *AIDS Behav.* 2009;13:1106-18.

[‡] Purcell, Mizuno, Metsch, et al. *J of Urban Health.* 2006;83:656-668.

HIV Risk Behaviors in Binge Drinkers

- 2008 Behavioral Risk Factor Surveillance System Binge Drinkers
(41,083 binge drinkers; 240,230 non-binge drinkers)
- HIV Risk Behaviors (past year)
 - IDU
 - Exchange of sex for money/drugs
 - Unprotected anal sex
- HIV risk behaviors higher among binge drinkers: 7.0% vs. 2.9% (OR 1.8, CI 1.58-2.00)

Alcohol Use and Risky Sex

- Meta-analysis (n=27 studies) found unprotected sex among HIV-infected individuals significantly associated with:
 - Alcohol consumption (OR 1.6, CI 1.4-1.9)
 - Problematic drinking (OR 1.7, CI 1.5-2.0)
 - Alcohol use in sexual contexts (OR 2.0, CI 1.6-2.4)

Alcohol Use and Vaginal HIV Detection

- HIV infected women (n=160)

	Recent Drinking (past 24 hrs.)		
	≤ 1 drink	≥ 2 drinks	p-value
Vaginal Detectable Virus	27%	40%	<.05

- When stratified by ART status, recent drinking effect only observed in those on ART (n=87)



Topics

Substance Use and HIV

- HIV epidemiology
- HIV risk behaviors
- **HIV testing**
- Engagement and retention in care
- Access to clean needles
- HIV disease progression
- ART adherence
- Addiction treatment

HIV Testing and Drug Users

1998-2002, 5 city study of IDUs (n=1543)

- Only 7% of IDUs reported no past HIV test
 - Syringe-exchange users more likely to have had an HIV test (OR 2.2, CI 1.3-3.9)

Behavior Change After Testing HIV Positive

- HIV Cost and Services Utilization Study (HCSUS) sample of HIV-infected persons in medical care in 1996 (n=2864)*
 - 80% of substance users quit or cut down drug use since diagnosis
 - Persons with CD4 counts <50 at some point were also more likely to quit or reduce substance use
- IDUs in the Ukraine (n=1798), after testing positive for HIV:†
 - Less unprotected sex (OR 0.6, CI 0.4-0.7)

* Collins, Kanouse, Gifford, et al. *Health Psychol.* 2001;20:351-60.

† Booth, Lehman, Dvoryak, Brewster, Sinitsyna. *Addiction.* 2009;104:1864-1873.



Topics

Substance Use and HIV

- HIV epidemiology
- HIV risk behaviors
- HIV testing
- **Engagement and retention in care**
- Access to clean needles
- HIV disease progression
- ART adherence
- Addiction treatment

Presenting to Medical Care



- Entry into care in two New England clinics, 1994-1996 (n=189)[†]
 - 39% delayed medical care for >1 year, 32% >2 years, and 18% >5 years after diagnosis
 - IDU (p<0.001) and history of alcohol problems in men (p=0.03) associated with delay
- Entry into care in 18 states, 2000-2004 (n=3942)[‡]
 - 28% delayed medical care for > 3 months
 - IDU associated with delay (OR 1.4, CI 1.08-1.82)

* Samet, Freedberg, Savetsky, Sullivan, Stein. *AIDS*. 2001;15:77-85.

† Samet, Freedberg, Stein, et al. *Arch Intern Med*. 1998;158:734-740.

‡ Reed, Hanson, McNaghten, et al. *AIDS Patient Care STDS*. 2009;23:765-773.

Alcohol Use and HIV Treatment

- HIV-infected Ugandans (n=421)
 - Persons abstinent in last year were 2.3 times more likely to receive ART

IDUs and HIV Treatment Engagement

- Global review of ART coverage for IDUs
 - In the five countries* with the largest IDU HIV epidemics, IDUs make up 67% of HIV cases, but only 25% of those receiving ART
 - Barriers to HIV Treatment Engagement of IDUs
 - Stigmatization of IDUs in health care settings
 - Separation of addiction and HIV care systems
 - Bans on ART in active IDUs
 - No HIV treatment of prisoners

* China, Vietnam, Russia, Ukraine, Malaysia

IDUs and HIV Treatment Engagement

“The doctor said that I had to deal with one thing first, and then the other. Because I had told her straight that I used drugs. So, she said that I had to quit first and then take care of the rest. But how? ... I’m actually afraid to discuss this issue of how to combine therapy and drugs. I don’t even want to ask the doctor... The doctor gave me such a look that I understood I’m kind of not entitled to ever feel good if I use drugs. So I made my conclusions. She made it clear to me that I had to deal with one thing first, then with the other.”

- Elena



Topics

Substance Use and HIV

- HIV epidemiology
- HIV risk behaviors
- HIV testing
- Engagement and retention in care
- **Access to clean needles**
- HIV disease progression
- ART adherence
- Addiction treatment

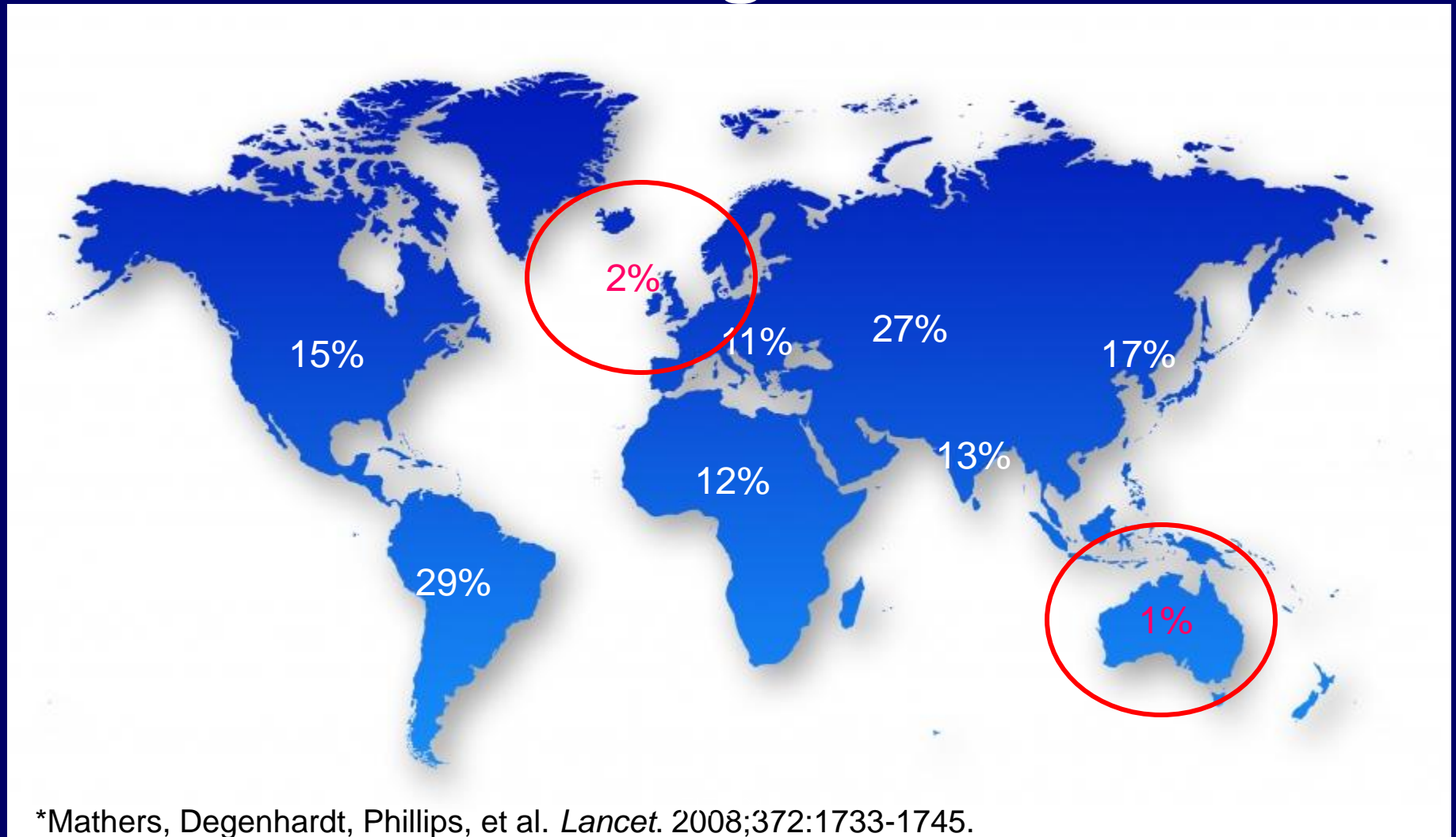
Needle Exchange Program (NEP)

- Review of 42 studies from 1989-1999 among IDUs*
 - Decrease in HIV risk behavior
 - Decrease in HIV seroconversion
- Review of 7 international studies from 1991-2001†
 - Cost-effective
 - Feasible to implement internationally
 - Applicable to special populations

* Gibson, Flynn, Perales. *AIDS*. 2001;15:1329-1341.

† Wodak & Cooney. *Substance Use & Misuse*. 2006;41:777-813.

Global HIV Prevalence Among IDUs



*Mathers, Degenhardt, Phillips, et al. *Lancet*. 2008;372:1733-1745.

Availability of Syringe Distribution and Exchange

- Great Britain and Australia have some of the lowest HIV prevalence rates among IDUs (~2%* and ~1%†)
- Reflects early adoption of harm reduction measures (c. 1986)†
 - Needle exchange programs
 - Opioid agonist treatment

* Mathers, Degenhardt, Phillips, et al. *Lancet*. 2008;372:1733-1745.

† Wodak, Maher. *NSW Public Health Bulletin*. 2010;21:69-73.

**AIDS
CAN
BLOW
YOUR
HIGH.**



**IF
YOU'RE
NOT GOING
TO STOP,
AT
LEAST
USE CLEAN
NEEDLES.**

CALL

HERO

Health Education Resource Organization

945-AIDS
BALTIMORE METRO

251-1164
DC METRO

1-800-638-6252
ELSEWHERE IN MARYLAND

FIT 2012

WHO/UNAIDS IDU Prevention Policy

- Needle and syringe programs
- Opioid agonist therapy
- HIV counseling and testing
- Antiretroviral therapy
- Prevention and treatment of STIs
- Condom programming
- Targeted information, education and communication
- Hepatitis diagnosis, treatment and vaccination
- TB prevention, diagnosis and treatment



Topics

Substance Use and HIV

- HIV epidemiology
- HIV risk behaviors
- HIV testing
- Engagement and retention in care
- Access to Clean Needles
- **HIV disease progression**
- ART adherence
- Addiction treatment

Injection Drug Use and HIV Disease Progression

- Hopkins* (n=1,851): Heroin and cocaine use and risk of opportunistic infections (OIs)

	OR	95% CI
Nonuser	1.0	
Intermittent user, abstinent	1.4	1.0 - 1.9
Intermittent user, active	2.3	1.5 – 3.0
Persistent user	2.1	1.4 – 3.1

Active drug use associated with HIV disease progression

* Lucas, Griswold, Gebo, Keruly, Chaisson, Moore. *Am J Epidemiology*. 2006;163:412-420. FIT 2012

Alcohol and HIV Disease Progression

- Pre-HAART, no association found*
- Heavy alcohol use associated with lower CD4 cell count in patients NOT on ART†
 - Adjusted mean decrease of 49 cells/ μ l compared with abstinence (p=0.03)
- Suggestive evidence from literature review that heavy alcohol use impacts disease progression.‡
 - Possible mechanisms:
 - Immune activation, increase GI bacterial translocation, interaction with ART metabolism

* Dingle, Oei. *Psychol Bull.* 1997;122:56-71.

† Samet, Cheng, Libman, Nunes, Alperen, Saitz. *JAIDS.* 2007; 46:194-199.

‡ Hahn, Samet. *Curr HIV/AIDS Rep.* 2010; 7:226-233. ^{51T} 2012

Cocaine and HIV Disease Progression

- HIV-infected drug users (n=222)
- Crack cocaine users (n=110) 2.1 times more likely to have a CD4 \leq 200 cells/ml
 - Higher HVL
 - Of those on ART, less likely suppress HVL
 - Of those not on ART (n=53), increased RR of CD4 cell decline $<$ 200 (HR 3.9, CI 1.1-14.9)

Tobacco and HIV Disease Progression

- HIV-LIVE cohort (n=462)
 - No significant association between CD4 or HVL and smoking status
 - True for the range of tobacco use compared to non-smokers

Mortality and Substance Use

- HIV-LIVE (n=595), mortality associated with*:
 - Heroin or cocaine use (HR 2.4, CI 1.1-5.3)
 - Homelessness (HR 2.9, CI 1.3-6.4)
 - No association with heavy alcohol use (HR 0.6, CI 0.2-1.4)
- Johns Hopkins HIV Clinical Cohort 1997-2006, (n=1030 women)†
 - Heavy drinking associated with increased mortality (HR 1.4, CI 1.0-1.97)

* Walley, Cheng, Libman, et al. *AIDS*. 2008; 22:415-420.

† Neblett, Hutton, Lau, McCaul, Moore, Chander. *J Women's Health*. 2011; 20:279-286.

IDU, HIV, and Mortality

- IDUs have the worst life expectancy among all transmission categories
- IDU life expectancy post-dx in the US (2005):
 - Male: 15.2 years (CI 14.8-15.5)
 - Female : 15.9 years (CI 15.1-16.6)
- IDU life expectancy almost half compared to those with sexual transmission risk



Topics

Substance Use and HIV

- HIV epidemiology
- HIV risk behaviors
- HIV testing
- Engagement and retention in care
- Access to clean needles
- HIV disease progression
- **ART adherence**
- Addiction treatment

Should continued substance use be a reason NOT to start ART?



Alcohol and ART adherence

- Meta-Analysis of 40 studies and over 25,000 participants*
 - Risky or dependent drinkers were less adherent than non-problem drinkers or abstainers (OR 0.5, CI 0.4-0.6)
- Study of African-Americans about beliefs of alcohol and ART (n=82)[†]
 - “Alcohol and ART do not mix.” (85%)
 - “I will not take my meds if I have been drinking.” (51%)

* Hendershot, Stoner, Pantalone, Simoni. *J AIDS*. 2009. 52:180-202.

[†] Sankar, Wunderlich, Neufeld, Luborsky. *AIDS Behav*. 2007; 11:195–203.

Efforts to Improve ART Adherence

Two RCTs to improve ART adherence among hazardous drinkers with motivational interviewing

■ ADHERE (n=151)*

- 4 session intervention
- No significant differences in medication adherence, CD4 count, VL, or alcohol consumption

■ Hazardous drinkers in New York City (n=143)†

- 8 session intervention
- Significant differences in VL, CD4 count at 3 months, but not 6 months

* Samet, Horton, Meli, et al. *Antivir Ther.* 2005;10:83-93.

† Parsons, Golub, Rosof, Holder. *J AIDS.* 2007;46:443-450.

IDUs and ART Adherence

- HIV-infected persons (n=578) first prescribed ART between 1996-2000*
 - Classified as current IDU, former IDU, or non drug user
 - Current IDUs were less likely to suppress their HVL compared to non-drug users
 - Former IDUs were NOT less likely suppress HVL compared to non-drug users
- Similar findings in Swiss Cohort between 1997-2006 (n=8669)[†]

* Palepu, Tyndall, Yip, O'Shaughnessy, Hogg, Montaner. *J AIDS*. 2003;32:522-526.

[†] Weber, Huber, Rickenbach, et al. *HIV Med*. 2009;10:407-416.

Interventions to Improve ART Adherence in Drug Users

- RCT of directly observed ART (DOT) in substance users (n=87):
 - Greater HVL suppression (OR 2.2, CI 1.0-4.7)
 - Estimated CD4 count improvement of 45 cells/ μ L (CI 5 - 85, p=0.03)

Treatment Options

- History of prior drug use is an insufficient reason for withholding ART
- Usually, it is possible to support active drug users such that acceptable ART adherence levels are achieved
 - Requires coordination of drug treatment, medical and psychiatric care, and harm reduction services (e.g., syringe exchange)

Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents*. Department of Health and Human Services. January 10, 2011; 1–166. Available at

<http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf> [Accessed March 15, 2012]



Topics

Substance Use and HIV

- HIV epidemiology
- HIV risk behaviors
- HIV testing
- Engagement and retention in care
- Access to clean needles
- HIV disease progression
- ART adherence
- **Addiction treatment**

Addressing Addiction in HIV Care

- HIV-infected adults (n=951) receiving care at 14 sites*
 - 71% using substances; 24% receiving substance use treatment
 - Less than half reported discussing substance use issues with HIV care provider
- Need for providers to address substance use problems
- Audio-tapes of physician-patient encounters (n=413)†
- Quality of patient-provider communication
 - Good for illicit drug users
 - Worse for those with unhealthy alcohol use (shorter visit length, fewer activating/engaging and psychosocial counseling statements)

* Korthuis, Josephs, Fleishman, et al. *J Subst Abuse Treat*. 2008;35:294-303.

† Korthuis, Saha, Chander, et al. *AIDS Behav*. 2011;15:832-841.

Alcohol Use among HIV/HCV-infected Persons

- HIV-LIVE (n=400)
- Those told about HCV diagnosis were more likely to report
 - Abstinence (AOR 1.60, CI 1.13 - 2.27)
 - Not drinking unhealthy amounts (AOR 1.46, CI 1.01 - 2.11)
- Awareness of HCV diagnosis associated with greater abstinence from alcohol and less unhealthy amounts of drinking

Addiction Pharmacotherapy

- Heroin*
 - Methadone
 - Buprenorphine
- Alcohol*
 - Naltrexone
 - Acamprosate
 - Disulfiram
- Cocaine = investigational†
 - Modafinil
 - GABA-ergic compounds (e.g. vigabatrin, topiramate)
 - Disulfiram
 - Vaccine (TA-CD)

* Bruce, Kresina, McCance-Katz. *AIDS*. 2010; 24:331-340.

† Kampman. *Curr Psychiatry Rep*. 2010; 12:441-447. ^{FIT 2012}

Opioid Agonist Therapy (OAT) & HIV Outcomes

- HIV-infected Vancouver IDUs on ART, 1996-2003 (n=278)*
 - Methadone OAT associated with
 - Adherence (OR 1.5; 95% CI 1.2-2.0)
 - HIV RNA suppression (OR 1.3, CI 1.0-1.8)
 - CD4 cell count rise (OR 1.6, CI 1.3-2.0)
- Prospective cohort of ART-naïve, HIV-infected IDUs in Vancouver, 1996-2008 (n=231)[†]
 - Methadone OAT associated with
 - Earlier ART initiation (RH 1.6, CI 1.2-2.3)

* Palepu, Tyndall, Joy, et al. *Drug Alcohol Depend.* 2006;188-194.

[†] Uhlmann, Milloy, Kerr et al. *Addiction.* 2010;105:907-913.

Integrated OAT & DOT

- RCT compared directly observed ART (DOT) to standard of care
- 12 methadone OAT clinics in the Bronx (n=77); 24-week follow-up
- DOT group at 24 weeks
 - Better adherence (86% vs. 56%, $p < 0.0001$)
 - More likely to have undetectable viral load (OR 3.1, CI 1.1-5.4)

Buprenorphine OAT

- Advantage of buprenorphine OAT*
 - Efficacy and retention comparable to methadone
 - Milder withdrawal symptoms
 - Very low risk of overdose
 - Decreased risk of abuse and diversion
(*buprenorphine/naloxone*)
- Can be delivered in the office through a collaborative nurse care-manager model†

* Johnson, Chutuape, Strain, Walsh, Stitzer, Bigelow. *New Engl J Med.* 2000; 343:1290-1297.

† Alford, LaBelle, Kretsch, et al. *Arch Intern Med.* 2011; 171:425-431.

Buprenorphine OAT

- Longitudinal analysis of HIV+ patients on *bup/nal* (n=166)
 - *bup/nal* associated with significant reductions in HIV sex and drug-related risk behaviors from baseline to 12 and 24 weeks

	BL	12 wks.	24 wks.	P value
IDU in past 3 months	37%	12%	7%	< 0.001
Sex while "high"	64%	13%	15%	< 0.001

Drug Interactions: ART Impacts Addiction Pharmacotherapy

- IDUs receiving ART and OAT (n=120)
 - Median methadone dose increase:
 - 20 mg/d ($p < 0.001$) with nevirapine
 - 7.5 mg/d ($p = 0.004$) with efavirenz
 - No significant increase required for patients on ritonavir-boosted lopinavir

Drug Interactions: Addiction Pharmacotherapy Impacts ART

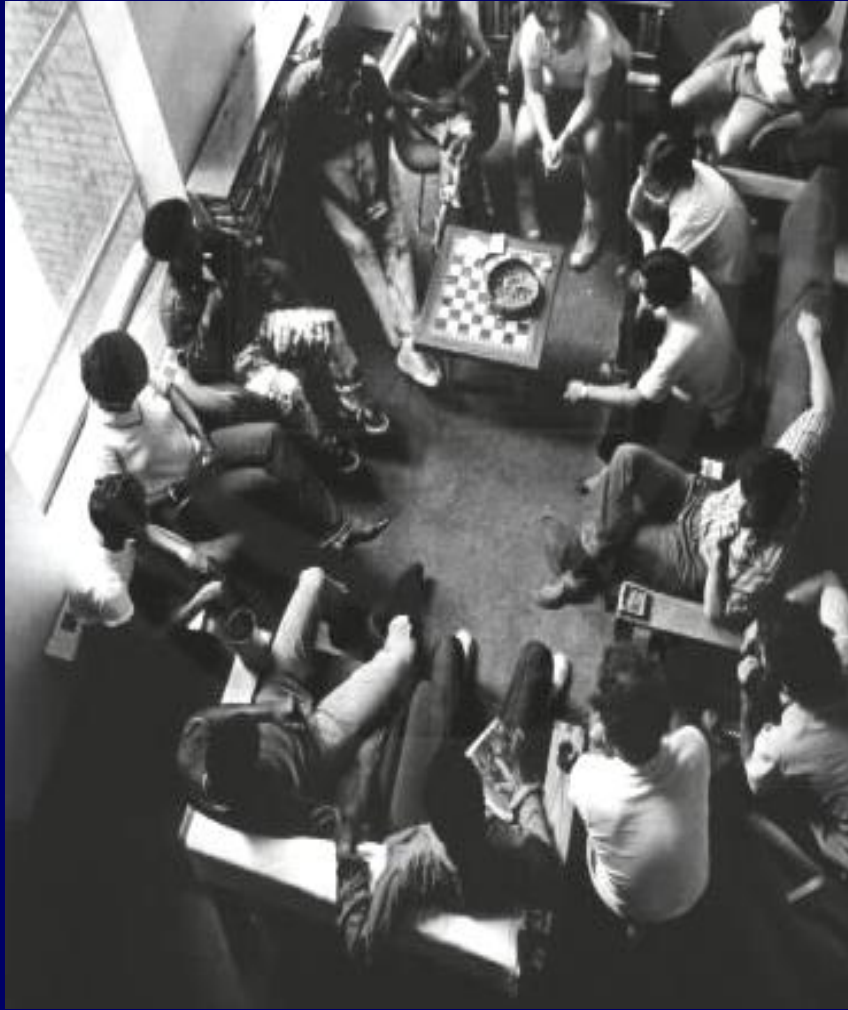
- Methadone increases serum zidovudine levels by 40%, but question if clinically relevant*
 - No such interaction observed with buprenorphine
- Buprenorphine had no effect on early and newer protease inhibitors (early PIs n=30)[†] (newer PIs n=21)[‡]

* Bruce, Kresina, McCance-Katz. *AIDS*. 2010;24:331-340.

† McCance-Katz, Moody, Smith, et al. *CID*. 2006;43:S235-246.

‡ Gruber, Rainey, Moody, et al. *CID*. 2012;54:414-423.

12-Step Programs (AA, NA, CA)



- Focus on abstinence
- Life long participation is emphasized

12-Step Programs & HIV-Infected Patients

- HIV-LIVE Study (n=400); 43% alcohol dependent, 43% drug dependent
- 56% attended 12-step meeting in past 6 months
- Less likely to attend:
 - Women (OR 0.6, CI 0.3, 0.9)
 - Alcohol-using social support system (OR 0.6, CI 0.4-0.8)
- More likely to attend:
 - HCV antibody positive (OR 2.3, CI 1.4-3.6)
 - Homeless (OR 1.6, CI 1.2-2.3)
 - Drug dependence diagnosis (OR 1.4, CI 1.1-1.8)

Addressing Substance Use: Talk Therapy- Beyond CAGE

- Physicians can play an important role in early detection and intervention.
- Assess patient's readiness to change alcohol or drug use behavior
- Brief intervention: 5-15 min counseling to motivate change
 - FRAMES: Feedback, Responsibility, Advice, Menu of Options, Empathy, Self-efficacy



“Only those who survive have a chance of coming off drugs.”

FIT 2012
-Marion Casper-Merk, Secretary of State for Drug Addiction, Germany